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Functional Abdominal Pain Syndrome: An Uncommon Entity Of Chronic Abdominal Pain.

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Abstract:
Background: Chronic abdominal pain (CAP) is a common condition and is often associated with significant health care utilization and impact on the quality of life. A functional aetiology, particularly, Functional abdominal pain syndrome (FAPS) in adults has psychosocial comorbidity and is a less extensively studied condition than other common functional gastrointestinal disorders. Hence, this study attempts to evaluate the patients with FAPS and to obtain a data for FAPS in adolescents and adults in a population from North India.
Methods: 150 patients in the age-group of 10-60 years with chronic abdominal pain were selected. A careful history, clinical examination and investigations were performed to find the aetiology.
Results: 105 out of 150 patients with CAP were found to be having underlying organic causes. FAPS was diagnosed in 3 patients (2%) on the basis of Rome III diagnostic criteria. The treatment of FAPS was commenced with a biopsychosocial approach with emphasis on an effective doctor-patient relationship and specific measures.
Conclusion: CAP has an extensive aetiology, yet a detailed history coupled with a complete physical examination and investigative profile help to a great extent in diagnosing the cause. FAPS should be diagnosed on the basis of a careful clinical history and characteristic pain behaviour during physical examination and only targeted investigations should be undertaken.

Key words: Chronic abdominal pain, Functional abdominal pain syndrome.

I. INTRODUCTION

Chronic abdominal pain is prevalent and is a leading cause of health care utilization with impact not only on the quality of life but a major economic impact as well. The diagnosis and management of chronic abdominal pain is often a challenging problem owing to its wide aetiology and poor sensitivity of history and physical examination of the patients. Unexplained abdominal pain is the sixth most common cause of hospital admission in women and the tenth most common cause in men.[1]

The vast aetiology of CAP ranges from organic to functional. Organic causes can be of anatomical, neurogenic, musculo-skeletal or metabolic in origin. Functional abdominal pain (FAP) is a more challenging condition and is difficult to diagnose and manage with no clear organic cause explaining the underlying symptoms.

FAP forms a distinct category in the classification of functional gastro-intestinal disorders (FGIDs). FGIDs include six major domains for adults: oesophageal, gastroduodenal, bowel, functional abdominal pain syndrome (FAPS), biliary and anorectal. FAP includes functional abdominal pain syndrome (FAPS), defined according to the Rome III diagnostic criteria and is characterized by chronic, recurrent or continuous abdominal pain for at least six months that is poorly related to gut functions or other physiological events, with some loss of daily functioning. FAP also includes unspecified functional abdominal pain, the condition which fails to meet the criteria for FAPS.[2]

The prevalence rates of pain-related FGIDs like Irritable bowel syndrome (IBS) is 10-20 %, that of functional dyspepsia is 20-30% and that of functional gall bladder and sphincter of Oddi disorders is 7.6-20.7 %. [3-5] The reported prevalence figures for FAPS from North America ranges from 0.5 to 2% and do not differ from those reported in other countries. The disorder is more common in

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females.[6-8] The data for FAPS in Indian population is sparse as majority of studies have either evaluated abdominal pain in paediatric age-group only or other common pain-related FGIDs like Irritable bowel syndrome (IBS) and Functional dyspepsia have been studied extensively. Evaluation of FAPS, however, should be emphasized as the syndrome imposes significant economic burden, the patients have high work absenteeism and have impact on their quality of life. According to a U.S Household survey of functional GI disorders (1993) people with FAPS miss an average of twelve days of work annually due to illness compared to four missed days for people without FAPS. Also, the number of doctors visited in a year was comparatively higher.[7] Despite its relative low prevalence in the community, patients with FAPS with refractory symptoms or unresponsive to standard medical therapy are often referred to the gastroenterology clinics for further invasive investigations. Also, the condition possesses high morbidity owing to its relation with psychological disorders. Hence, in the present study we attempted to evaluate and manage the patients with functional abdominal pain, a condition which is difficult to diagnose and treat and is a debilitating chronic abdominal pain disorder with associated psychosocial disturbances.

Materials and methods

It was a cross sectional study conducted on a population from North India. One Hundred and fifty patients, visiting Surgery out-patient department and those admitted in different wards of the hospital for chronic abdominal pain were selected over a period of one year. Written informed consent from the patients was obtained. The data was collected by taking patient's history, clinical examination and investigations charted in the proforma. This study has been approved from the Institutional Ethical Committee.

All the patients with chronic abdominal pain of more than 3 months duration were included in the study. However, patients with proven diagnosis for abdominal pain and follow up cases were excluded from the study. Patients were divided into 3 groups: A (0 to 18 yrs), B (19 to 40 yrs), C (41 yrs and above). Detailed history was taken about the pain regarding its location, type, duration, timing, frequency and factors that worsen or relieve the pain.

To evaluate functional abdominal pain and other functional GI disorders, a careful and comprehensive account of clinical history was taken regarding the pain events, with emphasis on the pattern of describing the pain events, intensity of pain and its variation, location, relation of pain with physiologic events like eating, defaecation, menstruation etc, history of previous abdominal surgeries, history of adverse or traumatic life events. The impact of pain on activities and quality of life was enquired. Presence of affective disorders like anxiety and depression and somatoform disorders was sought for, owing to the fact that FAPS is known to be associated with psychological disturbances.

Past medical history included Diabetes mellitus, Hypertension, Tuberculosis, abdominal surgeries, the results of previous investigations and treatment taken. Drug history included details concerning prescription as well as alcohol and other addictions. Family history of sickle cell trait or disease, familial Mediterranean fever, and porphyria were enquired upon. Presence of other GI symptoms were enquired such as nausea, vomiting, heart burn, gas bloating, post-prandial fullness, jaundice, haematemesis, malaena, anorexia, weight loss, and mucus or blood in the stool. Bowel symptoms, such as diarrhea, constipation, changes in stool consistency, color, or frequency were enquired upon.

Abdominal examination was done to find the areas of tenderness, hernial sites, scars, sinuses or fistulas. Presences of masses or organomegaly were noted and per rectal examinations were done wherever indicated. For the evaluation of FAPS, during examination, pain behaviour of the patients was carefully observed by different manoeuvres like distracting the patients and noting the pain behaviour, by firm application of the stethoscope at previously reported painful area of the abdomen, closed eye sign in which the patient was observed for the closure of the eyes during examination, which is thought to be an opposite feature in cases with acute abdomen.[9] Presence of abdominal scars were sought for. Autonomic arousal associated with pain was observed. Carnett's test was performed to rule out intra-abdominal cause, in which the patient was instructed to perform a sit-up against the resistance of the examiner's hand on the subject's forehead and painful area was palpated before and after the tensing of the abdomen.[10]

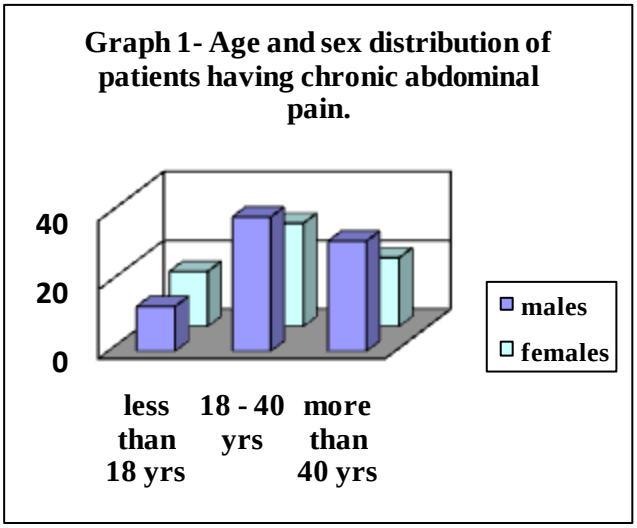
Patients underwent screening laboratory studies including urine analysis, complete blood Count, ESR (erythrocyte sedimentation rate), peripheral smear and blood sugar. Other investigations like Liver function tests, kidney function tests, serum amylase, serum lipase etc were done depending on the patient's history and findings. Stool examination was done in cases with GIT symptoms. Ultrasonography of the abdomen and pelvis was done in all the patients by experienced radiologists Other Special investigations like Contrast enhanced CT scan of the

abdomen and pelvis, upper GI endoscopy or colonoscopy and Barium studies were also done where indicated. Endoscopic retrograde cholangiopancreatography (ERCP), Magnetic resonance cholangiopancreatography (MRCP) and diagnostic laparoscopy were required in few cases.

The data from the 150 patients under study was recorded in Microsoft excel 2007 and findings were tabulated accordingly using statistical software SPSS version 19.

Observation & results

In the present study, 56% patients were males and 44% were females (graph 1).



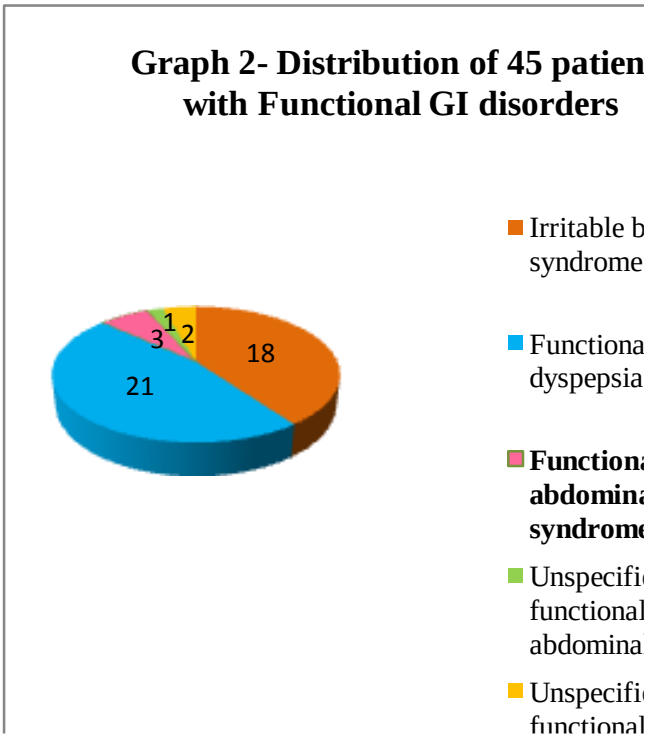
Most of the patients were in the age group of 18-40 yrs.

It was found that maximum patients (78) had pain for the duration of 3-6 months. Much higher percentage of adults had some type of chronic GI symptoms besides pain, including non ulcer dyspepsia and various other bowel disturbances. Maximum no. of patients (42) had pain in the upper abdomen i.e. epigastrium and hypochondrium and dull aching pain was the commonest type of pain (69 patients) because it is found in more than one disease. Twenty one patients had history of various abdominal surgeries including appendicectomy, hysterectomy/tubectomy, surgery for stones etc.

All patients underwent USG of abdomen and pelvis with 113 positive findings out of 150. CT scan was performed in 36 patients, which provided 34 positive findings. 2 cases had no findings and were the cases in which CT scan was done on request (suggestive of functional gastro-intestinal disorders). Upper GI endoscopy was done in 33 patients with 29 positive findings. Barium studies provided positive findings in 3 out of 12 patients. On the basis of final diagnosis, patients were found to have GIT disease as the cause of the pain in maximum i.e. 95 cases. 45 cases out of those 95 GIT diseases were found to be having functional gastrointestinal diseases (table 1, graph 2).

Table 1- Classification of patients with Gastro-intestinal disease after final diagnosis.

Gastro-intestinal disease	**No. of cases**
Oesophagitis	2
Oesophagitis with fundic ulcer	1
Carcinoma oesophagus	1
Gastritis	8
Alcoholic gastritis	3
Antral gastritis	1
Gastroenteritis	2
Gastric ulcer	4
Carcinoma stomach	3
Amoebiasis / worm infestation	5
Para- aortic lymphadenopathy	1
Colitis	1
Sub acute intestinal obstruction (TB abdomen)	1
Gastrointestinal stromal tumor	1
Carcinoma caecum	1
Carcinoma colon	1
Carcinoma rectum	1
Catarrhal appendicitis	2
Chronic recurrent appendicitis	7
Pancreatitis	4
Functional abdominal pain syndrome	***3***
Irritable bowel syndrome	***18***
Functional dyspepsia	***21***
Unspecified functional abdominal pain	***1***
Unspecified functional bowel disorder	***2***
Total	**95**

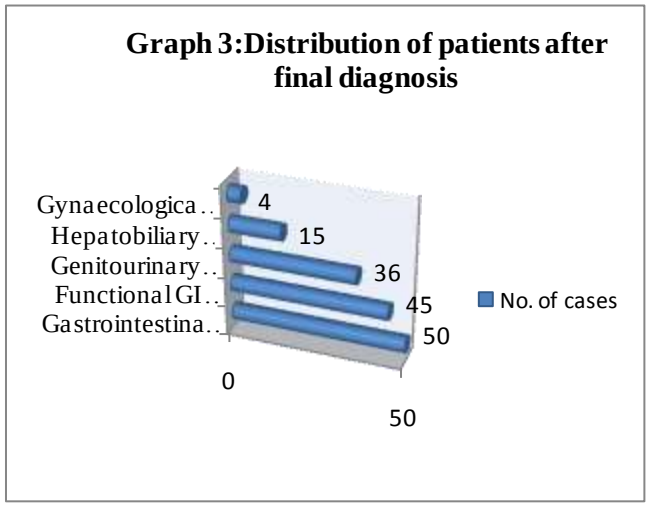


The diagnosis was based on Rome III diagnostic criteria, according to which 18 patients were found to be having irritable bowel syndrome, while 2 patients had unspecified functional bowel disorders. 21 patients were having functional dyspepsia and 4 patients were diagnosed as functional abdominal pain (category D) and out of those 4 patients, 3 fulfilled the criteria for FAPS (category D1) while one patient was diagnosed as Unspecified functional abdominal pain (category D2) as the clinical findings fail to meet the FAPS criteria (criteria was fulfilled for the last 3 months but symptom onset was less than 6 months prior to diagnosis) (table 2).

Table 2- Rome III diagnostic criteria for Functional abdominal pain

Must include all of the following: ***(Criteria fulfilled for the last three months with symptom onset at least six months prior to diagnosis)***
1. Continuous or nearly continuous abdominal pain
2. Poor 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 gastro-intestinal disorders that would explain the pain**.**

[2,11] GUT (genitor-urinary tract) disease was found in 36, hepato-biliary in 15 and gynecological disorder in 4 cases (graph 3).



Patients with FAPS were identified as having characteristic clinical history and some distinct features during physical examination (table 3).

Table 3- Characteristic features of clinical history and physical examination observed in four patients diagnosed as FAP.

	S.N	Characteristic features		No. of cases
Clinical history	1.	Description of pain events in emotional pattern		4
	2.	Pain with extreme intensity and not varying much with time		4
	3.	Location of pain	All over the abdomen	3
			Peri-umbilical	1
	4.	Duration of	>6 months	3

		pain	<6 months	1
	5.	Relation to physiologic events		Nil
	6.	Frequency of pain	Continuous	1
			Recurrent	2
	7.	History of abdominal surgeries		2
	8.	History of adverse or traumatic events		2
	9.	Response to previous treatments		Nil
Physical examination				
	1.	Presence of abdominal scars		2
	2.	Presence of autonomic arousal		Nil
	3.	Pain behaviour	i)Diminution of pain during distraction	4
			ii) Closed eye sign	3
			iii) Carnett's test-negative	4
Miscellaneous features	1.	Request for invasive investigations to discover organic cause		4
	2.	Request for increasing analgesia		3
	3.	Reluctant to consider the role of psychosocial factors in the genesis of the symptoms		4

The pain behaviour in these patients was noteworthy. Two patients had history of adverse life events few years back. In all the four cases the pain reported was severe in intensity and involving a large abdominal area, but noted to be diminished when the patient was distracted. The description of pain in emotional and bizarre pattern though noted in other organic causes of CAP too, was another feature. Closed eye sign was characteristically found in all four cases. Two patients had history of surgery few years back. All of them were seeking medical advice since a longer period, refractory to medical therapy and with no organic cause detected, despite all necessary investigations performed. Out of 3 patients diagnosed with FAPS, one was adolescent female (H2d1 category), and other two were in the age-group of 18-40 years (one male and one female).

Discussion

Patients with FAPS form a comparatively small fraction of functional GI disorders but present a difficult diagnostic and management issues to the clinicians. Patients have many referrals with numerous investigations performed and are refractory to the treatment in most of the cases. The condition, no doubt, imposes significant health care burden as well as worsens the quality of life. In tropical countries, where most of the population is of low socioeconomic status, a targeted investigational strategy to include standard hematological, biochemical, and immunological parameters is appropriate. In patients with alarm features, or red flag signs, an alternative diagnosis should be considered and investigated accordingly.

Present study revealed forty-five out of one hundred and fifty patients under study, to be having functional gastro-intestinal diseases. A diagnosis with functional aetiology often poses problems as clinicians are often trained to seek pathology and unneeded diagnostic studies might be pursued to find the organic cause. In this study, emphasis was given on a comprehensive clinical history and careful clinical examination to diagnose the condition. In the absence of alarm symptoms extensive diagnostic evaluation was not conducted. It was the clinical presentation with a well-structured medical history and physical examination that indicated the presence of functional gastrointestinal disorders in the individuals presenting with chronic abdominal pain. .

Rome III diagnostic criteria were applied for the diagnosis of functional GI disorders including FAPS. FAPS (category D1 and H2d1) was found to be present in 3 patients out of 150 (2%) while one patient did not fulfil the FAPS criteria and labelled as Unspecified functional abdominal pain (category D2) (criteria was fulfilled for the last 3 months but symptom onset was less than 6 months prior to diagnosis). The reported prevalence in various studies, for FAPS is 0.5-2% and is more common in females with 3:2 ratio.[6-8] In the present study, 2% of FAPS cases

were found, with a female preponderance. The study provides an FAPS data for adults and adolescents in a North Indian population. As follow-up study, the available data can be utilized further to evaluate the prognosis of this condition.

FAPS (category D) is primarily understood as amplified central perception of normal visceral input. The disorder has been placed in its own category and not included in functional bowel disorders (category C) unlike Rome II criteria, owing to the fact that it relates more to CNS amplification of normal regulatory visceral signals rather than functional abnormalities within the GI tract.

The treatment strategy for the patients with FAPS in the present study emphasized on establishing an effective doctor-patient relationship, involving validation of a patient's symptoms, reassurance and patient education regarding the pathophysiology of the condition; and setting realistic treatment goals. Patients were followed up after 2 months and pharmacological intervention in the form of low dose tricyclic antidepressants (Amitriptyline 10 mg once daily) was planned in the non-responders

A fundamental understanding of the pathophysiology of FAPS is essential for successful pharmacological intervention and management. A growing body of evidence suggests a disordered brain-gut communication as the cause of the chronic pain in FAPS. The importance of bidirectional brain-gut axis has been increasingly recognized in functional gastro-intestinal illness. The brain receives a constant stream of interoceptive input from the GI tract. In health, majority of these inputs reaching the brain are not consciously perceived but serve as the inputs to autonomic reflex pathways. In patients with FAPS, conscious perception of these interoceptive informations can occur in the form of constant or recurrent discomfort or pain owing to the activity in the stress and arousal circuits and by cognitive and emotional inputs to these circuits A model is proposed in patients with IBS and similar alterations in brain-gut interactions are extrapolated to patients with FAPS. [12]

Pain is thought to have two dimensions: a sensory-discriminative component and an affective-motivational component.[13] The discriminative component of gastro-intestinal pain encodes location, intensity and nature of pain and projects to primary (SI) and secondary somatosensory cortex (SII). [14] The affective-motivational component is thought to encode pain affect and suffering and projects to the limbic system, particularly the part called the anterior cingulated cortex (ACC). The ACC is a critical centre associated with the "unpleasantness" of the pain. Several studies demonstrated an increased activation of the anterior cingulated cortex in IBS patients compared to healthy controls. A successful pharmacological intervention in IBS patients with either alosetron, a 5-HT3 antagonist or amitriptyline, a tricyclic antidepressant have been found to be associated with reduced activation of the anterior cingulated cortex. [15, 16] Apart from these ascending pathways a variety of descending inhibitory pathways play a part in the perception of normal visceral sensation. These are the pathways arising from the opioid-rich ACC, where inhibitory signals are transmitted to the periaqueductal gray either directly or via second-order neurons from the amygdala. Third-order opioidergic, serotonergic, and second-order noradrenergic neurons project to the dorsal horn neurons in the spinal cord where they 'gate' or modulate ascending visceral afferent signals. It is hypothesized that emotional processes like anxiety and cortical factors like previous experience of pain, coping mechanisms and psychosocial stressors could interact with limbic circuits to amplify the pain experience.[17]

Abnormal visceral pain perception

The neurophysiological dysfunctions leading to chronic pain in this condition may be due to peripheral augmentation of the visceral pain afferent impulses, central sensitization around the dorsal horn of the spinal cord, alterations in descending modulation, or central amplification.

Peripheral augmentation of visceral afferent impulses may occur after repeated injury or inflammation. A recent important case control study demonstrated that 15.3% of patients undergoing gynaecological surgery, for non-pain-related conditions, developed abdominal pain at twelve months compared with 3.6% of healthy controls who did not undergo surgery.[18] Another study demonstrated significantly reduced rectal perceptual thresholds in IBS, but interestingly, not in FAP, suggesting that pain reporting in FAP is less likely to be attributable to visceral hypersensitivity. [19]

Central sensitization due to increased responsiveness of the dorsal horn neurons has been suggested as a pathophysiology for FAPS.[20] Repetitive experimental stimulation or gut injury also have been reported in various studies to induce hyperalgesia owing to both peripheral augmentation as well as central sensitization in the GI tract after gut injury.[21]

Disturbances in central descending modulation of pain have been proposed to account for the

pronociceptive state encountered in FAP. The central descending modulatory systems in the ACC that control visceral pain connect with the spinal dorsal horn, facilitating gating of afferent signals from the periphery and thereby allowing amplification or diminution of this signal. There is increasing evidence in FGIDs that cognitive, emotional, autonomic, and spinal reflex pathways coordinate supraspinal and spinal pain modulation.[22]

Stressful events are known to be the contributory factors in FAPS. One of proposed mechanisms in which stress could modulate symptoms in functional pain syndromes is through the Corticotrophin releasing factor (CRF), one of the important hormones involved in the stress response. CRF can induce an increase in colonic motility and in IBS this motility effect is markedly increased compared to normal individuals. [23] The exact neural and hormonal pathways causing increased gut sensitivity and contractility during stress are not defined. Psychological stress can lead to permanent alterations in the hypothalamo-pituitary-adrenal (HPA) -axis, the descending pain modulatory system, the immune system and the gut microbiota. Mechanisms by which physical stress such as infections mediate visceral hypersensitivity are likely to be different and may involve altered immune system functioning.[24]

Conclusion

Clinical evaluation of FAPS should include a comprehensive clinical history and physical examination and a targeted investigational strategy should be adopted. A correct identification of this subgroup should be the priority for the clinicians which will guide a successful outcome in the management of this uncommon condition with a comparatively higher socio-economic impact. Treatment strategy should include an effective doctor-patient relationship with a variable combination of pharmacological interventions, cognitive behavioural therapy and psychotherapy. The present study can further be extended to evaluate the prognosis of this condition. More researches are necessitated regarding the studies on pathophysiology of FAPS, as most of the basic mechanisms suggested to account for symptom genesis in FAPS are extrapolated from research in other chronic pain syndromes.

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