Pediatric Functional Gastrointestinal Disorders: Pathophysiology, Diagnosis, and Management

Reviewed by:
Dr. Ankur Chawla
MD (Pediatrics),
Consultant Pediatrics,
Kailash Hospital, Noida

Introduction

Functional Gastrointestinal Disorders (FGIDs) are chronic or recurrent gastrointestinal conditions that cannot be explained by structural or biochemical abnormalities. The term "functional" emphasizes that symptoms may occur as part of normal development, such as infant regurgitation, or as responses to otherwise normal internal or external stimuli, such as constipation following painful stooling.[1] In children, FGIDs are highly prevalent and are influenced by multiple factors, including disturbances in gut motility, visceral hypersensitivity, mucosal and immune dysfunction, altered gut microbiota, and central nervous system processing. These conditions impose a considerable burden by causing psychological distress, reduced quality of life, school absenteeism, increased healthcare utilization, and work disruption for parents. Importantly, FGIDs in childhood often persist into later life, with evidence showing that up to 25% of children experiencing recurrent abdominal pain may develop Irritable Bowel Syndrome (IBS) in adulthood.[2]

FFGIDs, more recently referred to as disorders of gut–brain interaction, represent a spectrum of conditions with distinct features across developmental stages. The ROME criteria, established in the late 20th century and revised periodically with new scientific evidence, provide standardized diagnostic guidelines. The latest version, ROME IV has been in use since 2016. Pediatric FGIDs are classified into 2 main groups: Neonates/toddlers (<4 years) and children/adolescents (4–18 years). In infants and toddlers, FGIDs include regurgitation, rumination syndrome, cyclic vomiting syndrome, colic, functional diarrhea, infant dyschezia, and functional constipation. In older children and adolescents, they encompass functional nausea and vomiting disorders (cyclic vomiting syndrome, functional nausea, functional vomiting, rumination syndrome, aerophagia), functional abdominal pain disorders (functional dyspepsia, IBS, abdominal migraine, functional abdominal pain not otherwise specified), and functional defecation disorders (functional constipation, non-retentive fecal incontinence). Diagnosing and managing pediatric FGIDs remains challenging because of children's limited ability to describe their symptoms and the influence of developmental factors on disease presentation and course.[3]

Table-1: Presents the Rome IV FGIDs in children and adolescents[4]

H1. Functional nausea and vomiting disorders
H1a. Cyclic vomiting syndrome
H1b. Functional nausea and functional vomiting
H1c. Rumination syndrome
H1d. Aerophagia
H2. Functional abdominal pain disorders
H2a. Functiona dyspepsia
H2b. Irritable bowel syndrome
H2c. Abdomina migraine
H2d. Functional abdominal pain — not otherwise specified
H3. Functional defecation disorders
H3a. Functiona constipation
H3b. Nonretentive fecal incontinence

Diagnosis

Diagnosing FGIDs is often challenging, as physicians frequently perform extensive investigations to rule out organic causes, leading to high costs. The ROME IV criteria are primarily symptom-based, with limited reliance on investigations. A detailed history and thorough clinical

examination are essential, including the assessment of stressors, psychosocial factors, and past medical or drug history. Awareness of red flag signs is crucial, such as poor weight and height gain, delayed puberty, painful swallowing, bile-stained or persistent vomiting, bleeding, localized pain away from the umbilicus, fever, arthritis, perianal disease, and a family history of inflammatory bowel disease or celiac disease.

Neonate/Toddler FGIDs

Infant Regurgitation: Involuntary movement of gastric contents into the mouth, nose, or esophagus is common in infants aged 3 weeks to 12 months. Diagnosis requires at least 2 episodes per day for a minimum of 3 weeks, without retching, failure to thrive, apnea, feeding difficulty, or posturing. The estimated prevalence is 41–67%

Infant Rumination Syndrome: This rare condition involves effortless regurgitation of food, which is chewed and re-swallowed, accompanied by repetitive abdominal muscle contractions, persisting for at least 2 months. Its estimated prevalence is 1.9%. Onset occurs between 3 to 8 months of age, without distress, and it is absent during sleep. It is considered a self-stimulatory behavior in children experiencing maternal emotional or sensory deprivation or neglect.

Infant Colic: Onset occurs before 5 months of age and is marked by recurrent, prolonged irritability, fussing, and crying without an identifiable cause, with no evidence of failure to thrive. Episodes last at least 3 hours per day, 3 days per week, or 3 hours of crying with fussing in a 24-hour diary. The estimated prevalence is 5–19%.

Child/Adolescent FGIDs

Cyclical Vomiting: Diagnosis in older children follows the same criteria as in younger children, with a focus on excluding other medical conditions. The estimated prevalence is 0.2–1.0%.

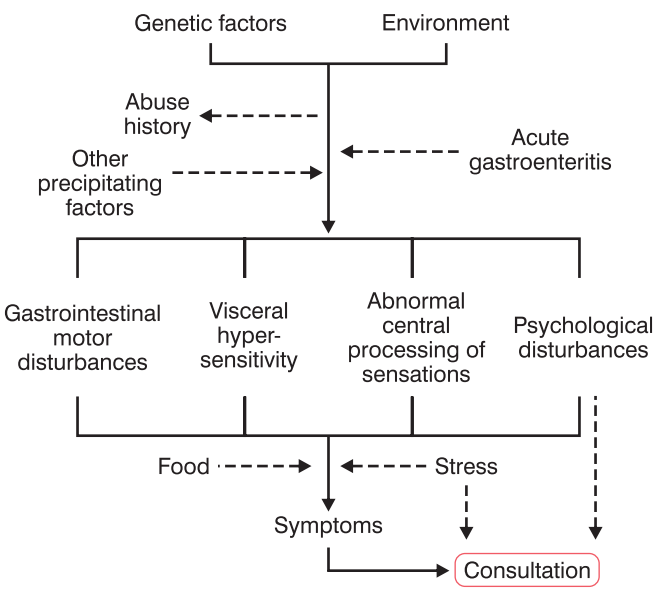
Functional Dyspepsia: Characterized by postprandial fullness, early satiety, or epigastric pain not attributable to other conditions, symptoms must occur at least 4 days per month for 2 months. It can be subclassified into postprandial distress syndrome or epigastric pain syndrome based on predominant features. Prevalence is about 1.4% in children and 5–10% in adolescents.

Irritable Bowel Syndrome (IBS): IBS is categorized as IBS with diarrhea, IBS with constipation, or unspecified IBS. Diagnostic criteria include abdominal pain related to defecation, changes in stool frequency, or stool consistency, present at least 4 days per month for a minimum of 2 months, and not explained by other medical conditions. The estimated prevalence is 1.2–5.4% in children. Red flag signs such as blood in stools or failure to thrive should prompt evaluation for organic causes, including celiac disease and inflammatory bowel disease.[3]

Pathophysiology

Most diseases are multifactorial, unlike simple anatomical lesions where treatment is straightforward. FGID pathophysiology is complex, involving interactions among the digestive system, nervous system, and microbiota. Key mechanisms include intestinal dysmotility, visceral hypersensitivity, disrupted reflexes, psychological factors, and dysbiosis (Figure 1). The varying combinations of these mechanisms explain the different manifestations of FD and IBS. Rome IV defines FGIDs as gut–brain interaction disorders, with symptoms linked to motility disturbance, visceral hypersensitivity, altered mucosal or immune function, microbiota changes, and CNS processing.[5] There is increasing evidence of gut microbiota dysbiosis, particularly a reduction in species with anti-inflammatory effects, such as *Bifidobacterium* and *Faecalibacterium*, in FGIDs, especially IBS. Stress, early life events, diet, and antibiotic therapy may alter gut microbiota, while some probiotic strains have shown potential in improving gastric emptying and alleviating FGIDs.[3]

Figure-1: FGIDs pathophysiology is extremely complex, with digestive, neural, and microbiota interplays



Management

FGIDs in children require a multifaceted approach combining medical, behavioral, and dietary strategies, as single interventions are rarely effective. A biopsychosocial model—addressing triggers, educating parents, and involving multidisciplinary care—is central to management. While 60–70% of children recover over time, many remain at risk of migraine, anxiety, and other disorders in adulthood, underscoring the need for proper transition of care between pediatric and adult providers.

Table-2: Lactase enzyme research results[6]

	Active (median)	Placebo (median)	% Reduction	*p*
Intention to treat (*n*=46)				
Breath hydrogen	6.0 p.p.m.	11.5 p.p.m.	50.0%	<0.0001
Cry time	657.5 min	847.5 min	22.4%	=0.09
Compliant (*n*=32)				
Breath hydrogen	6.0 p.p.m.	9.5 p.p.m.	36.8%	=0.0007
Cry time	520.0 min	872.5 min	40.4%	=0.0052

Dietary: Low-FODMAP (Low Fermentable Oligo saccharides, Di-saccharides, Mono-saccharides and Polyols") diet, lactose/gluten-free diet, fiber supplements, probiotics, nutraceuticals.

Psychosocial: Cognitive behavioral therapy, hypnotherapy, yoga etc.

Pharmacological: Antispasmodics, antibiotics, antidepressants, laxatives, prokinetics, antidiarrheals.[3]

Lactose intolerance has been identified as a potential contributing factor in infant colic. To investigate this, a double-blind, randomized, placebo-controlled crossover study was conducted in 53 infants with colic symptoms. Pre-incubation of feeds with lactase significantly reduced breath hydrogen levels and total crying time by at least 45% compared with placebo in 26% of the overall trial group (95% CI: 12.9%–44.4%) and in 38% of compliers (95% CI: 18.8%–59.4%). The remaining infants did not show the same level of response. These results indicate that infant colic may have multiple causes, with transient lactose intolerance being an immediate factor in some cases. In such infants, pretreatment of feeds with lactase can provide notable symptomatic relief.[6]

In infants where colic is attributed to lactose intolerance, the use of lactase is likely to result in symptomatic relief.[6]

Narang *et al.* investigated the role of oral lactase in infantile colic through a randomized, double-blind, placebo-controlled trial in an urban hospital in Delhi, India. A total of 162 healthy infants under five months of age, meeting Rome IV criteria for infantile colic, were randomly assigned to receive either lactase (*n*=80) or placebo (*n*=82) with feeds, 4 times daily for 4 weeks. Primary outcomes assessed were daily crying/fussing duration and number of days with colic >3 hours/day, while secondary outcomes included parental satisfaction and adverse events.

At 4 weeks, infants in the lactase group had significantly shorter crying/fussing time [89.9 (115.2) *vs.* 178.5 (153.2) min/day; $p=0.001$] and fewer colic days [12.1 (7.8) *vs.* 17.6 (8.4); $p<0.001$] compared with placebo. Parental satisfaction regarding infant mood, activity, comfort, and oral intake was higher in the intervention group, with adverse events comparable between groups. The study concluded that oral lactase provided symptomatic relief in infantile colic by reducing crying duration and improving parental satisfaction.[7]

Table-3: Parental satisfaction score and adverse events during 4 weeks of treatment in both the groups[7]

Outcome	Lactase Median (IQR) (*n*=78)	Placebo Median (IQR) (*n*=76)	*p*
At the end of Treatment			
Mood	5 (4, 5)	3 (2, 4)	<0.001
Activity	5 (4, 5)	4 (3, 5)	0.005
Alertness	5 (4, 5)	4 (3, 5)	0.002
Comfort	5 (4, 5)	3 (2, 4)	<0.001
Vomiting	5 (4, 5)	4 (3, 5)	0.021
Fluid intake	5 (4, 5)	4 (3, 5)	0.033
Adverse events	12	31	0.27
Constipation	0	1	
Diarrhea	3	3	
Vomiting	4	9	
Regurgitation of feeds	3	11	
Eating poorly than usual	1	0	
Cutaneous reaction	0	1	
Fever	1	4	
Others	0	2	

Ahmed *et al.* conducted a double-blind randomized controlled trial to assess the efficacy of lactase enzyme supplementation in infant colic. Infants aged 0–6 months with colic, defined as excessive crying for 3 hours/day on 3 days/week for at least 3 weeks, were randomized into 2 groups: Group A received lactase enzyme, and Group B received placebo. Five drops of the assigned preparation were given before each feed for 2 weeks, with drug codes ensuring blinding. Crying duration was recorded at baseline, and after the 1st and 2nd weeks of intervention.

A total of 104 infants were enrolled, with 52 in each group and 48.1% being boys. At baseline, all had colic. After 2 weeks, significant improvement in crying duration was observed in Group A [45 (86.5%)] compared to Group B [31 (59.6%)] ($p<0.05$). The study concluded that lactase enzyme supplementation significantly reduced crying duration in infants with colic.[8]

Kearney *et al.* investigated the role of transient lactose intolerance in infant colic through a randomized, double-blind, crossover trial. Infants diagnosed with colic based on Wessel's modified criteria were randomly assigned to receive either lactase or placebo drops added to formula feeds for 1 week, followed by a 2-days washout, and then crossed over for the 2nd week. Parents maintained diaries recording daily crying time.

Thirteen infants completed the trial, including 9 boys, with a mean birth weight of 3.7 kg. Colic symptoms began within the first month of life in 12 infants. Lactase supplementation significantly reduced crying time by a mean of 1.14 hours per day (CI 0.23–2.05; t=2.75; $p=0.019$) compared to placebo. The study concluded that transient lactose intolerance may contribute to infant colic, and that lactase drops—when pre-incubated with formula—can significantly reduce symptoms, supporting the role of intestinal spasm in infant discomfort.[9]

Table-4: Evaluation outcome after 1st and 2nd week of intervention[8]

Evaluation Outcome	Intervention received		Total	Sig. levelt
	Group A (Lactase)	Group B (Placebo)		
Duration of Crying after 1st week of Intervention				0.012
<3 hours per day	45	34	79	
≥ 3 hours per day	7	18	25	
Total	52	52	104	
Duration of Crying after 2nd week of Intervention				0.002
<3 hours per day	45	31	76	
≥ 3 hours per day	7	21	28	
Total	52	52	104	

Table-5: Mean crying time (h/day) of babies receiving Lactaid or placebo[9]

	Placebo ($n=6$)	Lactase ($n=7$)	Difference
Mean (s.e.)	2.57	1.43	1.14 (0.413)

Conclusion

Pediatric FGIDs are multifactorial conditions influenced by motility, hypersensitivity, microbiota, immune, and CNS interactions, often persisting into adulthood with significant impact on quality of life. Diagnosis relies on Rome IV symptom-based criteria, with attention to red flag signs to exclude organic disease. Management of pediatric FGIDs requires a biopsychosocial approach combining dietary changes, psychosocial therapies, and pharmacological interventions. Lactose intolerance has been identified as a contributing factor in infant colic, with multiple randomized trials showing that lactase supplementation significantly reduces crying duration and improves parental satisfaction. Early targeted interventions are essential to relieve symptoms, reduce disease burden, and improve long-term outcomes.

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