

Literature Review

Functional Abdominal Pain in Children

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Abstract:

Background: Functional abdominal pain (FAP), often affecting girls and those with mental health issues, is a prevalent pediatric disorder characterized by persistent symptoms without a clear identifiable organic pathology. The Rome IV Criteria classify it into subtypes, which have distinct symptoms and required tailored management approaches.

Discussion: Subtypes classified by the Rome IV Criteria include irritable bowel syndrome (IBS), functional dyspepsia, abdominal migraine, and FAP - not otherwise specified (NOS). The pathophysiology involves gut hypersensitivity, hyperalgesia, genetic predispositions, and psychosocial triggers. Diagnosis relies on medical history, physical examination, the presence of alarm signs, and the characteristic of pain. Treatment strategies encompass dietary modifications, psychological interventions, pharmacology treatment including proton pump inhibitors, prokinetics, and antidepressants like amitriptyline.

Conclusion: Recognizing the specific subtypes, as defined by the Rome IV Criteria, allows healthcare professionals to implement individualized care strategies for optimal outcomes.

Keywords: functional abdominal pain, pediatric disorder, rome IV criteria

Introduction

Functional abdominal pain is a disorder frequently found in children, typically diagnosed following a comprehensive medical evaluation, with manifestations that cannot be attributed to other medical conditions and the absence of clinical evidence indicating an organic disease.¹ The prevalence among children globally is 13,5% with a higher occurrence observed among girls and children with accompanying mental health conditions.²

The subtypes of functional abdominal pain were classified based on the Rome IV Criteria, consisting of Irritable Bowel Syndrome (IBS), Functional Dyspepsia, abdominal migraine, and functional abdominal pain - not otherwise specified (functional abdominal pain – NOS).^{1,3} Functional abdominal pain disorder in children and adolescents have varying classifications with different diagnosis, approaches, and treatments. Therefore, a clinician must be able to understand and determine the proper evaluation and monitoring needed to care for patients with such functional abdominal pain.¹

Pathophysiology

Functional abdominal pain occurs due to changes in gut hypersensitivity and hyperalgesia, resulting from previous medical disturbance such as abdominal distention, gut motility disorders, inflammation (due to infection or allergy), and genetic predisposition that occurs in early life or is triggered by psychosocial factors including depression, anxiety, family-related stress, adapted lifestyle, secondary changes due to puberty, history of abuse, or stress. These factors lead to the abdominal pain and digestion disorder (**Figure 1**).¹

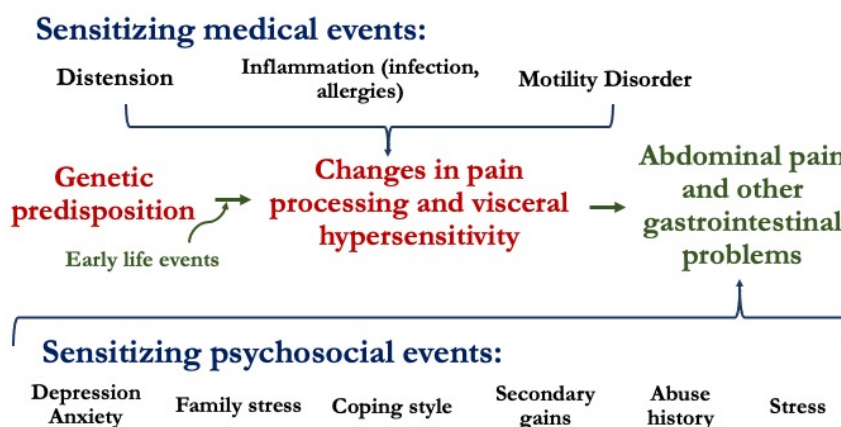


Figure 1. Pathophysiology of Functional Abdominal Pain¹

Classifications of Functional Abdominal Pain

Below is the classification of Childhood Functional GI Disorders (FGID) in children or adolescent as described in **Table 1**, Abdominal Pain Classification Based on FADP Criteria and its approach depicted in **Figure 2**, and **Table 2** shows potential alarm signs in children with Chronic Abdominal Pain.¹

Table 1. The classification of childhood Functional GI Disorders (FGID) in Child/Adolescent⁴

H1. Functional nausea and vomiting disorders
H1a. Cyclic vomiting syndrome (CVS)
H1b. Functional nausea and functional vomiting
H1b1. Functional nausea
H1b2. Functional vomiting
H1c. Rumination syndrome
H1d. Aerophagia
H2. Functional abdominal pain disorders (FADP)
H2a. Functional Dyspepsia
H2a1. Postprandial distress syndrome
H2a2. Epigastric pain syndrome
H2b. Irritable Bowel Syndrome (IBS)
H2c. Abdominal migraine
H2d. Functional abdominal pain – NOS
H3. Functional defecation disorders
H3a. Functional constipation
H3b. Non-retentive fecal incontinence

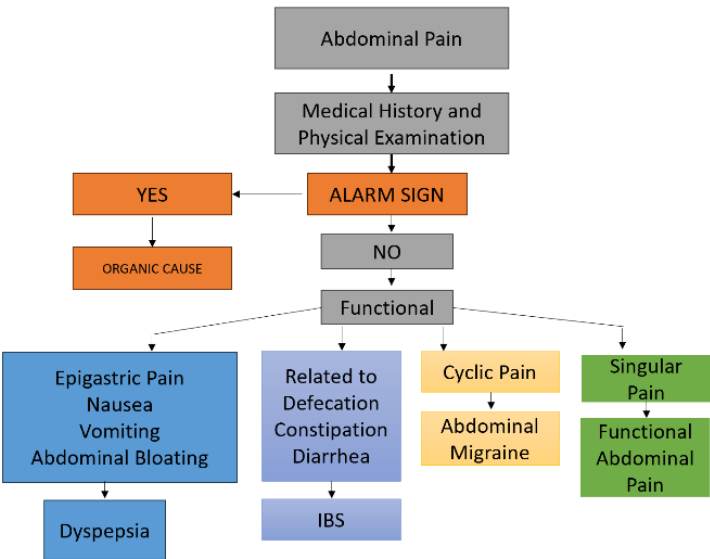


Figure 2. Abdominal Pain classification based on FADP criteria⁵

Table 2. Potential alarm signs in children with Chronic Abdominal Pain¹

Family history of bowel inflammation, IBD, Celiac disease, or peptic ulcer disease
Persistent upper-right quadrant or lower-right quadrant pain
Dysphagia
Odynophagia
Persistent vomiting
Gastrointestinal blood loss
Nocturnal diarrhea
Joint inflammation
Perirectal diseases
Unexplained weight loss
Slow linear growth
Delayed puberty
Fever of unknown origin
Uveitis, oral lesions, skin rash, anemia, hepatosplenomegaly, icterus
Family history of bowel inflammation, IBD, Celiac disease, or peptic ulcer disease
Persistent upper-right quadrant or lower-right quadrant pain
Dysphagia

Pediatric Functional Abdominal Pain (Rome IV)

Irritable Bowel Syndrome

Irritable Bowel Syndrome is a medical condition characterized by chronic, recurrent abdominal pain and discomfort, along with changes in defecation habit that are not influenced by other organic gastrointestinal diseases. While IBS often manifests in childhood, its prevalence peaks during early adulthood. Women are 2 times more likely diagnosed with IBS than men. The prevalence of IBS ranges from 10 – 20%, with an occurrence rate of 1 – 2 % per year. Studies conducted on school children in Colombia shows a prevalence of 4,9%, while in Sri Lanka the prevalence rate was 5.4%, and in the United States, it ranges from 1.2 – 2.9%.⁶

IBS does not have a specific etiology, but several probable causes include visceral hypersensitivity, stressful periods especially if occurring in early life, genetic factors, food intolerance, mental health conditions, such as depression and anxiety, microbiological factors such as SIBO (small intestinal bacterial overgrowth), inflammation, post-infection, gut motility disorder, or heavy metal poisoning.⁷

The pathophysiology of IBS is often considered to involve a disorder between the gut-brain axis, characterized by symptoms such as diarrhea versus constipation, severe pain, and psychosocial distress. While several children with IBS exhibit rectal hyperalgesia but not gastric disorders, the reverse can also occur with some children with functional abdominal pain with no organic causes (FAPNOS).^{8,9}

Visceral hypersensitivity occurs during psychological stress, including anxiety, depression, impulsivity, anger, and emotional management problems.¹⁰ Pro-inflammatory cytokines in the mucosa can be induced by acute/post-infectious IBS, as well as changes in the gut microbiome.^{11, 12}

The history of noxious events in early life such as past surgeries is also linked with the risk of childhood functional abdominal pain, including IBS.¹³

IBS can be suspected in patients experiencing recurrent abdominal pain occurring on average at least one day per week, with symptom onset typically occurring 2 months before diagnosis.¹

The diagnosis of IBS is based on the Rome IV criteria, which include:¹

1. Abdominal pain occurring at least four days per month, accompanied by one or more of the following symptoms:
 - a. Related to defecation;
 - b. Changes in defecation frequency;
 - c. Changes in stool shape;
2. Pain does not subside after treatment of constipation;
3. Not related to other medical conditions.

The Bristol Stool chart is depicted in **Figure 3**. There are 4 categories in IBS:¹

1. IBS-C, characterized by predominantly constipation, is defined as having more than 25% of stools with Bristol type 1 or 2 stool shape and less than 25% with Bristol type 6 or 7 stools;
2. IBS-D, characterized by predominantly diarrhea, is defined as having more than 25% of stools with Bristol type 6 or 7 shape and less than 25% Bristol type 1 or 2 stools;
3. IBS-M, which involves alternating diarrhea or constipation, is defined as having more than 25% defecation with Bristol type 1 or 2 stools and more than 25% with Bristol type 6 or 7 stools;
4. IBS-U, classified as unclassified IBS, occurs when a patient's defecation habits cannot be categorized into one of the three previous criteria.

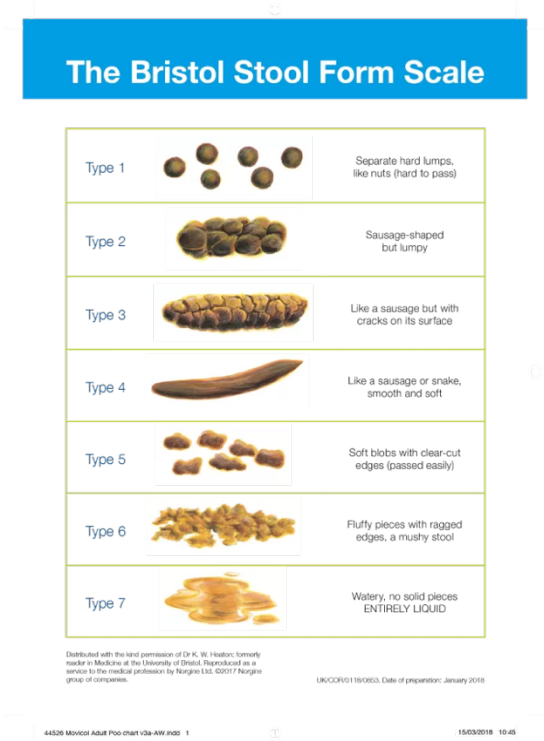


Figure 3. The Bristol Stool Chart¹⁴

Common symptoms of IBS in children and adolescents consist of abdominal pain and changes in defecation habits. Other symptoms may include bloating with or without abdominal distention, excessive gaseous abdominal bloating, and nausea (Figure 4).¹⁵

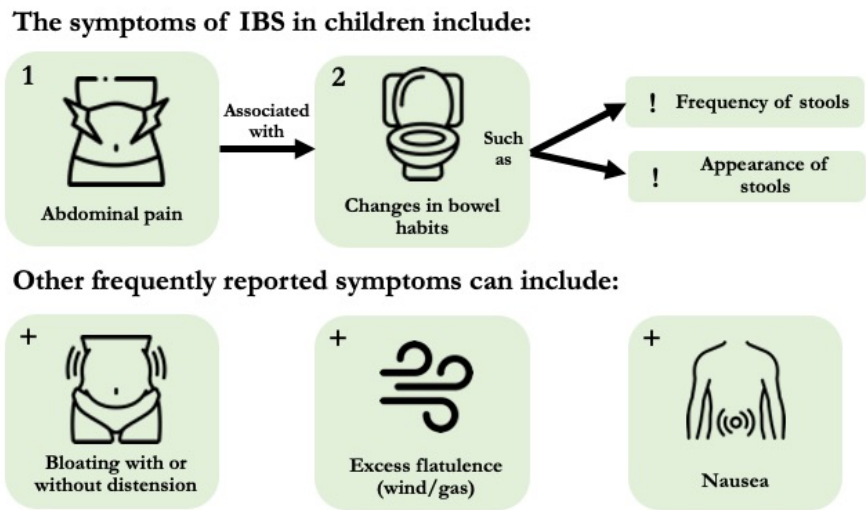


Figure 4. Pediatric IBS Symptoms¹⁵

Clinical evaluations of IBS consist of thorough history-taking and physical examination. Tests are performed to determine the presence of functional constipation, diarrhea, infection, Celiac disease, carbohydrate malabsorption, and inflammatory bowel disease (IBD). The more alarm symptoms discovered, the more likely it is to be an organic disease. Non-invasive testing such as stool calprotectin is preferable over C-reactive proteins to determine the presence of mucosal inflammation or IBD.¹⁶ Several studies have demonstrated that probiotics can reduce bloating symptoms in IBS and improve the patient’s quality of life.¹⁷

Treatments of IBS prioritizes functional treatments over specific therapeutic options. This includes encouraging FAPD diet and several studies also suggests the administration of other remedies such as probiotics and peppermint oil.¹ Additionally, there are additional options, such as amitriptyline, fibers, and hypnotherapy.¹⁸⁻²⁰

1. FODMAP

In all IBS subtypes, dietary elimination by reducing intake of fermentable oligosaccharide, disaccharide, monosaccharide, and polyol (FODMAP) is highly beneficial. FODMAP is a category of foods containing short-chain carbohydrates that are difficult to digest for many people (**Table 3**). All FODMAP substances in food can trigger IBS symptoms by drawing excess water to the small intestines and subsequently to the large intestines, where they are fermented by bacteria, potentially mimicking the symptoms of IBD.^{21, 22}

Table 3. FODMAP Diet Treatment for IBS²³

Initial Therapy	Avoiding foods that can produce intestinal gas, lactose avoidance, and following a FODMAP diet are recommended. Once symptoms are controlled, patients can gradually introduce new foods (1-2 new foods per week). If symptoms reappear with newly added foods, the patient will need to avoid those foods long-term.
Avoiding sources of bowel gas	The patient needs to avoid beans, pork, cabbages, broccoli, Brussel sprouts, wheat, high-carbohydrate foods, fructose, and dietary gluten. Patients who avoid gaseous foods demonstrate alleviation of symptoms.
Lactose avoidance	The patient is subjected to a lactose breath test. If lactose intolerant, the patient will then limit their lactose intake. If lactose tolerant, the patient can reduce their lactose intake when all other therapeutic approaches fail. FODMAP refers to food that increases the amount of gas in the intestines which can cause abdominal discomfort. Patients who follow low FODMAP diet demonstrates score improvements for abdominal pain, bloating, and stool consistency.

The FODMAP limitation approach is effective in adults, but more data is needed to assess its efficacy in children. Furthermore, this diet does not support the limitation of lactose.²²

Table 4. The types of FODMAP²³

	Consume foods with low FODMAP	Avoid foods with high FODMAP
Fruits	Bananas, berries, melons (except watermelons), cranberry, grapes, oranges.	Apples, mangoes, pears, dried fruits, canned fruits, watermelon, peaches, prunes, plums
Vegetable	Bok Choy, beansprouts, red bell pepper, lettuce, spinach, carrots, green onions, cucumber, eggplants, mung beans, tomatoes, potatoes, chestnuts.	Artichoke, asparagus, sweet peas, cabbages, onions, shallots, scallions, garlic, cauliflower, mushroom, pumpkin, green bell pepper
Milk Products	Milk: almond, coconut, nutmeg, flaxseed milk, rice, lactose free milk, kefir, ice cream, butter, cream cheese, cheeses (cheddar, Swiss, brie, blue cheese)	Milk: cow, sheep, lamb, soy, evaporated milk, sweetened and thickened yogurt, cottage cheese, ricotta, mascarpone, ice cream, frozen yogurt, sherbet
Grains	Red Rice, oats, quinoa, corn, gluten free bread, cereals, pastas, and flours.	Wheat, barley
Legumes	Tofu, nuts	Peas, hummus, red bean, baked beans, edamame, soy milk, lentils
Seeds	1-2 tablespoons of almond, macadamia, pecans, pine nuts, walnuts, pumpkin seeds, sesame seeds, sunflower seeds	Pistachios
Sweeteners	Sugar, glucose, pure maple syrup, aspartame	Honey, agave, high fructose corn syrup, sorbitol, mannitol, xylitol, maltitol, Splenda.
Proteins	Fish, chicken, turkey, eggs, meat	
Oils	Olive and Canola oil, olive, avocado	

2. Peppermint Oil

Peppermint Oil (PO) is a natural carminative mixture, containing L-menthol compound, which blocks calcium channels in smooth muscles, thereby producing antispasmodic effects on antimicrobial channels, anti-inflammatory properties, antioxidant effects, immunomodulation, and anesthesia.²⁴

In various meta-analyses, PO has been proven to be a safe and effective therapy for pain and common symptoms in adults with IBS. Other studies have demonstrated that PO acts as an antispasmodic fiber, and its administration is superior to placebo.²⁴ Studies on children measuring the motility effect of PO demonstrate an average decrease in intestinal contraction, alleviating IBS pain, but it does not significantly affect the effect of gastrointestinal transit time. Peppermint oil is usually well tolerated at commonly suggested doses.²⁴

However, Peppermint Oil is contraindicated on patients with hiatal hernia or Gastroesophageal Reflux Disease (GERD) due to its deleterious effect on reflux symptoms and its effect on lower esophageal sphincter function.²⁵

3. Amitriptyline

Tricyclic antidepressants, known for their good safety profile, operate by blocking the reuptake of norepinephrine (NE) and serotonin (5-HT), while also acting as antagonists of H₁, M, and α_1 receptors. They play a crucial role in altering gastrointestinal sensors, motor functions, and brain-gut plasma peptide concentration. At doses ranging from 0.5 – 1 mg/Kg body weight, Amitriptyline (AMT) demonstrates clinically and statistically significant efficacy in controlling symptoms of irritable bowel syndrome. Additionally, low-dose AMT has been shown to reduce gastric sensitivity, making it a recommended option for managing functional gastrointestinal disorders.¹⁸

4. Fibers

A systematic review has revealed no evidence supporting the use of fiber supplementation in the treatment of functional gastrointestinal disorders (FGID) in children.¹⁹

5. Hypnotherapy

Hypnotherapy can be recommended to alleviate functional abdominal pain disorder or IBS. Typically, it involves six sessions over a three-month period. During these sessions, children and parents are advised not to discuss pain, and to engage in breathing exercises, along with progressive relaxation techniques.²⁰

Positive suggestions provided during hypnotherapy sessions aid in reducing discomfort, anxiety, and stress. Consequently, hypnotherapy proves beneficial in treating chronic functional abdominal pain or IBS.²⁰

Functional Dyspepsia

Functional Dyspepsia is a functional gastrointestinal disorder that occurs in children and is a chronic condition. Symptoms often manifest in upper abdominal pain as in

epigastric pain or discomfort, with no organic, systemic, or metabolic disorders that can explain the symptoms. The prevalence of Functional Dyspepsia in developing countries are 1.8 – 3.5%, while in developed countries, it ranges from 5 – 10%.²⁶

The Rome IV criteria are utilized to determine the diagnosis of Functional Dyspepsia when there are complaints about the following symptoms occurring approximately four times a month within the span of 2 months before diagnosis:^{1, 26}

1. Feeling of fullness after eating;
2. Initial sensation;
3. Epigastric pain that is not related to defecation disorders;
4. Not related to other medical conditions.

Functional Dyspepsia is divided into two subtypes:

1. Postprandial Distress Syndrome. This involves early or debilitating postprandial fullness, leading children to eat less than they used to. It also includes symptoms, such as upper abdominal bloating, postprandial nausea, or excessive burping episodes.¹
2. Epigastric Pain Syndrome. This subtype includes debilitating localized epigastric pain or a burning sensation. The pain is not generalized or localized to other abdominal regions, and it does not subside with flatulence and/or defecation. Criteria for Epigastric Pain Syndrome include:
 - a. Burning pain quality with no involvement of retrosternal components.
 - b. Pain is usually induced or relieved by swallowing food, but can occur during fasting.¹

The pathogenesis of Functional Dyspepsia includes the presence of gastroduodenal motility disorder, visceral hypersensitivity, psychosocial factors, gastric acid, *Helicobacter pylori* infection, post-infection, genetic factors, as well as food and lifestyle factors.²⁷

The treatment of Functional Dyspepsia involves an integrated approach that considers physiological, biological, psychological, and social factors. Clinicians need to exclude organic factors and perform tests to determine the presence of *Helicobacter pylori* infection, subsequently eradicating the infection if detected.¹ **Figure 5** presents an algorithm for uninvestigated dyspepsia, systematic approach to diagnosis and treatment of Functional Dyspepsia.²⁷

Patients are advised to avoid dietary triggers that can exacerbate dyspeptic symptoms, such as foods and drinks rich in caffeine, spices, and fat, as well as the use of Non-Steroidal Anti-Inflammatory Agents (NSAIDs). Psychological factors contributing to symptom exacerbation should also be addressed. For patients experiencing

accompanying pain symptoms, acid blockade with histamine receptor antagonist and proton-pump inhibitors can be prescribed.²⁸

The use of proton pump inhibitors (PPI) is effective to alleviate symptoms of Functional Dyspepsia. Additionally, the administration of prokinetics has also demonstrated effectiveness in symptom relief. Successful treatment of Functional Dyspepsia is defined as symptom reduction after 4 weeks of medical treatment. Administration of 0.4 – 1 mg/KgBW Omeprazole with a frequency of 1 – 2 oral dose is superior to the administration of oral Ranitidine given at 2 – 5 mg/KgBW given 2 – 3 times orally, Famotidine 0.5 – 1 mg/KgBW 1 – 2 times orally, and Cimetidine 5 – 10 mg/KgBW 2 times orally.²⁹

In children with more difficult-to-treat symptoms, such as nausea, bloating, and early fullness, PPIs and prokinetic agents such as Cisapride 0.2 mg/KgBW (up to a maximum dose of 10 mg) given 3 – 4 dose orally, along with oral Domperidone 0.2 – 0.5 mg/KgBW given 3 times, can be considered. A retrospective, open-label study has shown that Cyproheptadine with a dose of 0.1 mg/KgBW given 3 times orally is safe and effective in treating dyspeptic symptoms in children.³⁰

Other research has investigated the administration of the extract of the Ikkunshito herbs (TJ-43). In addition, low-dose tricyclic antidepressants, such as Amitriptyline and Imipramine can be considered in severe cases, despite the lack of available data.¹

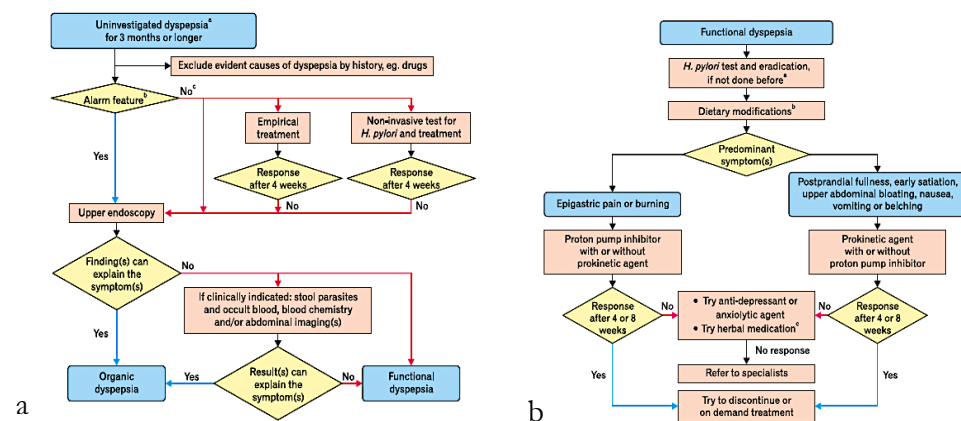


Figure 5. Algorithm. a. Algorithm for uninvestigated dyspepsia; b. Functional Dyspepsia diagnostic and its treatment algorithm.²⁷

Abdominal Migraine

Abdominal migraine is classified as a functional abdominal pain disorder, with a prevalence rate ranging from 0.2 – 4.1% among children. Its symptoms typically include recurrent paroxysmal abdominal pain that may manifest in the midline, periumbilical region, or other areas, often occurring in acute episodes. These episodes

are accompanied by symptoms, such as pallor, nausea, vomiting, anorexia, headache, and photophobia. Between episodes, patients may return to a symptom-free state. Diagnosis of abdominal migraine is based on the Rome IV criteria and International Classification of Headache Disorders III.³¹

The highest incidence of abdominal migraine is observed between the ages of 5 and 10 years old. The presence of parents with migraines increases the likelihood of developing abdominal migraine, with a probability ranging from 65 – 75%. Abdominal migraine can persist until the end of adolescence, with 38 – 70% of patients experiencing migraine headaches.³¹

Various triggers can precipitate acute episodes of abdominal migraine, including:³¹

- Stress related to school and/or familial life
- Insufficient sleep or irregular sleep patterns
- Prolonged fasting
- Dehydration
- Travel
- Exercise
- Consumption of foods rich in amine (such as citrus fruits, chocolate, cheese, vegetables such as eggplants and mushrooms, and meat: salami and ham)
- Foods containing taste and colour additives, and Monosodium Glutamate (MSG)
- Exposure to flashing lights.

The diagnostic criteria for abdominal migraine must encompass all of the following features at least twice:¹

1. Acute paroxysmal periumbilical episode: Intense, midline or diffuse abdominal pain, lasting for 1 hour or more (must be the most severe or debilitating symptom).
2. Episodes are separated by intervals from weeks to months.
3. Pain significantly interferes with daily activities.
4. Presence of stereotypical patterns and symptoms in the individual.
5. Pain is accompanied by two or more of the following symptoms:
 - a. Anorexia
 - b. Nausea
 - c. Vomiting
 - d. Headache
 - e. Photophobia
 - f. Pallor
6. Following a thorough evaluation, symptoms cannot be explained or attributed to other medical conditions.

These diagnostic criteria must be present at least six months before a diagnosis can be made.¹

The treatment of abdominal migraine is shown in **Table 5**.¹

Table 5. Abdominal Migraine Treatments¹

Non-pharmacologic Treatment: STRESS Mnemonic

- S: (stress) stress management ± Cognitive Behavioral Therapy
- T: (Travel) traveling tips
- R: (Rest) rest and adequate sleep hygiene
- E: (Emergency) monitoring for emergency symptoms
- S: (Sparkling) avoid bright and flashing lights; rest in dark and quiet places
- S: (Snacking) snack often – avoid long fasting periods and foods high in amines

Preventive Medications

- Propranolol: 10-20 mg BID or TID
- Cyproheptadine: 0.25-0.50 mg/kgBW daily, syrup: 0,1 mg/kg/times 2 – 3 times
- Flunarizine: 5,0-7,5 mg per day
- Pizotifen: 0,25 mg BID; syrup

Abortive Medications

- Analgesics: Ibuprofen 10 mg/kg, acetaminophen 15 mg/kg
 - Sumatriptan: 10 mg intranasal
-

Functional Abdominal Pain with No Specific Cause

Functional Abdominal Pain - Not Otherwise Specified Epidemiology (FAPNOS) is a disorder that accounts for approximately one-third of children diagnosed with the Rome Criteria for Functional Abdominal Pain Disorders (FAPD). According to the Rome III criteria, the prevalence of FAPNOS is reported to be 2.7% in Colombia and 4.4% in Sri Lanka among school-age children.^{6, 32} Studies relying on parental reports have found that the prevalence of FAPNOS are 1.2% in the United States and 2% in Germany among school-age children.^{6, 33}

The difference between FAP-NOS and IBS lies in the fact that children with FAP-NOS typically do not exhibit rectal hypersensitivity, unlike children with IBS.^{8, 9}

Previous studies indicate that children with FAP-NOS exhibit lower antral contractions and slower emptying of liquid food compared to healthy controls. However, the clinical significance of this characteristic remains unclear.³³ Evidence suggests a correlation between psychological stress and chronic abdominal pain in children and adolescents.^{11, 34, 35} Stressful life events such as parental divorce, hospitalization, bullying, and childhood abuse also contribute to the development of FAP-NOS.^{32, 36, 37}

The diagnostic criteria for FAP-NOS stipulate that symptoms must occur at least four times a month and include the following:¹

1. Episodic or continuous abdominal pain occurring during physiological activities (such as meals or menstruation);
2. Insufficient criteria to diagnose IBS, Functional Dyspepsia, or abdominal migraine;
3. Following a thorough examination, abdominal pain cannot be attributed to a specific medical condition.

Symptoms must be present for at least 2 months before the time of diagnosis. Clinical examination of children with FAP-NOS often reveal somatic and non-specific findings, and extraintestinal symptoms do not typically necessitate laboratory testing or imaging studies.¹

The coping mechanisms employed by children and their families in response to FAPD pain can significantly impact their ability to manage and accommodate the pain. The scoring of pain episodes experienced by a child plays a crucial role in this regard. When a child is unable to address the risk factors or when protective factors prove ineffective, it can lead to the development of maladaptive response, resulting in chronic abdominal pain for those with FAP-NOS.³⁸

While small-scale studies have shown that administration of amitriptyline can have beneficial effects, large multi-center studies have not demonstrated a clinically significant effect.^{39, 40} Studies on the use of citalopram have demonstrated its effectiveness compared to placebo in treating children with FAP.⁴¹ Additionally, parental support is important in the management of FAP and can be facilitated through the use of hypnotherapy and cognitive behavioral therapy (CBT), both of which have demonstrated long and short-term effects for patients with FAP.^{42, 43}

Conclusion

In conclusion, functional abdominal pain (FAP) is a common disorder among children, diagnosed following a thorough medical evaluation when symptoms cannot be attributed to other medical conditions. The recognition and timely management of functional abdominal pain (FAP) in children are important. Subtypes of FAP, delineated by the Rome IV Criteria, encompass various disorders such as Irritable Bowel Syndrome (IBS), Functional Dyspepsia, abdominal migraine, and functional abdominal pain - not otherwise specified (FAPNOS), each demanding tailored diagnostic and therapeutic approaches.

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Conflict of Interest

None declared.

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