Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-023-04730-6

REVIEW ARTICLE

Functional Diarrhea in Children

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Received: 11 January 2023 / Accepted: 9 June 2023

Abstract
Functional diarrhea in children is a disease that has been focused on by both general pediatricians as well as pediatric gastroenterologists across the world. Although it is seen across the pediatric age group from late infancy to adolescence, most still believe that functional diarrhea only occurs in younger children. Recent epidemiological studies have shown that functional diarrhea is prevalent in all subcontinents. The classic clinical features include chronic loose stools with undigested food particles without growth faltering. Although known for long years, pathophysiological mechanisms and therapeutic options are not well explored, and the existing literature is outdated. In this article, authors review the available literature on functional diarrhea, with a reminder that a fresh look is needed to broaden the horizons of understanding of this disease.

Keywords Functional diarrhea · Chronic diarrhea · Toddles diarrhea

Introduction

Functional diarrhea is emerging as a common disease in children. Although formally named toddlers' diarrhea, and chronic non-specific diarrhea, adding a connotation that it is a disease of early childhood, emerging evidence shows that it is found in children as well as in adolescents. The cardinal features of functional diarrhea include loose stools with undigested food particles in an otherwise healthy and growing child. Although the pathophysiology of the disease is not fully elucidated, it is generally believed that alteration of intestinal motility, consumption of highly osmotically active drinks, and a diet low in fat contribute to the development of symptoms. Functional diarrhea in children is a clinical diagnosis using the current iteration of the Rome criteria. However, many clinicians tend to investigate them to rule out other possible sinister diseases such as celiac disease, inflammatory bowel disease (IBD), malabsorption syndromes, and gastrointestinal infections. There is no clearly defined guideline for the management of functional diarrhea. However, reassurance with an explanation of the potential mechanisms of diarrhea is the only management option, as most children outgrow the condition. Research exploring the potential pathophysiological mechanisms and therapeutic options is urgently needed to ensure the well-being of children as well as improve the quality of life of parents. This article reviews the currently available literature on epidemiology, pathophysiology, clinical evaluation, and management strategies and also addresses the future perspective of functional diarrhea in children.

Epidemiology

Functional diarrhea is prevalent in all age groups from infancy to adolescent age. Several epidemiological studies involving young children in Asia [1, 2], Europe [3] South America [4, 5] and North America [6, 7] have reported varying prevalence of functional diarrhea. Except one study, all the other studies have used Rome IV criteria for the diagnosis (Table 1). A systematic review noted a prevalence of functional diarrhea in 0.07% of primary care and 12.3% in the community among infants and young children [8]. One drawback of the Rome criteria was that it assumed that functional diarrhea only occurred in infants and young children and excluded it as a diagnosis from children and adolescents, although the disease entity exists in adults as well [9, 10].

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Published online: 29 July 2023

Table 1 Prevalence of functional diarrhea

Region	Country	Diagnostic criteria	Age group	Prevalence
Asia	Vietnam	Rome IV	0–48 mo	0%
	China	Rome IV	7–12 mo	2.2%
			12–48 mo	2.7%
Europe	Belgium, Italy, and The Netherlands	Rome IV	0–12 mo	0.1%
			13–48 mo	0.6%
South America	Colombia	Rome IV	0–48 mo	0.04%
	El-Salvador	Rome IV	0–48 mo	1.5%
North America	USA	Rome IV	0–36 mo	0%
		Rome III	0–36 mo	6.4%
	USA	Rome III	0–36 mo	2.4%

Pathophysiology

The pathophysiology of functional diarrhea is not clearly described, and most of the literature is outdated. Consumption of excess fluid and fruit juices, a diet low in fat, and abnormal motility in the gastrointestinal tract are thought to be involved in the pathogenesis.

Dietary Factors

Consumption of highly osmotically active fruit juices such as apple juice, grape juice, and pear juice have been implicated in the pathogenesis of functional diarrhea in children [11]. Most of them, specially apple juice has high percentage of fructose over glucose which is thought to be a potential pathophysiological mechanism [12]. Concentrations of fructose and sucrose in apple juice may vary with the type of apples used and the preparation and storage process. In addition, sorbitol in apple juice has also been suggestive of inducing functional diarrhea. The capacity of the small intestine for absorption of fructose is limited in children, specially in toddlers, compared to older children [13, 14].

Hyams and Leichtner reported five children ingesting 240 ml (non-excessive) of apple juice developed diarrhea with evidence of significant carbohydrate malabsorption in breath-hydrogen testing. Diarrhea resolved with the withdrawal of apple juice [15]. These subjects were proven to have no lactose malabsorption after the breath-hydrogen test. A Dutch study compared the effects of clear apple juice and unprocessed apple juice in developing functional diarrhea and noted that clear apple juice contributes to increased stool frequency and breath hydrogen excretion [16].

Dietary fat content has been implicated in functional diarrhea. However, the evidence is conflicting. In a retrospective study, a low-fat diet to prevent coronary artery disease has been shown to induce functional diarrhea [17, 18]. Other researchers have found no such evidence and, in fact, improvement of symptoms [19, 20]. Excessive fluid intake has also been suggested as a pathophysiological mechanism [21]. However, it is implausible to be a mechanism for functional diarrhea as the small and large intestines can handle a large amount of fluid without inducing diarrhea. It has been shown that excess clear fluid >50% over basal consumption does not influence stool frequency and consistency [16]. More evidence is needed in the modern day before clearly implicating these factors as pathophysiological mechanisms, as they have a significant impact on the health of children.

Intestinal Motility

Although many believe that the cause of functional diarrhea, as in most other functional gastrointestinal disorders, is disturbed intestinal motility, the available evidence is timeworn and non-convincing. In an otherwise healthy child, the duodenal migratory motor complexes (MMC) occur frequently during fasting and tend to disappear after a meal. Fenton et al. studied three groups of children to understand intestinal motility in response to an intraduodenal bolus of 5% dextrose. After intraduodenal dextrose, healthy children and children with chronic gastrointestinal problems showed inhibition of MMC, while children with toddlers' diarrhea showed no disruption of MMC [22]. The researchers speculated the persistence of MMC after dextrose infusion as an indicator of the failure of food induced disruption of MMC. The persistence of MMC could push undigested food particles into the colon and induce diarrhea. However, the study had a small number of children, and it is questionable that the glucose infusion could mimic a meal in real life. In addition, although speculated, the researchers could not demonstrate the shortening of small bowel or whole gut transit. More studies are needed using novel technical modalities to assess small intestinal function in children with functional diarrhea before concluding this single study.

Clinical Picture and Diagnostic Criteria

A high degree of suspicion is needed to identify children with functional diarrhea. Typically, they present to the clinician with a history of chronic loose stools several times a day. Stools are characteristically mushy or watery with undigested food particles (described as the presence of ingested food particles such as carrots, beans, etc.). The diarrhea is painless, and the stools are foul smelling, and light in color with no blood. Stool frequency is usually more than four times a day. Although it typically occurs in children between 1–5 y of age, and the Rome criteria described it only in children under 5 y, the clinical picture is seen across childhood to adolescence. It is imperative to explore the details of bowel habits and the nature of stools in older children and adolescents who present with chronic diarrhea to identify cases of functional diarrhea and to carefully rule out other common causes in this age group such as diarrhea predominant irritable bowel syndrome and inflammatory bowel disease.

Children with functional diarrhea are otherwise well and have no constitutional symptoms. Their appetite is normal, and they have normal feeding patterns. The physical examination is generally unremarkable, with normal growth parameters and normal systemic findings. The Rome IV diagnostic criteria for functional diarrhea are given in Box 1. Since there are no criteria to diagnose functional diarrhea in children older than 5 y, and it is evident that cases do exist up to adolescents, future iteration of the Rome criteria should carefully consider changing the age as a criterion from late infancy to 18 y.

Box 1 Rome IV Criteria for Functional Diarrhea

Must include all of the following criteria

- Daily painless, recurrent passage of four or more large, unformed stools
- Symptoms last more than 4 wk
- Onset between 6 and 60 mo of age
- No failure to thrive if caloric intake is adequate

Differential Diagnosis

Although the diagnosis is evident after careful evaluation, the following differential diagnosis must be considered during clinical evaluation.

Malabsorption Syndromes

Common malabsorption syndromes such as celiac disease, cystic fibrosis, and small intestinal bacterial overgrowth need to be considered and excluded before making a firm diagnosis. However, in both celiac disease and cystic fibrosis, failure to thrive would be clearly evident during clinical evaluation. Small intestinal bacterial overgrowth may also mimic functional diarrhea.

Parasitological Diseases

The commonest parasitological diseases that cause chronic diarrhea include *Giardia lamblia* and cryptosporidium infections. Giardiasis is a common problem in developing and developed countries, and the transmission is usually feco-oral. Children often present with chronic diarrhea with watery and foul-smelling stools. Cryptosporidium often presents with watery diarrhea associated with nausea, vomiting, flatulence, and anorexia, which are not very common in functional diarrhea.

Lactose Intolerance

Lactose intolerance due to post-infectious enteropathy or gradual loss of lactase activity over the years presents with chronic diarrhea. Children and adolescents from Asia and Africa have a genetic tendency to develop hypolactasia. However, the typical features of lactose intolerance, such as abdominal pain/cramps, bloating, flatus, borborygmi, and perianal excoriation due to acidic stools, are uncommon in children with functional diarrhea [23].

Inflammatory Bowel Disease

Inflammatory bowel disease may present at any age. Cohort studies have described early onset IBD in children less than six years (very early onset IBD) as a common problem [24]. However, in contrast to functional diarrhea, these children may show blood in their stools, clear growth faltering, and abdominal pain.

Diarrhea Predominant Irritable Bowel Syndrome (IBS-D)

IBS-D is a common problem among children and adolescent [25]. They usually present with a history of loose stools associated with abdominal pain. There is also a clear history of abdominal pain relieved with the passage of stools.

Clinical Evaluation

Clinical evaluation of children with functional diarrhea demands a detailed clinical history and a meticulous physical examination. The most critical parts of the clinical history are given in Table 2. The physical examination usually reveals a happy and active child with normal growth parameters. The abdominal examination should be completely normal, and the perianal examination should have normal skin. The rest of the system examination is also normal, and the child should have normal developmental milestones.

Functional diarrhea is a clinical diagnosis, and no investigations are necessary after fulfilling Rome IV criteria. However, investigations are invaluable in confirming the diagnosis of a child with atypical features. The commonly useful investigations in such situations are depicted in Box 2.

Box 2 Investigations to Rule Out Organic Disorders in Children Suspected to Have Functional Diarrhea

- Full blood count
- Inflammatory markers (ESR/C-reactive protein)
- Stool microscopy and culture
- Celiac screening
  - Anti-tissue transglutaminase antibodies
  - Total serum IgA
- Serum albumin
- Serum immunoglobulin
- Stool Calprotectin

ESR Erythrocyte sedimentation rate

Management

There is no specific therapy for functional diarrhea. Once the diagnosis is certain after clinical evaluation and basic investigations whenever necessary, the mainstay of treatment is counselling the parents (Fig. 1). Most of the parents who have gone through many doctors with a large pile of investigation reports are naturally agitated as well as frustrated. A thorough explanation of the possible mechanisms with reassurance and a follow-up plan are essential components of the care package. It is helpful to request parents to keep a diet and defecation diary for them to understand that diarrheal episodes do not have a specific relationship to mostly blamed food items. During the follow-up, showing that the child's growth parameters are maintaining along appropriate centile lines, would alleviate parental concerns. Many families tend to avoid food items that they think precipitate loose motions as well as food that appear in the stools. Proper counselling to offer a balanced diet without highly restrictive diets is paramount to prevent nutritional deficiencies and maintain a good quality of life for affected children. Although suggested, pharmacological interventions such as aspirin and loperamide have no place in managing functional diarrhea [26].

Future Perspectives

Functional diarrhea is one of the most poorly understood pediatric functional gastrointestinal disorders. Abnormal intestinal motility may play a role in pathogenesis. Therefore, evaluation of small and large bowel motility in children using modern-day assessment methods may help unravel mechanisms responsible for functional diarrhea. In addition, studying the microbiome of children with functional diarrhea would also improve our understanding of the pathogenesis. Clinicians must realize that the frequency of diarrheal stools is the most distressing part to the parents. Therefore, proper clinical trials using old and novel anti-motility agents and probiotics with realistically defined clinical and laboratory endpoints would be of utmost importance to ensure rational therapeutic options for children with functional diarrhea.

Table 2 Clinical history of evaluating children with functional diarrhea

Component of the history	Details of the findings
Onset	Gradual and lasting for at least 4 wk Usually, age of onset 1–5 y
Frequency of stools	Four or more times per day
Nature of the stool	Mushy to watery with undigested food particles Often light colored and foul smelling
Nocturnal diarrhea	Not present
Blood in stools	Not a feature
Pain while passing stools	Not a feature
Food intake	No anorexia or food refusal and has an adequate intake of calories
Precipitating factors	Low fat in diet Excessive consumption of fruit juices

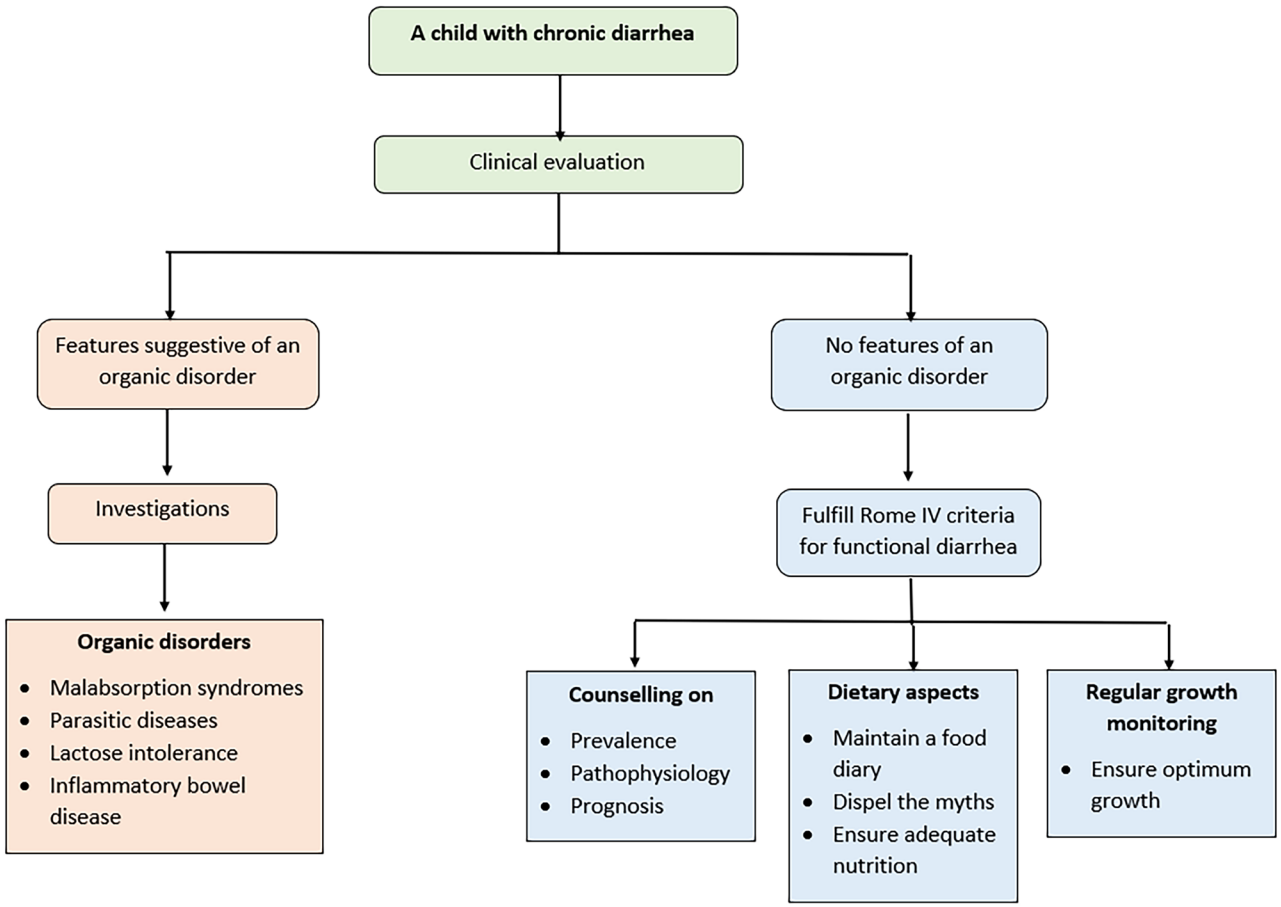

Fig. 1 Management of functional diarrhea in children

Authors' Contributions SR conceptualized the paper and wrote the first draft. WH and NMD supported with data collection, and reviewing the first draft. All authors agree with the final content. SR will act as guarantor for this manuscript.

Declarations

Conflict of Interest None.

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