THE OUTCOME OF ALARM SYMPTOMS AND COLONOSCOPY IN FUNCTIONAL BOWEL DISORDERS AND FUNCTIONAL ABDOMINAL PAIN SYNDROME

Dissertation submitted to

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

DM BRANCH – IV
MEDICAL GASTROENTEROLOGY

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

August 2007

CERTIFICATE

This is to certify that the dissertation titled **"THE OUTCOME OF ALARM SYMPTOMS AND COLONOSCOPY IN FUNCTIONAL BOWEL DISORDERS AND FUNCTIONAL ABDOMINAL PAIN SYNDROME"** is the bonafide original work done by **JIJO V. CHERIAN** in partial fulfillment of the requirements for DM Branch – IV (Medical Gastroenterology) Examination of the Tamilnadu DR. M.G.R Medical University to be held in August 2007 under our supervision and guidance.

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DECLARATION

I, **JIJO V. CHERIAN,** hereby declare that the dissertation titled **"THE OUTCOME OF ALARM SYMPTOMS AND COLONOSCOPY IN FUNCTIONAL BOWEL DISORDERS AND FUNCTIONAL ABDOMINAL PAIN SYNDROME"** is a bonafide work done by me under the guidance and supervision of Prof. Dr. V. Jayanthi, the Professor & Head, Department of Medical Gastroenterology, during the period between January and December 2006 at the Govt. Stanley Medical College and Hospital**.**

This dissertation is submitted to the Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of DM Degree (Branch – IV) in Medical Gastroenterology.

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ACKNOWLEDGEMENT

My sincere thanks to Dr**. T. RAVEENDRAN MD.,DTCD** Dean,Govt. Stanley Medical College and Hospital, for permitting me to avail the infrastructure and facilities of the Govt. Stanley Medical College and hospital that were needed for the completion of this dissertation.

I am deeply indebted to my Chief, **Prof. V. JAYANTHI, MD., DM** Professor and Head, Department of Medical Gastroenterology, not only for guiding me through this project, but also for the constant support, inspiration and motivation throughout the period of my three year training which has molded me into what I am today.

I am grateful to my Assistant Professors **Dr. A. MURALI MD., DM, Dr. M.S. REVATHY MD., DM, Dr. T. RAJKUMAR SOLOMON MD., DM** and **Dr. K. CAROLENE SELVI MD., DM** for the knowledge and training they have imparted to me, for their patience towards my mistakes, incessant guidance and encouragement.

Mr. A. VENGATESAN, lecturer in statistics, Institute of Social Paediatrics, Stanley Medical College performed the statistical analysis and my sincere thanks to him.

My family and friends have stood by me during my times of need and my heartfelt thanks go to all of them.

My heart goes out to all my patients, who ungrudgingly bore the added pain and anxiety of the investigations along with their illness. I can but pray for their speedy recovery and hope that this research project of mine be of use to them and the patient community at large

CONTENTS

INTRODUCTION

Functional gastrointestinal disorders such as the Functional bowel disorders and functional abdominal pain are the most common disorders encountered by the gastroenterologist and constitute a considerable economic burden to the health care system.[1] However, the accuracy of a diagnosis based purely on the presenting gastrointestinal symptoms continues to worry practicing physicians.[2] Traditionally, a diagnosis of a functional bowel disorder is based on the classical symptom patterns in the absence of an organic explanation by appropriate testing. Thus functional bowel disorders are diagnosed when unexplained abdominal pain and bowel symptoms coexist while the role of other potential diagnostic criteria remains unclear.[3]

There is a limit to the repertoire of gastrointestinal symptoms and hence it is understandable that symptoms alone may not be accurate enough to identify functional from organic disease. However, in the absence of a reproducible and accepted biological marker, symptoms currently remain the primary means of identifying patients in clinical practice and recruiting patients for research studies. Several diagnostic approaches that are based on the patient's symptoms, such as the Manning criteria,[4] the Kruis scoring system,[5] or the Rome criteria,[6] have been proposed to assist the diagnostic process. However, the available literature suggests that symptom based diagnostic algorithms, although often used for clinical and research studies, have poor sensitivity.[7] Although diagnostic algorithms such as the Manning criteria or the Rome criteria can discriminate IBS from health or upper gastrointestinal tract conditions, studies do not provide convincing evidence that the criteria can discriminate IBS from organic disease of the colon.[8] Thus, in clinical practice functional gastrointestinal disorders are still often identified by exclusion.

In daily clinical practice, history taking includes a search for leading symptoms, as suggested by diagnostic algorithms for functional bowel disorders, as well as an intensive clinical search for

evidence of organic disease (alarm symptoms or features), such as older age at symptom onset, weight loss, gastrointestinal bleeding, etc. Current guidelines recommend a full diagnostic workup in patients who present with such alarm features.[9] Vanner and colleagues[10] suggested that evaluating alarm symptoms in combination with the Rome I criteria improved the predictive value for diagnosing IBS. However, the value of these symptoms in discriminating organic disease from functional disorders remains uncertain, especially as alarm features are common, even in younger people in the general population.[11]

AIM OF THE STUDY

1. To assess the value of alarm features in differentiating organic disease from functional bowel disorders and functional abdominal pain syndrome
2. To assess the outcome of colonoscopy in diseases of the lower gastrointestinal tract

REVIEW OF LITERATURE

Throughout recorded history, and alongside structural diseases of the intestinal tract, are maladies that have produced multiple forms of pain, nausea, vomiting, bloating, diarrhea, constipation, or difficult passage of food or feces. Although structural diseases can be identified by pathologists and at times cured by medical technology, the nonstructural symptoms that are described as "functional" remain enigmatic and less amenable to explanation or effective treatment. Often considered "problems of living," there are physiological, intrapsychic and sociocultural factors that amplify perception of these symptoms so they are experienced as severe, troublesome or threatening, with subsequent impact on daily life activities. Those suffering from such symptoms attribute them to an illness and self treat or seek medical care. Traditionally trained physicians then search for a disease in order to make a diagnosis and offer treatment specific to the diagnosis. In most cases, no structural etiology is found, the doctor concludes that the patient has a "functional" problem and the patient is evaluated and treated accordingly.

Functional Bowel Disorders

Functional bowel disorders are functional gastrointestinal disorders with symptoms attributable to the middle or lower gastrointestinal tract. These include the IBS, functional bloating, functional constipation, functional diarrhea, and unspecified functional bowel disorder.

To separate these chronic conditions from transient gut symptoms, they must have occurred for the first time ≥ 6 months before the patient presents, and their presence on ≥ 3 days a month during the last 3 months indicates current activity.

Previous diagnostic criteria presumed the absence of a structural or biochemical disorder. However, research will likely confirm that functional gut disorders manifest such findings. Moreover, IBS, functional bloating, functional constipation and functional diarrhea may have multiple etiologies.

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The functional bowel disorders are classified into

C. Functional bowel disorders
C1. Irritable bowel syndrome
C2. Functional bloating
C3. Functional constipation
C4. Functional diarrhea
C5. Unspecified functional bowel disorder

C1. Irritable Bowel Syndrome

Definition

IBS is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit, and with features of disordered defecation.

Epidemiology

Throughout the world, abort 10% - 20% of adults and adolescents have symptoms consistent with IBS, and most studies find a female predominance.[12] IBS

symptoms come and go over time, often overlap with other functional disorders,[13] impair quality of life,[14] and result in high health care costs.[15]

C1. Diagnostic criteria* for irritable bowel syndrome

Recurrent abdominal pain or discomfort** at least 3 days per month in the last 3 months associated with 2 or more of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset 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.

** Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation for subject eligibility.

Supportive symptoms that are not part of the diagnostic criteria include abnormal stool frequency ([a] ≤ 3 bowel movements per week or [b] > 3 bowel movements per day), abnormal stool form ([c] lumpy/hard stool or [d] loose/ watery stool), [e] defecation straining, [f] urgency, or also a feeling of incomplete bowel movement, passing mucus, and bloating.

The Rome II working team suggested 2 systems for classifying patients into diarrhea – predominant and constipation – predominant subgroups based on the first 6 of these features.[16,17] The Rome II book classification based on the first 6 supportive symptoms includes: diarrhea predominant: 1 or more of b, d, f, and none of a, c, e, or ≥2 of b, d, f, or ≥ 2 of a, c,e, and 1 of b, d, f.

Both variations exclude patients with hard stools from the diarrhea subtype, but 1 version can include patients with watery stools in the constipation subgroup. Investigators have used these methods and modifications of them to select patients for treatment trials targeting a specific bowel pattern.

Sub typing IBS by predominant stool pattern

1. IBS with constipation (IBS-C) – hard or lumpy stools ≥25% and loose (mushy) or watery stools < 25% of bowel movements.
2. IBS with diarrhea (IBS-D)- loose (mushy or watery stools ≥25% and hard or lumpy stool <25% of bowel movements.
3. Mixed IBS (IBS-M) – hard or lumpy stools ≥25% and loose (mushy) or watery stools ≥25% of bowel movements.
4. Unsubtyped IBS – insufficient abnormality of stool consistency to meet criteria for IBS-C, D, or M.

Patient reports of “diarrhea” and “constipation” may mislead physicians. The stool may be solid, though defecation is frequent (pseudodiarrhea).[18] Conversely, straining to defecate may occur with soft or watery stools. Some patients feel constipated because they have unproductive urges to defecate or feelings of incomplete evacuation that prompt them to strain after passing stool. The need for accurate symptom description is corroborated by reports of straining, urgency, and incomplete evacuation across the spectrum of stool form.[19] In subgroups identified by cluster analysis or symptoms, most patients have a stool frequency within the normal range regardless of bowel pattern. However, stool form (from watery to hard) reflects intestinal transit time.

Researchers and practitioners use the Bristol stool form scale[18] (table 3) to identify constipation as types 1 and 2 and diarrhea as types 6 and 7.

The Bristol stool form scale

Type	Description
1	Separate hard lumps like nuts (difficult to pass)
2	Sausage shaped but lumpy
3	Like a sausage but with cracks on its surface
4	Like a sausage or snake, smooth and soft
5	Soft blobs with clear-cut edges (passed easily)
6	Fluffy pieces with ragged edges, a mushy stool
7	Watery, no solid pieces, entirely liquid

Rationale for changes in the diagnostic criteria

The symptom criteria are useful for clinical practice, epidemiologic surveys, pathophysiology research, and therapeutic trials. The symptom frequencies suggested for the FBDs are arbitrary and may need to be modified for different purposes. Epidemiologists should explore several frequencies to understand their significance. In therapeutic trials, the higher the symptom frequency threshold for subject enrollment, the larger the potential treatment effect and the smaller the number of subjects that may be needed to show a significant difference. However, such patients may be less likely to achieve satisfactory relief, and such studies are less applicable to the general population. Hence, enrollment symptom criteria are critical. The recommended threshold for pain or discomfort of $\geq$ 2 days a week for pathophysiology studies and clinical trials is reported by a majority of IBS patients.[20] About three fourths of patients who rated their pain as at least moderate (not ignorable, but without affect on lifestyle) also had pain $\geq$2 days a week.[21] Because relief of pain/discomfort with defecation may be incomplete, *improved* with defecation replaces *relieved*.

The Rome II sub typing using multiple criteria were complex and difficult to use in practice. We therefore simplified them by using only the most reliable criterion, stool form. Current evidence indicates that bowel pattern sub typing is best done according to stool form rather than bowel frequency, particularly IBS-M; however, we emphasize that bowel pattern subtypes are highly unstable. In a patient population with approximately 33% prevalence rates of IBS-D, IBS-C, and IBS-M, 75% of patients change subtypes and 29% switch between IBS-C and IBS-D over1 year.

Other investigators report the IBS-M subtype in about 50% of referred patients according to 3 sets of criteria, and IBS-M is the most prevalent group in primary care. In addition, a majority of patients have rapidly fluctuating symptoms lasting from <1 hour to <1 week. Therefore, the rate of documented bowel pattern change is a function of the data collection frequency, and there are insufficient data upon which to recommend a time period for defining IBS-A. In drug studies on patients sub typed by stool form, investigators may want to assess pharmacologic effects on stool frequency, straining, urgency and incomplete evacuation as well as stool form. Although the committee recommends a change in sub typing from the multi symptom Rome II classification to one based on stool form only, there are insufficient data to exclude either classification at this time. Further validation studies are needed.

Because of the characteristic symptom instability, we prefer the terms IBS with constipation and IBS with diarrhea instead of constipation and diarrhea predominant IBS. In this categorical system, many people whose features place them close to a subtype boundary change pattern without a major change in pathophysiology. Moreover, the heterogeneity and variable natural history of IBS significantly limit clinical trials of motility-active drugs and drug therapy in practice. In both research and practice, it may be desirable to base drug use on a stronger bowel pattern predominance than the requirements of this system.

Clinical Evaluation

Diagnosis depends on careful interpretation of the temporal relationships of pain/ discomfort, bowel habit, and stool characteristics. Pain/discomfort related to defecation is likely to be of bowel origin, whereas that associated with exercise, movement, urination, or menstruation usually has a different cause. Fever, gastrointestinal bleeding, weight loss, anemia, abdominal mass, and other ”alarm” symptoms or signs are not due to IBS, but may accompany it.

In women, so-called pelvic pain,[22] worsening of IBS symptoms during menstruation, and dyspareunia or other gynecologic symptoms may obscure the diagnosis.

Incorrect symptom attribution can lead to hospitalization and surgery; especially cholecystectomy, appendectomy, and hysterectomy. The recognition and evaluation of bowel dysfunction in patients with “pelvic” or abdominal pain may reduce unnecessary surgery.

Heartburn, fibromyalgia, headache, backache, genitourinary symptoms, and others are often associated with IBS, but are not useful in diagnosing it. These symptoms increase as the severity of IBS increases and may be associated with psychological factors. Obviously, a common disorder such as IBS may coexist with organic gastrointestinal disease. There are no discriminating physical signs of IBS, but abdominal tenderness may be present. Tensing the abdominal wall increases local tenderness associated with abdominal wall pain, whereas it lessens visceral tenderness by protecting the abdominal organs (Carnet test).[23]

Few tests are required for patients who have typical IBS symptoms and no alarm

features.[24] Unnecessary investigations may be costly and even harmful. Testing is based on the patient's age, duration and severity of symptoms, psychosocial factors, alarm symptoms and family history of gastrointestinal disease. Investigations may include a sigmoidoscopy or colonoscopy to rule out inflammation, tumors, or melanosis coli owing to regular laxative use. Stool examination for occult blood, leukocytes, or ova and parasites (e.g., giardia) where they are endemic may be indicated, but routine rectal biopsy and abdominal ultrasonography usually are not. Many people who report severe lactose intolerance absorb lactose normally with negligible symptoms, undermining the value of documenting lactase deficiency. The discovery of diverticulosis does not change the diagnosis of IBS.[25] Some patients with celiac sprue have IBS symptoms. In IBS patients who were HLA-DQ2-positive and had intestinal antibodies to gliadin and other dietary proteins, stool frequency and intestinal IgA levels decreased after gluten restriction. However, the available data suggest testing for celiac disease only if indicated by clinical features and local prevalence.

A confident diagnosis that holds up over time can usually be made through careful history taking, examination, and limited laboratory and structural evaluations individualized to each patient's needs. IBS is often properly diagnosed without testing. After diagnosis, a change in the clinical features may warrant additional investigation. However, persistence and recurrence is expected, and needless investigation may undermine the patient's confidence in the diagnosis and in the physician.

Physiologic Features

IBS is best viewed as an interaction of important biological and psychosocial factors. Altered motility, visceral hyperalgesia, disturbance of brain-gut interaction, abnormal central processing, autonomic and hormonal events, genetic and environmental factors, post infectious sequels, and psychosocial disturbance are variably involved, depending on the individual.[26]

Psychosocial Features

Psychological disturbance, especially in referred patients, includes psychiatric disorders (e.g., panic disorder, generalized anxiety disorder, mood disorder, and posttraumatic stress disorder), sleep disturbance, and dysfunctional coping. A history of childhood abuse is common.[27] Although stressful life events sometimes correlate with symptom exacerbation, the nature of the link between psychosocial factors and IBS is unclear.

Treatment

Management depends on a confident diagnosis, explanation of why symptoms occur, and suggestions for coping with them. Education about healthy lifestyle behaviors, reassurance that the symptoms are not due to a life-threatening disease such as cancer, and establishment of a therapeutic relationship are essential, and patients have a greater expectation of benefit from lifestyle modification than drugs.[28] For such counseling, individual or group interactions are effective.

Most IBS patients present to primary care where physicians are best positioned to know their histories, personalities, and families. Specialists' patients are more likely to have severe symptoms, depression, anxiety, panic, or other complicating psychosocial disorders that require special treatment. In addition to allaying fear, physicians should recover any unstated worries or aggravating factors. It is important to assess the patient's quality of life and level of daily functioning, personality, recent life stress (e.g., divorce, bereavement, or job loss), and any psychological disturbance.

The type and severity of symptoms and the nature of associated psychosocial issues determine treatment.[29] Psychological factors may alter symptom perception, and the patient's reaction to the symptoms may be more important than the symptoms themselves. Most patients respond to psychological support, a strong physician patient relationship, and multicomponent treatment approaches that reduce health care utilization. The physician should be understanding, maintain patient contact, and prevent over testing and harmful treatments. Unsatisfied patients may consult many physicians, undergo unjustified and hazardous investigation, take unproven medication, and have unneeded surgery.

Patients should avoid nutritionally depleted diets and have regular, unhurried meals. Lactose restriction usually fails to improve symptoms, and dietary calcium restriction may be harmful. Excessive fructose and artificial sweeteners, such as sorbitol or mannitol, may cause diarrhea, bloating, cramping, or flatulence. More data are necessary before testing for 1gG antibodies to certain foods can be recommended.[30] Dietary fiber for IBS is time honored, inexpensive, and safe, but poorly substantiated by clinical trials. Indeed, many patients believe bran exacerbates their symptoms, and the only substantial randomized controlled trial of bran suggested

it exacerbated flatulence and did not relieve pain.

Possible drugs for a dominant symptom in IBS

Symptom	Drug	Dose
Diarrhea	Loperamide	2-4 mg when necessary/maximum 12g/d
	Cholestyramine resin	4g with meal
	Alosetron	0.5-1 mg bid (for severe IBS, women)
Constipation	Psyllium husk	3.4 g bid with meals, then adjust
	Methylcellulose	2g bid with meals, then adjust
	Calcium polycarbophil	1g qd to qid
	Lactulose syrup	10-20g bid
	70% sorbitol	15 ml bid
	Polyethylene glycol 3350	17g in 8 oz water qd
	Tegaserod	6mg bid (for IBS, women)
	Magnesium hydroxide	2-4 tbsp qd
Abdominal pain	Smooth-muscle relaxant	qd to qid ac
	Tricyclic antidepressants	start 25-50 mg hs, then adjust
	Selective serotonin reuptake inhibitors	begin small dose, increase as needed

Drug therapy is directed toward the dominant symptoms. Their changeable nature and the complex interactions between the central and enteric nervous systems circumscribe the effectiveness of specific therapies. Researchers are searching for biomarkers and genetic polymorphisms that might identify patients most likely to respond to drugs. Early therapeutic trials had significant methodological inadequacies, and deficiencies and publication bias persist. Drugs help only some symptoms in

selected patients. Loperamide may prevent diarrhea when taken before a meal or an activity that often leads to the symptom. Constipation is treated initially with dietary fiber supplementation. If response is unsatisfactory, commercial fiber analogs may help. The heterogeneous smooth-muscle relaxants are questionably beneficial for pain; trial deficiencies leave their efficacy in doubt.[31] Furthermore, their availability varies in Australia, Canada, Europe, and the United States. Antidepressant drug therapy in lower than antidepressant doses may be beneficial even if there is no major psychiatric co morbidity. For example, desipramine benefits women with moderate to severe IBS who do not discontinue the drug owing to side effects, and the effect appears unrelated to the drug dose. Paroxetine improves the physical component of quality of life of patients with severe IBS and is more effective than a high-fiber diet in improving global status. The narrow therapeutic window for antidepressants suggests they be limited to patients with moderate or severe IBS.

Alosetron, a selective serotonin 5-HT3 receptor antagonist, can decrease pain, urgency, stool frequency, and increase global status in women with diarrhea and IBS. Based on rigorous studies, the number needed to treat (NNT) is 7.[32] Ischemic colitis and severe obstipation led to its withdrawal, but it was reintroduced only in the United States with restricted access and a risk management program. It was efficacious and safe in a 48- week trial. Well-designed studies of tegaserod, a partial 5-HT4 receptor agonist, found it can improve overall status, stool frequency and form, ease of evacuation, and bloating in women with IBS and constipation. In 8 studies, the NNT for daily doses of 12mg and 4mg was 14 and 20, respectively, and it is as effective in re treating patients as during initial therapy. Published trials comparing alosetron and tegaserod with conventional anti diarrheals and laxatives, respectively, are not available, and interpretation of NNT values calculated from older studies of these

agents is compromised by trial deficiencies.

Preliminary trials of probiotics are encouraging, especially symptom improvement and normalization of the blood mononuclear cell ration of an anti-inflammatory to a pro inflammatory cytokine in patients taking bifidobacterium infantis, but these studies need repeating in larger numbers of patients before they can be considered established treatments. Small bowel bacterial overgrowth, as diagnosed by lactulose hydrogen breath testing is a suggested but disputed cause of IBS, and antibiotics provide only transient benefit and risk clostridium difficile infection, allergic reactions, anti microbial resistance, and chronic functional symptoms.

Cognitive- behavioral therapy, standard psychotherapy, and hypnotherapy may help selected IBS patients. Weekly cognitive- behavioral therapy for 12 weeks was better than weekly educational sessions, but depressed patients did not respond; quality of life but not pain, improved. Hypnotherapy, the most thoroughly evaluated psychological treatment, normalizes rectal sensation, [33] and 12 sessions benefit quality of life, anxiety, and depression in refractory patients (except men with IBS and diarrhea), and the benefits last ≥5 years. However, trials of psychological therapy cannot be double blind, and treatment is time consuming, costly, and often unavailable.

C2.Functional Bloating

Definition

Functional bloating is a recurrent sensation of abdominal distention that may or may not be associated with measurable distention, but is not part of another functional bowel or gastro duodenal disorder.

Epidemiology

Most of the research on bloating has dealt with subjects who also have other functional gastrointestinal disorders; up to 96% of IBS patients report this symptom. Community surveys reveal that about 10%-30% of individuals report bloating during the previous year. It is about twice as common in women as men, and is often associated with menses. Typically, it worsens after meals and throughout the day and improves or disappears overnight. Abdominal inductance plethysmography confirms increased abdominal girth in some bloated IBS patients.[34]

C2. Diagnostic criteria* for functional bloating

Must include both of the following:

1. Recurrent feeling of bloating or visible distention at least 3 days/month in 3 months
2. Insufficient criteria for a diagnosis of functional dyspepsia, IBS, or other functional GI disorder

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Rationale for the criteria

Because *abdominal* as a modifier of *bloating* is redundant, it was omitted. Fullness was also deleted, because it may imply postprandial satiety, yet bloating occurs throughout the day. Importantly, bloating overlaps with other functional disorders (e.g., functional constipation, IBS, and functional dyspepsia), epidemiologic surveys and factor analyses do not convincingly demonstrate a distinct bloating group, and physiologic studies of bloating have mainly been done on patients with IBS. Because of the lack of data on bloating frequency, the frequency criterion is arbitrary and may need to be modified for different purposes. Additional epidemiologic research should investigate functional bloating.

Clinical evaluation

Bloating is distinguished from other causes of abdominal distention by its diurnal pattern. It may follow ingestion of specific food. Excessive burping or flatus is sometimes present, but these may be unrelated to the bloating. Diarrhea, weight loss, or nutritional deficiency should prompt investigation for intestinal disease.

Physiologic features

No unified pathophysiologic mechanism can be applied to all patients. Food intolerance, abnormal gut bacterial flora, weak abdominal musculature, and abnormal retention of fluid inside and outside the gut do not appear to be significant factors. However, studies have documented both increased intestinal gas accumulation and abnormal gas transit. Visceral hyperalgesia may be important in some patients.

Psychosocial features

No uniform psychological factors have been identified.

Treatment

Although the functional bloating criteria require the absence of other disorders, most research has been done on patients who have IBS or another disorder; therefore, treatment of bloating is similar whether it is isolated or associated with another functional disorder. Most treatments are designed to reduce flatus or gut gas, which are of unproved importance in bloating, and most are of unproven efficacy. Bloating may decrease if an associated gut syndrome such as IBS or constipation is improved. If bloating is accompanied by diarrhea and worsens after ingesting dairy products, fresh fruits, or juices, further investigation or a dietary exclusion trial may be worthwhile. However, even patients with proven lactase deficiency experience little or no bloating after drinking 240 mL of milk. Avoiding flatogenic foods, exercising, losing excess weight, and taking activated charcoal are safe but unproven remedies.[35] Data regarding the use of surfactants such as simethicone are conflicting. Antibiotics are unlikely to help, but trials of probiotics are encouraging. Beano, an over-the-counter oral ß-glycosidase solution, may reduce rectal passage of gas without decreasing bloating and pain.[36] Pancreatic enzymes reduce bloating, gas, and fullness during and after high-calorie, high-fat meal ingestion. Tegaserod improves bloating (a secondary outcome measure) in some constipated female IBS patients.

C3. Functional constipation

Definition

Functional constipation is a functional bowel disorder that presents as persistently difficult, infrequent, or seemingly incomplete defecation, which do not meet IBS criteria.

Subjective and objective definitions of constipation include straining, hard stools or scybala (hard, inspissated stool), unproductive calls ("want to but cannot"), infrequent stools, or incomplete evacuation; >3 bowel movements per week, daily stool weight <35 g/day, or straining >25% of the time; and prolonged whole gut or colonic transit. Stool frequency correlates poorly with colonic transit, but one can estimate gut transit using the Bristol stool form scale. Usually, there is no demonstrable physiological abnormality.

Epidemiology

Constipation occurs in up to 27% of people depending on demographic factors, sampling, and definition. It affects all ages and is most common in women and non-whites. In 1 survey, the prevalence was sought by 3 means: patient complaint, Rome I Criteria, and transit time[37] (using the Bristol scale). Approximately 8% had constipation by each definition, but only 2% were constipated by all 3. Therefore, the concept of constipation is complicated by disagreement among patients and doctors about its nature.

C3. Diagnostic criteria* for functional constipation

1. Must include 2 or more of the following:
    a. Straining during at least 25% of defecations
    b. Lumpy or hard stools in at least 25% of defecations
    c. Sensation of incomplete evacuation for at least 25% of defecations
    d. Sensation of anorectal obstruction / blockage for at least 25% of defecations
    e. Manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation, support of the pelvic floor)
    f. Fewer than 3 defecations per week
2. Loose stools are rarely present without the use of laxatives
3. There are insufficient criteria for IBS

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Rationale for changes to diagnostic criteria

A required frequency of "≥25%" is substituted for ">25%" to maintain consistency with other FBD criteria. Studies using Rome II criteria yield a lower prevalence than those using Rome I criteria because the Rome II criteria did not allow for laxative-induced loose stools, an anomaly that is corrected in the Rome III criteria.

Clinical evaluation

The physician should clarify what the patient means by constipation. Manual maneuvers to assist defecation or straining to expel soft stools suggest anorectal dysfunction, but are diagnostically unreliable.[38] Transit time can be estimated using the Bristol scale. Evaluation of the patient's gut symptoms, general health, psychological status, use of constipating medications, dietary fiber intake, and signs

of medical illnesses (e.g., hypothyroidism) should guide investigation. Physicians should perform perianal and anal examination to detect fecal impaction, anal stricture, rectal prolapse, mass, or abnormal perineal descent with straining. Laboratory tests are rarely helpful. Endoscopic evaluation of the colon may be justified for patients >50 years with new symptoms or patients with alarm features or a family history of colon cancer.

If fiber supplementation fails to help or worsens the constipation, measurements of whole gut transit time may identify cases of anorectal dysfunction or colon inertia. Using radio opaque markers, measurement of whole gut transit time (primarily colon transit) is inexpensive, simple, and safe. Several methods produce similar results. Retention of markers in the proximal or transverse colon suggests colonic dysfunction, and retention in the recto sigmoid area suggests obstructed defecation. A radioisotope technique involves less radiation than plain x-rays and may provide more information, helping to differentiate proximal colon emptying, pancolonic inertia, and dyssynergic defecation.

Physiologic Factors

Severe, intractable constipation may be due to colonic inertia or anorectal dyssynergia. These disorders may coexist, but most patients complaining of constipation have normal colonic transit and anorectal function.

Psychosocial Factors

No uniform psychological profile is applicable to patients with constipation; however, patients with severe constipation and normal intestinal transit often have

increased psychological distress, and depressed patients may have constipation.

Treatment

Reassurance may convince some patients that failure to evacuate for 2 or 3 days is harmless. Increased fluid intake and physical exercise are unproven measures.[39] Physicians should stop or reduce any constipating medication the patient may be taking and treat depression and hypothyroidism when present. Pharmacologic therapy is not advisable until general and dietary measures are exhausted. There are few published trials of some commonly used medical therapies.

The severity and nature of the symptoms guide further treatment. The indigestible matter in dietary fiber increases fecal bulk by promoting fecal water holding capacity and bacterial proliferation. Other bulking agents include psyllium, methylcellulose, and calcium polycarbophil. Although stimulating laxatives such as bisacodyl, sodium picosulphate, or sennosides may be tried, their effectiveness and long-term safety have not been determined by placebo – controlled trials; they were introduced in an era when high quality trials were not performed. Polyethylene glycol solution, lactulose, and sorbitol may be useful. Tegaserod is superior to placebo for patients with chronic constipation.[40] Recent studies suggest that prostaglandin analogs may be helpful.

C4. Functional diarrhea

Definition

Functional diarrhea is a continuous or recurrent syndrome characterized by the

passage of loose (mushy) or watery stools without abdominal pain or discomfort.

Epidemiology

There are few studies in which functional diarrhea was specifically diagnosed as distinct from IBS-D, so it is impossible to provide a precise frequency. 9.6% of Minnesota residents and 4.8% of people throughout the United States reported unspecified diarrhea; however, its duration and frequency are uncertain. Although a common reason for consulting a gastroenterologist, diarrhea was a presenting complaint of <2% of general practice patients.

C4. Diagnostic criterion* for functional diarrhea Loose (mushy) or watery stools without pain occurring in at least 75% of stools **Criterion fulfilled for the last 3months with symptom onset at least 6 months before diagnosis*

Rationale for the criteria

Most people apply the term diarrhea to loose or watery stools. Fewer individuals relate it to increased frequency and urgency. Because rapid transit increases the percentage of water in stool, stool form correlates well with transit. Safe stools are 85% water, and watery stools 90% with greatly reduced stool viscosity.[41] Stool viscosity is critical because watery stool is difficult to retain, and anal contact with fluid causes extreme urgency. However, urgency alone unreliably indicates diarrhea and may be reported by individuals with hard, pellet like stools. Thus, stool form, not frequency, defines diarrhea. How often a symptom must occur to be significant depends on its troublesomeness. Just 1 episode of fecal incontinence is a serious

problem for a patient, whereas an occasional loose stool may not be.

Clinical Evaluation

The combination of abdominal pain with intermittent diarrhea and constipation is highly suggestive of IBS, and small-volume, frequent defecation is likely functional. Pseudodiarrhea (frequent defecation and urgency with solid stools) is not diarrhea. A stool diary incorporating the Bristol stool form scale is a useful method to verify stool form. Dietary history can disclose poorly absorbed carbohydrate intake, such as lactose by patients with hypolactasia, or " sugar-free" products containing fructose, sorbitol, or mannitol. Alcohol can cause diarrhea by impairing sodium and water absorption from the small bowel. Physical examination should seek signs of anemia or malnutrition. An abdominal mass suggests crohn's disease in the young patient and cancer in the elderly patient. Rectal examination, colon endoscopy, and biopsy can exclude villous adenoma, microscopic colitis, and inflammatory bowel disease.

Abnormal results of blood or stool tests or other alarm features necessitate further tests. Features of malabsorption (malnutrition, weight loss, non-blood-loss anemia, or electrolyte abnormalities) should provoke the appropriate antibody tests and /or duodenal biopsy for celiac disease. Where relevant, giardiasis and tropical sprue should be excluded. Barium small bowel radiography may be necessary. Rarely, persistent diarrhea may require tests for bile acid malabsorption or, more practically, a trial of the bile acid-binding resin cholestyramine.

Physiologic factors

Few studies have addressed the physiology of functional diarrhea. One such study found decreased non-propagating colonic contractions and increased propagating colonic contractions.

Psychosocial factors

Psychosocial factors have also received little research attention apart from the finding of accelerated colonic transit inducible by acute stress.

Treatment

Discussion of possible psychosocial factors, symptom explanation, and reassurance is important. Restriction of foods such as those containing sorbitol or caffeine, which seem provocative, may help. Empiric antidiarrheal therapy (e.g., diphenoxylate or loperamide) is usually effective, especially if taken prophylactically, such as before meals or public engagements.[42] Alosetron slows transit and reduces the gastrocolonic response in normal volunteers and may improve diarrhea. However, it is expensive and of limited availability only in the United States; there are no published, randomized, controlled trials in patients with functional diarrhea. Cholestyramine, an ion-exchange resin that binds bile acids and renders them biologically inactive, is occasionally very effective. The prognosis of functional diarrhea is uncertain, but it is often self-limited.

C5. Unspecified functional bowel disorder

Individual symptoms discussed in the previous sections are very common in the population. These occasionally lead to medical consultation, yet are unaccompanied by other symptoms that satisfy criteria for a syndrome. Such symptoms are best classified as unspecified.

C5. Diagnostic criterion* for unspecified functional bowel disorder
Bowel symptoms not attributable to and organic etiology that do not meet criteria for the previously defined categories
* Criterion fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis

Functional abdominal pain syndrome

Functional abdominal pain syndrome (FAPS) represents a chronic pain disorder localized to the abdomen with features that differentiate it from other painful functional gastrointestinal disorders. Like other functional gastrointestinal disorders, symptoms are not explainable by a structural or metabolic disorder by using currently available diagnostic methods. FAPS appears highly related to alterations in endogenous pain modulation systems, including dysfunction of descending pain modulation and cortical pain modulation circuits. There is only 1 recognized diagnosis in this category of functional gastrointestinal disorders

D. Functional abdominal pain syndrome

Definition

FAPS represents a pain syndrome attributed to the abdomen that is poorly related to gut function, is associated with some loss of daily activities, and has been present for at least 6 months. The pain is constant, nearly constant, or at least frequently recurring. The principal criterion differentiating FAPS from other functional gastrointestinal disorders, such as irritable bowel syndrome (IBS) and functional dyspepsia, is the lack of symptom relationship to food intake or defecation. FAPS commonly is associated with a tendency to experience and report other somatic symptoms of discomfort, including chronic pain thought to be related to the gynecologic or urinary systems. Psychological disturbances are more likely when pain is persistent over a long period of time, is associated with chronic pain behaviors, and/ or dominates the patient's life. In psychiatric nosology, FAPS would qualify as a

somatoform pain disorder and satisfy a pain criterion toward the diagnosis of somatization disorder.

Epidemiology

The epidemiology of FAPS is incompletely known because of limited available data and methodological difficulties in establishing a diagnosis that can be differentiated from other more common functional gastrointestinal disorders, such as IBS and functional dyspepsia, however, it is generally considered that FAPS is a less common functional disorder than either IBS or functional dyspepsia. Reported prevalence figures in North America range from 0.5% to 2% and do not differ from those reported in other countries. The disorder is more common in women[43] (female: male=3:2), with prevalence peaking in the fourth decade of life. Patients with FAPS have high work absenteeism and health care utilization and, thus, impose a significant economic burden.

D. Diagnostic criteria* for functional abdominal pain syndrome must include all of the following:

1. Continuous or nearly continuous abdominal pain
2. No or only occasional relationship of pain with physiological events (e.g., eating, defecation, or menses)
3. Some loss of daily functioning
4. The pain is not feigned (e.g., malingering)
5. Insufficient symptoms to meet criteria for another functional gastrointestinal disorder that would explain the pain

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months

Rationale for changes from previous criteria

Studies determining the reliability of these criteria in identifying a homogeneous population are lacking, and subjects with various different explanations for pain (in particular, chronic pain attributed to pelvic viscera) may be represented.[44] A lack of relationship of pain in FAPS with defecation separates this diagnosis from the functional bowel disorders, but the distinction from IBS has acknowledged difficulties and is not clearly based on scientific evidence. The requirements for some loss of daily functioning and that pain is not feigned are derived from the diagnostic criteria for somatization disorder and undifferentiated somatoform disorder. Qualifiers in the criteria (e.g., “occasional” and “some”) remain subjectively defined. Although discussed in the context of this article as a functional gastrointestinal disorder, FAPS also would qualify as a pain symptom contributing toward these diagnoses in psychiatric nosology.

Clinical evaluation

A host of disorders can produce chronic abdominal pain, and the clinician should be aware of the extended differential diagnosis. Algorithms to diagnose and treat FAPS are empirical because objective scientific evidence to support a singular approach does not exist. It is suggested that evaluation consist of a clinical/psycho social assessment, observation of symptom reporting behaviors and a detailed physical examination. By answering a few questions, the physician effectively can appraise the clinical features of FAPS identify the key psychosocial contributions to the disorder, and increase confidence in the diagnosis.[45]

Symptom-related behaviors often seen in patients with FAPS

Expressing pain of varying intensity through verbal and nonverbal methods, may diminish when the patient is engaged in distracting activities, but increase when discussing a psychologically distressing issue or during examination
Urgent reporting of intense symptoms disproportionate to available clinical and laboratory data (eg, always rating the pain as "10" on a scale from 1 to 10)
Minimizing or denying a role for psychosocial contributors, or of evident anxiety or depression, or attributing them to the presence of the pain rather than to understandable life circumstances
Requesting diagnostic studies or even exploratory surgery to validate the condition as "organic"
Seeking health care frequently
Taking limited personal responsibility for self-management, while placing high expectations on the physician to achieve symptom relief
Making requests for narcotic analgesics when other treatment options been implemented

Typically, FAPS patients describe abdominal pain in emotional terms,[46] as

constant and not influenced by eating or defecation, as involving a large anatomic area rather than a precise location, as one of several other painful symptoms, and as a continuum of painful experiences beginning in childhood or recurring over time. For patients meeting diagnostic criteria for FAPS who exhibit a longstanding history of pain behaviors and certain psychosocial correlates, the clinical evaluation typically fails to disclose any other specific medical etiology to explain the illness. In the absence of alarm features common to the functional gastrointestinal disorders, conservative efforts should be taken to exclude other medical conditions in a cost-effective manner.

Questions for appraising clinical features of FAPS while identifying key psychosocial contributors

1. What is the patient's life history of illness?
2. Why is the patient presenting now for medical care?
3. Is there a history of traumatic life events?
4. What is the patient's understanding of the illness?
5. What is the impact of the pain on activities and quality of life?
6. Is there an associated psychiatric diagnosis?
7. What is role of family or culture?
8. What are the patient's psychosocial impairments and resources?

Physiological features

The observations that symptoms are reported as constant and unrelated to physiological events along with the common responsiveness of FAPS symptoms to low-dose tricyclic antidepressants point toward central neuropathic pain as a likely pathophysiological process. The common comorbidity of FAPS with psychiatric disorders (in particular, anxiety, depression, and somatization) and the fact that chronic abdominal pain is common in major depressive disorder suggest a prominent role of the central nervous system in altering pain modulation (cognitive or emotional). This does not exclude the possibility that, as in other neuropathic pain conditions, peripheral factors play a role in initiating or perpetuating this chronic pain state; scientific evidence to support such a mechanism, however, is not available. Descending pain modulation systems (opoidergic, serotonergic, and noradrenergic pathways) originate in distinct brainstem regions and modulate spinal cord excitability. It has been speculated that patients with various chronic pain syndromes, including fibromyalgia and FAPS, have compromised ability to activate such endogenous pain inhibition systems or exhibit an imbalance between facilitatory and inhibitory systems. Recent studies performed by using functional brain-imaging techniques identify interactions between prefrontal cortical regions, limbic regions, and brainstem regions that could provide the neurobiological substrate for the influence of cognitive factors on symptom perception in FAPS. Belief systems and coping styles characteristically seen in FAPS patients are consistent with the possibility of altered influences of cortical networks (including prefrontal and parietal cortical regions) on limbic and pain modulation circuits.[47]

Psychological features

FAPS shows a close relationship with a variety of psychiatric and psychological conditions. Clinical evidence suggests that there is a strong association of aversive early life events and certain types of psychosocial stressors with increased pain reports among patients with functional gastrointestinal disorders.[48] The combination of genetic factors, vulnerability factors, and adult stress may determine in part the effectiveness of endogenous pain modulation systems and thereby influence development of FAPS. Population and patient- based studies have confirmed the significant association between chronic abdominal pain and affective disorders, especially anxiety and depression. Symptom-specific anxiety has been proposed recently as having a more direct influence on pain than general anxiety, and this construct also has been investigated in functional gastrointestinal disorders including abdominal pain. FAPS may be seen with other somatoform disorders (e.g., somatization disorder, conversion disorder, and hypochondriasis). In a study of somatization disorder identified in a primary-care population, abdominal pain was present in 30% of subjects and was the third most frequent somatic symptom (after headache and back pain).

Pain beliefs and coping strategies are important in chronic pain and somatoform disorders and are significant predictors of quality of life impairment and treatment response. Patients may exhibit ineffective coping strategies (e.g., “catastrophizing”) or have poor social or family support. Unresolved losses, including onset or exacerbation of symptoms after the death of a parent or spouse, personally meaningful surgery (e.g., hysterectomy and ostomy), or interference with the outcome of a pregnancy (abortion, stillbirth), are common in FAPS. Histories of sexual and physical abuse are prevalent, but elevated rates are not specific for this diagnosis. These histories predict poorer health status, medical refractoriness, increased diagnostic and therapeutic procedures, and more frequent health care visits.

Such trauma may increase awareness of bodily sensations, although visceral pain thresholds are not reduced.

Treatment

In contrast to IBS, treatment recommendations for patients with FAPS are empirical and not based on results from well-designed clinical trials. The accepted basis for clinical management of FAPS relies on establishing an effective patient-physician relationship, following a general treatment approach, and offering more specific management that often encompasses a combination of treatment options. Factors that contribute to an effective patient-physician relationship include empathy toward the patient, patient education, validation of the illness, reassurance, treatment negotiation, and establishment of reasonable limits in time and effort. Before implementing specific forms of therapy (e.g., antidepressants and anticonvulsants), the following general aspects of care should be considered: setting of treatment goals, helping the patient take responsibility, basing treatment on symptom severity and the degree of disability, and referring to a mental health care professional or, if available, to a multidisciplinary pain treatment center in selected patients, particularly those with refractory symptoms. Unfortunately, establishing a diagnosis, an effective patient physician relationship, and a general treatment plan often is overlooked. Lack of confident diagnosis, non therapeutic physician attitudes, excessive testing and treatment (including unnecessary surgery), and patient cognitions often contribute to a cycle of ineffective, costly management.[49]

Pharmacological therapies. Antidepressants, particularly tricyclic antidepressants (TCAs) in low daily dosages, are helpful in treating chronic pain and other painful functional gastrointestinal disorders, such as IBS, and may be useful for

the treatment of FAPS for both direct pain management effects and antidepressant effects. However, evidence from controlled clinical trials for the effectiveness of antidepressants in FAPS or superiority of any 1 agent or antidepressant class in this disorder is not available. In other chronic pain conditions, trials with TCAs generally have been more successful than those using selective serotonin-reuptake inhibitors. Newer agents with combined serotonin and nor epinephrine reuptake activity (SNRIs, such as venlafaxine and duloxetine) have recognized pain- reducing effects in some somatic pain conditions and may prove useful in FAPS. Both selective serotonin reuptake inhibitors and SNRIs may be useful in the patient with comorbid depression or anxiety. Most analgesics (e.g., aspirin and nonsteroidal anti-inflammatory drugs) offer little benefit, possibly because their actions primarily are peripheral in location. Narcotic analgesics should be avoided because of the likelihood of addiction and possibility of narcotic bowel syndromes, such as chronic neuropathic pain, as alternatives to TCAs with fewer side effects. The most studied have been gabapentin, carbamazepine, and lamotrigine. They have not been examined specifically in abdominal pain disorders or FAPS, although there is a rationale and evidence of efficacy in chronic pain management remains limited despite rather widespread use. These agents are relatively safe and non-habituating, also may interrupt the cycle between pain and depression[50] and might prove beneficial as adjunctive agents in some refractory patients, although direct evidence is lacking. In summary, anecdotal reports and observed benefits of some compounds in other chronic pain conditions provide the basis for pharmacological treatment of FAPS not scientific evidence from controlled clinical trials.

Psychological therapy. No psychological treatment study specifically has targeted adult FAPS. However, studies in other painful functional gastrointestinal disorders and non-gastrointestinal pain conditions suggest that psychological

treatments would be beneficial. Interventions of potential benefit include cognitive behavioral therapy, dynamic or interpersonal psychotherapy, hypnotherapy, and stress management. Referral to pain treatment centers for multidisciplinary treatment programs may be the most efficient method of treating disability from refractory chronic pain. Although the various psychological treatments described earlier have been shown to improve mood, coping, quality of life, and health care costs, they have less demonstrable impact on specific visceral or somatic symptoms, suggesting that their best use may be in combination with symptomatic treatment. Psychological treatment may be most accepted if presented as a parallel intervention with ongoing medical care, a means for managing pain, and an attempt to reduce psychological distress from the symptoms.

Complementary therapies. Patients with chronic pain disorders, including FAPS, commonly use complementary and alternative therapies, such as spinal manipulation,[51] massage,[52] and acupuncture[53] although data supporting their use are limited. Few reports have described the use of transcutaneous electrical nerve stimulation in patients with FAPS, and uncontrolled results are indeterminant. Although uncontrolled studies suggest a significant diagnostic and therapeutic benefit of laparoscopy with intended adhesiolysis in patients with chronic abdominal pain tentatively attributed to adhesions from prior surgical procedures, the outcome may be placebo related and unsuspected diagnoses are rare. A blinded, randomized trial of 100 patients undergoing either laparoscopic adhesiolysis or diagnostic laparoscopy alone found no advantage to adhesiolysis. This study also reported a significant improvement in chronic abdominal pain over 6 months whether laparoscopy alone or laparoscopic adhesiolysis were performed, suggesting spontaneous improvement in these patients over time.

MATERIALS AND METHODS

All patients who attended the Gastroenterology Outpatient clinic of the Stanley Medical College Hospital between July 2006 and December 2006 for a lower gastrointestinal complaint requiring a colonoscopy for evaluation were included in the study. At their first visit, data was collected in a structured proforma (annexure I) incorporating the bowel symptom questionnaire and were offered a full diagnostic workup, as considered appropriate based on the presenting symptoms. The data recorded included the age, gender, educational status (illiterate, primary, middle, high school and college), duration of symptoms, clinical symptomatology, relevant findings on clinical examination, basic laboratory data, imaging and findings at colonoscopy. Questionnaire data were collected prospectively in the above mentioned time period. Data were then retrospectively audited. Ethics committee approval was obtained prior to the initiation of the study.

All patients of functional bowel disorders (FBS) and functional abdominal pain syndrome (FAPS) were diagnosed based on the history, physical examination and appropriate negative diagnostic tests, including lower endoscopy. All patients underwent a full-length colonoscopy. In those patients in whom the caecum and terminal ileum could not be intubated were excluded from the analysis. Also patients were excluded if they had not completed a full diagnostic workup or had a colonoscopy for an indication other than a lower GI disorder. Alarm features, gastrointestinal symptoms, and factors that might indicate an organic disease on laboratory evaluation were considered for analysis. Patients were finally grouped into those having a functional disorder (Group I) and those with an organic disorder (Group II). The ability of the symptoms, alarm features and abnormalities on laboratory investigations to predict an underlying organic disease was then assessed by statistical analysis.

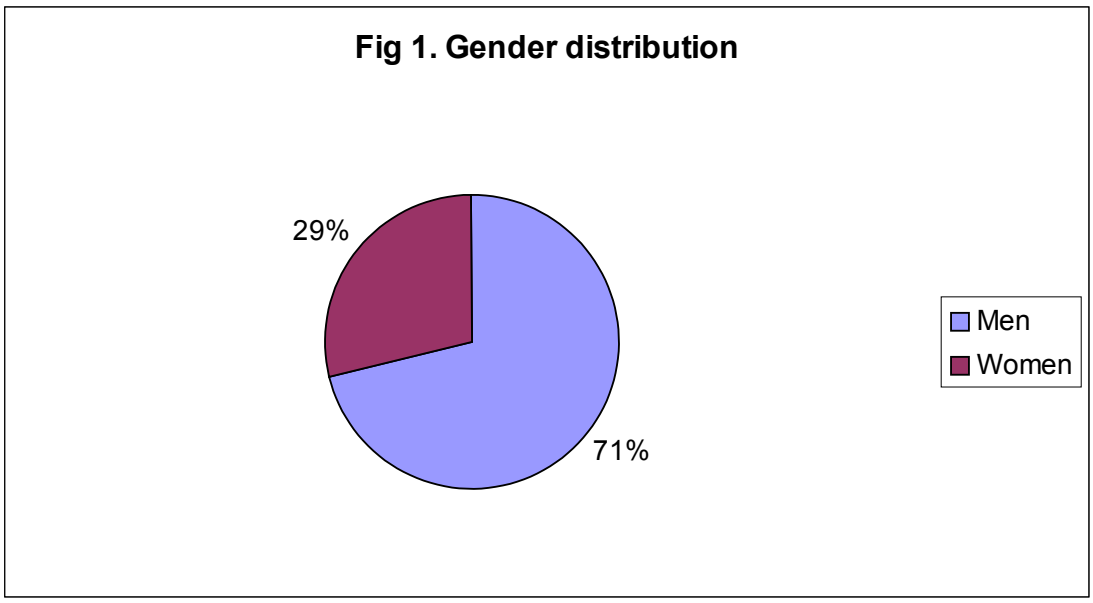
STATISTICAL ANALYSIS

Prevalence estimates were reported for all symptoms and for all disease risk factors, stratified by diagnostic group membership; univariate associations were assessed using Pearson's χ^2 test. Comparisons were performed between functional bowel disorders and organic illnesses of the lower gastrointestinal tract. Student's independent "t test" was used for quantitative data.

Logistic regression was used to assess the value of alarm features in discriminating functional disorders from organic disease Alarm features were entered into a regression model, and backward stepwise elimination was used to identify the best subset of symptoms that predicted a diagnosis of organic disease. For significant risk factors identified on univariate and multivariate analysis, odds ratio was calculated and their 95% confidence intervals were recorded. P values of < 0.05, were considered significant.

RESULTS

A total of 104 patients underwent colonoscopy during the study period. Twenty one patients were excluded in accordance with the following criteria: 11 had functional illnesses that did not meet the ROME III criteria for functional bowel disorders or functional abdominal pain syndrome, 5 had an incomplete colonoscopy due to inadequate preparation or technical difficulty, 5 had not undergone all diagnostic procedures that were considered necessary.



In total, 83 patients entered the study following the inclusion and exclusion criteria. There were 59 (71%) men and 24 (29%) women in the study group (Fig 1). Mean patient age was 44 $\pm$ 15.32. Men were older than women 45.83 $\pm$ 15.01 Vs 39.5 $\pm$ 15.47, though statistically not significant (p=0.09).

Of the 83 patients, 54 (65.1%) patients had a functional disorder (Group I) and 29 (34.9%) had an organic lower GI illness (Group II). The functional LGI disorders that were diagnosed were IBS – C in 8 (14.8%), IBS – D in 12 (22.2%), functional constipation in 16 (29.6%), functional diarrhea in 4 (7.4%) and functional abdominal pain syndrome in 14 (25.9%) patients.

The distribution of LGI organic diagnoses were Colorectal malignancy in 5 (17.3%), lymphoma in 1 (3.4%), benign polyp in 4 (13.8%), tuberculosis in 4 (13.8%), ulcerative colitis in 2 (6.9%), crohn's disease in 1 (3.4 %), perianal disease

in 11 (40%) and systemic illness causing lower GI symptoms in 1 (3.4%) patient.

Table 1. Age distribution

	Mean age	≥ 40 yrs	≥ 50 yrs	≥ 60 yrs
Group I (54)	44.11 ± 15.5	30	26	12
Group II (29)	43.79 ± 15.3	17	11	4
p value	0.93	0.78	0.37	0.35

The mean age of patients in group I was 44.11 ± 15.5 years and for those in group II was 43.8 ± 15.3 years; the differences were not statistically significant (p=0.93). Sub stratification of the study group into ≥ 40 yrs, ≥ 50 yrs and ≥ 60 yrs also did not reveal any significant differences between the two groups. (Table 1)

Table 2. Gender ratio and literacy status of the study population

		Group I No. (%)	**Group II No. (%)**	**P value**
Gender	Male	40 (74.1)	19 (65.5)	
	Female	14 (25.9)	10 (34.5)	0.41
Education	Illiterate	12 (22.2)	5 (17.2)	
	Primary	8 (14.8)	7 (24.1)	
	Middle	10 (18.5)	10 (34.5)	
	High school	20 (37)	6 (20.7)	0.26
	College	4 (7.4)	1 (3.4)	

Both groups of disorders were male predominant and the ratios were 2.9 and 1.9 for groups I and II respectively, with differences between the two groups being statistically insignificant ($p = 0.41$). The differences in literacy status between the two groups were also not significant ($p = 0.26$). (Table 2)

The mean duration of symptoms in group I was 95.56 ± 193.58 weeks and in group II was 24.28 ± 37.34 weeks ($p = 0.01$).

Table 3. Significance of symptoms in diagnosis

		Group I No. (%)	Group II No. (%)	p value	Odds ratio (95% CI)
Nocturnal symptoms	**Yes**	**2 (3.7)**	**5 (17.2)**	**0.03**	**5.4 (1.01 - 43.8)**
	No	**52 (96.3)**	**24 (82.8)**		
Blood in stools	**Yes**	**4 (7.4)**	**13 (44.8)**	**0.001**	**10.2 (26.3 – 43.7)**
	No	**50 (92.6)**	**16 (55.2)**		
Mucus in stools	Yes	10 (18.5)	7 (24.1)	0.55	-
	No	44 (81.5)	22 (75.9)		
Rectal symptoms	Yes	10 (18.5)	4 (13.8)	0.58	-
	No	44 (81.5)	25 (86.2)		
Incomplete evacuation	Yes	25 (46.3)	10 (34.5)	0.30	-
	No	29 (53.7)	19 (65.5)		
Mass descending PR	**Yes**	**0 (0)**	**4 (13.8)**	**0.005**	**-**
	No	**54 (100)**	**25 (86.2)**		
Abdominal pain	Yes	32 (59.3)	14 (48.3)	0.34	-
	No	22 (40.7)	15 (51.7)		
Digital evacuation	Yes	6 (11.1)	5 (17.2)	0.43	-
	No	48 (88.9)	24 (82.8)		
Anorexia	Yes	26 (48.1)	19 (65.5)	0.13	-
	No	28 (51.9)	10 (34.5)		
Weight loss	**Yes**	**2 (3.7)**	**11 (37.9)**	**0.001**	**15.9 (2.9 – 115.6)**
	No	**52 (96.3)**	**18 (62.1)**		
Tuberculosis in the past	Yes	2 (3.7)	4 (13.8)	0..09	-
	No	52 (96.3)	25 (86.2)		
Comorbid illness	Yes	10 (18.5)	10 (34.5)	0.10	-
	No	44 (81.5)	19 (65.5)		
Surgery	Yes	18 (33.3)	12 (41.4)	0.47S	-
	No	36 (66.7)	17 (58.6)		
Family H/O	Yes	2 (3.7)	1 (3.4)	0.95	-
	No	52 (96.3)	28 (96.6)		
UGI symptoms	Yes	18 (33.3)	6 (20.7)	0.22	-
	No	36 (66.7)	23 (79.3)		

The clinical symptomatologies that were statistically significant on univariate analysis (Table 3) were presence of nocturnal symptoms (p = 0.03), blood in stools (p = 0.001), mass descending per rectum (p = 0.005) and weight loss (p = 0.001). Symptoms like mucus in stools, rectal symptoms, sense of incomplete evacuation, presence, character or location of pain, digital evacuation of stools, anorexia, comorbid illness, abdominal surgery or tuberculosis in the past, family history of cancer or the presence of associated upper GI symptoms were not statistically significant to differentiate an organic from a functional LGI disease. None of the

symptoms evaluated favored the diagnosis of a functional LGI disorder by inclusion.

Table 4. Significance of abnormalities on clinical examination and investigations

		Group I No. (%)	Group II No. (%)	p value	Odds ratio (95% CI)
Anemia	**Yes**	**4 (7.4)**	**11 (37.9)**	**0.001**	**7.6 (1.9 – 33.2)**
	No	**50 (92.6)**	**18 (62.1)**		
Lymphadenopathy	Yes	0 (0)	1 (3.4)	0.17	-
	No	54 (100)	28 (96.6)		
Mass abdomen	**Yes**	**0 (0)**	**2 (6.9)**	**0.05**	**-**
	No	**54 (100)**	**27 (93.1)**		
Tenderness	**Yes**	**8 (14.8)**	**10 (34.5)**	**0.04**	**3.03 (1.01 – 10.1)**
	No	**46 (85.2)**	**19 (65.5)**		
Per rectal exam.	**Yes**	**0 (0)**	**3 (10.3)**	**0.02**	**-**
	No	**54 (100)**	**26 (89.7)**		
Low hemoglobin	**Yes**	**10 (18.5)**	**16 (55.2)**	**0.001**	**3.6 (1.2 – 11.1)**
	No	**44 (81.5)**	**13 (44.8)**		
Total Count	Yes	1 (1.9)	2 (6.9)	0.57	-
	No	53 (98.1)	27 (93.1)		
Raised ESR	**Yes**	**8 (14.8)**	**10 (34.5)**	**0.04**	**3.03 (1.01 – 10.1)**
	No	**46 (85.2)**	**19 (65.5)**		
Stool occult blood	**Yes**	**0 (0)**	**4 (22.2)**	**0.001**	**-**
	No	**52 (100)**	**14 (77.8)**		
High blood sugar	Yes	2 (3.7)	2 (6.9)	0.91	-
	No	52 (96.3)	27 (93.1)		
Low total protein	**Yes**	**0 (0)**	**4 (13.8)**	**0.005**	**-**
	No	**54 (100)**	**25 (86.2)**		
Low S. Albumin	**Yes**	**2 (3.7)**	**5 (17.2)**	**0.03**	**5.4 (1.01 – 43.8)**
	No	**52 (96.3)**	**24 (82.8)**		
Abnormality on USG	**Yes**	**0 (0)**	**3 (10.3)**	**0.02**	-
	No	**54 (100)**	**26 (89.7)**		
Abnormal colonoscopy	**Yes**	**0 (0)**	**28 (82.8)**	**0.001**	**-**
	No	**54 (100)**	**1 (3.4)**		

The presence of anemia (p = 0.01), mass abdomen (p = 0.05) and a positive finding on per rectal examination (p = 0.02) suggested an organic pathology. Moreover a low hemoglobin (p = 0.001), an elevated ESR (p = 0.04), stool occult blood positivity (p = 0.001), low total protein (p = 0.005), albumin (p = 0.03), abnormality on ultrasonogram (p=0.02) and colonoscopy (p=0.001) also suggested the probability of diagnosing an organic LGI disease with statistical significance. The total count (p = 0.57) and blood sugar (p = 0.91) were not significant variables. (Table 4)

Table 5. Multivariate logistic regression using backward elimination

Variables	p value	Odds ratio	95% CI
Duration of illness	0.01	1.03	1.01 – 1.05
Blood in stools	.021	5.5	1.29 – 25.0
Weight loss	.001	17.5	1.33 - 90.9
Tenderness	.004	11.1	4.45 – 41.6
Anemia	0.007	6.25	1.66 –23.8
Mass	0.01	4.33	1.33 - 19.4
Abnormal colonoscopy	0.02	3.22	1.12 – 8.6

(Variable(s) entered on step 1: nocturnal symptoms, blood in stools, rectal symptoms, mass descending per rectum, anorexia, weight loss, tuberculosis, comorbid illness, family history, anemia, lymphadenopathy, mass abdomen, per rectal examination, abnormality on ultrasonogram and colonoscopy)

The variables that showed statistical significance in differentiating an organic from a functional lower GI disease on multivariate analysis (Table 5) were passage of blood in stools ($p = 0.02$), weight loss ($p = 0.01$), abdominal tenderness ($p = 0.004$), anemia ($p = 0.007$), presence of mass abdomen ($p = 0.01$) and abnormalities on colonoscopy ($p=0.02$).

Table 6. Sensitivity, Specificity, PPV, NPV & Efficacy of Clinical Vs final diagnosis

		95% Confidence interval
Sensitivity	69%	54% to 80%
Specificity	62%	42% to 79%
Positive predictive value	77%	62% to 88%
Negative predictive value	51%	34% to 69%
Efficacy	66%	55% to 76%

The clinical differentiation between functional and organic LGI disease on clinical and laboratory investigations had a sensitivity of 69%, specificity of 62%, positive predictive value of 77%, negative predictive value of 51%, efficacy of 66% with the kappa statistics showing a fair agreement (k=0.29, p=0.007) (Table 6)

DISCUSSION

The presence of alarm features in patients with symptoms suggestive of IBS should shift the physician's differential diagnosis towards structural or inflammatory conditions based on the present results. However, the present data demonstrate that the actual diagnostic yield of most of the alarm features assessed is limited when the ROME III criteria are taken as the basis of the diagnosis. In the present study certain alarm features, including signs of rectal blood loss, mass abdomen and weight loss, had some value in discriminating functional from lower gastrointestinal organic disease. Although only three of the evaluated alarm features were significant discriminators of functional from organic lower gastrointestinal diseases, the present results suggest that a symptom based diagnosis, combined with a limited amount of alarm feature data, improve the diagnostic yield of the history, as captured by a questionnaire.

This study detected that functional constipation was more common than IBS per se, which is the more predominant form of functional bowel disorder reported from other countries. This adds to the contention that pain is not a major component of functional disorders in this population. The finding that literacy status does not influence the diagnosis may be due to a bias that this center caters to the health needs of a population with low literacy and socioeconomic status, free of cost. Larger studies with more representative population should be incorporated to clarify this issue.

In a study by Hammer et al[54] age 50 years at symptom onset and blood on the

toilet paper emerged as alarm features that discriminated organic lower gastrointestinal illness from IBS. A diagnosis of IBS was typically associated with female sex, pain on six or more occasions in the previous year, pain that radiated outside of the abdomen, and pain associated with looser bowel motions. In the present study the presence of nocturnal symptoms, blood in stools, mass descending per rectum and weight loss helped differentiation of functional LGI disorders from organic diseases. However, in contrast to other studies,[54] age of onset of symptoms was not a significant factor. Moreover, none of the symptoms evaluated, or female gender favored the diagnosis of a functional LGI disorder by inclusion. In contrast to several other studies[54] men were affected by functional LGI disorders than women, though the differences were not statistically significant. This corroborates with a previous report from this center[55] wherein it was found that 70.3% of patients with IBS were men and 29.7% were women.

The development of criteria to positively diagnose functional bowel disorders has evolved since the Manning criteria[4] were first described. Kruis et al[5] developed a different scoring system that included key gastrointestinal symptoms but also incorporated the results from a physical examination and basic laboratory tests. As both the Manning criteria and the Kruis scoring system have shown unsatisfactory sensitivity and the Kruis scoring system has proved to be too cumbersome for clinical practice, there have been a number of adaptations, with the Rome III symptom based criteria being the most recent and widely accepted. In a study by Vanner et al[10] of the Rome I criteria, found a sensitivity of only 35% in diagnosing IBS. However, when alarm symptoms were included in the diagnostic workup, sensitivity increased to 63% with a specificity of 100%. In a prospective arm of the same study, the Rome I criteria in combination with alarm symptoms had a positive predictive value of 98% in diagnosing IBS.

A previous study[56] evaluated whether extensive diagnostic testing might improve the diagnostic yield in IBS. Laboratory tests, including erythrocyte

sedimentation rate as well as stool tests for microorganisms, provided no increased diagnostic yield in the study. The authors concluded that these diagnostic tests should not be part of the routine evaluation for IBS unless there is a specific clinical indication from the history or physical examination. The present study assessed the value of laboratory tests in the diagnostic workup of functional bowel disorders. Thirty seven patients with a functional LGI disease and 18 patients with an organic LGI disease were correctly diagnosed clinically while 17 patients in the functional group and 11 patients in the organic group were misclassified as having an organic LGI disease and functional LGI disease respectively. Thus alarm features in combination with the basic laboratory evaluation has a sensitivity of 69%, specificity of 62% and positive predictive value of 77% and suggest that laboratory tests though useful do not have sufficient sensitivity or specificity to diagnose or refute the possibility of an underlying organic illness. Moreover, addition of colonoscopy to the diagnostic algorithm, a sensitivity and specificity of 100% was obtained, thereby indicating that it would be appropriate to perform a colonoscopy in all patients with a lower GI symptom to exclude an underlying organic disease and to allay patient anxiety.

Newer tests to document colonic inflammation may be useful; Tibble et al[57] showed that faecal calprotectin was of value in the differential diagnosis of functional versus organic gastrointestinal disorders in a tertiary referral center although the authors did not include alarm features in their evaluation of intestinal disease. However until the discovery of a test specific for functional bowel disorder/ functional abdominal pain syndrome, it would remain a diagnosis of exclusion.

The present study had fewer references during the study period resulting in fewer organic diseases in the sample and less cancers than would have been ideal for analysis. Only 34.9% of patients had a diagnosis of organic disease while the rest had a functional bowel disorder. However, most patients with organic disease had symptoms that were judged to be most likely explained by the

underlying condition. Moreover all known alarm features were evaluated and the chances that a few of the alarm symptoms that have not yet been identified could have been inadvertently excluded; the value of these other alarm symptoms cannot be determined here. Confirmation of the results that were obtained with the functional LGI disorder group will require another study with a larger group of such patients.

In conclusion, the Rome criteria have standardised the field of functional gastrointestinal disorders and promoted new clinical and epidemiological research. The present study, as well as those of Vanner et al[10] and Hammer et al,[54] allow to conclude that the Rome criteria and Manning criteria identify fewer patients as having functional GI disorders than are diagnosed by clinicians, suggesting a need to adjust the current diagnostic guidelines. However, it may be appropriate that the Rome criteria for functional bowel disorders and functional abdominal pain syndrome be expanded to include key alarm features, basic investigations and colonoscopy.

SUMMARY AND CONCLUSIONS

1. The incidence of organic and functional disorders in patients presenting with lower gastrointestinal complaints are 34.9% and 65.1% respectively.

2. The commonest organic disorder to be diagnosed was perianal disease (40%) and the commonest functional disorder was functional constipation (29.6%).

3. No significant differences in the mean age or age group distribution were discernible between the two groups of disorders

4. There were no significant differences in the gender ratio or educational status of patients in the two groups

5. The clinical symptoms that were helpful in distinguishing an organic illness from a functional disorder were the presence of nocturnal symptoms, blood in stools, mass descending per rectum and weight loss. None of the symptoms evaluated favored the diagnosis of a functional LGI disorder by inclusion.

6. The presence of anemia, mass abdomen and abnormalities on per rectal examination suggested an organic disease

7. The laboratory investigations that differentiated an organic from functional disease include a low hemoglobin, elevated ESR, stool occult blood positivity, low serum proteins and albumin, abnormalities on ultrasonography and colonoscopy with terminal ileoscopy

8. The clinical differentiation between functional and organic LGI disease had a sensitivity of 69%, specificity of 62%, positive predictive value of 77%, negative predictive value of 51%, efficacy of 66% with fair agreement on Kappa statistics.

9. It may be appropriate that the Rome criteria for functional bowel disorders and functional abdominal pain syndrome be expanded to include key alarm features, basic investigations and colonoscopy.

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ANNEXURE - I

THE OUTCOME OF ALARM SYMPTOMS AND COLONOSCOPY IN FUNCTIONAL BOWEL DISORDERS AND FUNCTIONAL ABDOMINAL PAIN SYNDROME

Name: Age/sex MGE No. SGE No.

Address: Education:

Clinical diagnosis: Provisional diagnosis:

Colonoscopy diagnosis:

Clinical parameter	**Status**	**Duration**
Bowel frequency		
Day/ Night		
Consistency	Hard/ Normal/ Semi formed/ Liquid	
Blood in stools		
Mucus in stools		
Incomplete evacuation		
Tenesmus		
Painful defaecation		
Mass descending PR		
Abdominal pain		
Character		
Location		
Intestinal obstruction		
Digital evacuation		
Intolerance to milk		
Anorexia		
Weight loss		
Mass abdomen		
Symptoms of anemia		
Fever		
Diabetes mellitus		
Hypertension		
Ischemic heart disease		
Tuberculosis		
Drugs (specify)		
Surgery (specify)		
Family history	Ca colon/ Polyp/ IBD/ TB	
Associated symptoms		
Dyspepsia	Ulcer/ reflux/ dysmotility	
Others (specify)		
Cardiovascular		

Respiratory		
Neurological		
Others (specify)		

Clinical examination	**Status**
Anemia	
Clubbing	
Edema	
Lymphadenopathy/ site	
Mucocutaneous manifestations (specify)	
Weight/ Height/ BMI	
Pulse	
Blood pressure	
Abdomen	
Tenderness - site	
VIP	
Scar	
Mass	
Others (specify)	
Per rectum	

Investigations	**Report**
Hemoglobin	
Total Count	
Differential count	
ESR	
Peripheral smear	
Stool	
Ova	
Cyst	
Occult blood	
Blood sugar	
TSH	
Total protein	
Albumin/ globulin	
LDH	
Others (specify)	
CXR	
AXR	

USG abdomen:

CT/ MRI abdomen:

Barium meal follow through/ Barium enema:

Colonoscopy:

Histopathology:

Interventions: Surgical/ endoscopic (specify with details)