

## Guideline



# Saudi Experts Consensus on Diagnosis and Management of Pediatric Functional Constipation

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## ABSTRACT

Although functional gastrointestinal disorders (FGIDs) are very common in pediatric patients, there is a scarcity of published epidemiologic data, characteristics, and management patterns from Saudi Arabia, which is the 2nd largest Arabic country in terms of area and the 6th largest Arabic country in terms of population, with 10% of its population aged <5 years. Functional constipation (FC) is an FGID that has shown a rising prevalence among Saudi infants and children in the last few years, which urges us to update our clinical practices. Nine pediatric consultants attended two advisory board meetings to discuss and address current challenges, provide solutions, and reach a Saudi national consensus for the management of pediatric constipation. The pediatric consultants agreed that pediatricians should pay attention to any alarming signs (red flags) found during history taking or physical examinations. They also agreed that the Rome IV criteria are the gold standard for the diagnosis of pediatric FC. Different therapeutic options are available for pediatric patients with FC. Dietary treatment is recommended for infants with constipation for up to six months of age. When non-pharmacological interventions fail to improve FC symptoms, pharmacological treatment with laxatives is indicated. First, the treatment is aimed at disimpaction to remove fecal masses. This is achieved by administering a high dose of oral polyethylene glycol (PEG) or lactulose for a few days. Subsequently, maintenance therapy with PEG should be initiated to prevent the re-accumulation of feces. In addition to PEG, several other options may be used, such as Mg-rich formulas or stimulant laxatives. However, rectal enemas and suppositories are usually reserved for cases that require acute pain relief. In contrast, infant formulas that contain prebiotics or probiotics have not been shown to be effective in infant constipation, while the use of partially hydrolyzed formula is inconclusive. These clinical practice recommendations are intended to be adopted by pediatricians and primary care physicians across Saudi Arabia.

**Keywords:** Constipation; Gastrointestinal diseases; Saudi Arabia; Consensus; Feeding

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## INTRODUCTION

Pediatric gastrointestinal (GI) disorders, including diarrhea, constipation, colic, and regurgitation, are highly prevalent and nonspecific, especially in the Gulf and Middle-Eastern countries [1]. GI disorders can be classified into organic (OGIDs) and functional (FGIDs) according to their etiology. OGIDs are GI disorders with a recognizable etiology, such as cow's milk allergy, celiac disease, or inflammatory bowel disease. By contrast, FGIDs define a wide range of GI symptoms that cannot be attributed to an apparent organic cause after appropriate medical evaluation [2]. The most common pediatric FGIDs are irritable bowel syndrome and functional constipation (FC) [3,4]. During infancy, regurgitation, colic, dyschezia, and FC are the most frequent FGIDs [3,4].

FGIDs mostly present with vague non-specific symptoms; therefore, their diagnosis is challenging. The clinical approach for children with GI symptoms must start with a comprehensive history taking and thorough clinical examination, including disease onset, course duration, severity, aggravating or relieving factors, previous history of the same condition, and any family history of the same condition with meticulous examination for alarming signs. Only a limited indications have been investigated for the diagnosis of FGIDs and to rule out OGIDs. The diagnostic approach for FGIDs is mainly established by the application of the Rome IV criteria [5].

According to its etiology, constipation can be classified into several categories which include: functional (non-organic), anatomic, abnormal motility (neurointestinal dysplasia/or aplasia), iatrogenic (caused by drugs), metabolic (such as hypokalemia or hypercalcemia), and endocrinal [6]. FC is highly prevalent among children worldwide and accounts for 90–95% of all constipated infants [7–9]. FC shows a variable prevalence across different continents and countries, as reported in 9.6% of European infants/toddlers [10], 20% of Japanese children [11], and 31.4% of African children [12].

Most FGIDs occurring during infancy resolve before or around the age of 1 year, except for FC, which persists through different age groups. For example, an infant's colic resolves at the age of 4–5 months, dyschezia resolves at 8–9 months, and regurgitation resolves at 12 months [13]. Therapeutic options for FGIDs include dietary, pharmacological, behavioral, and complementary approaches [14]. Despite the availability of multiple treatment options, more effective treatments are still needed for many of them.

The present consensus was developed to reach a national Saudi consensus for practical considerations and clinical implications of pediatric FC. This consensus panel aimed to provide solutions for the current challenges regarding the prevalence and management of FC among Saudi infants and children. In addition, the consensus panel highlighted the current status of FGIDs in Saudi Arabia from the clinical perspective of participating experts.

## CONSENSUS DEVELOPMENT

To address the current challenges, provide solutions, and reach a national consensus for the management of constipation in Saudi infants/children, two advisory board meetings were held. The Delphi method was used to develop the consensus, as nine pediatric consultants (eight from the Kingdom of Saudi Arabia and one from Belgium) were invited to participate in both meetings and share their opinions through rounds of anonymous electronic voting

**Table 1.** Strength of recommendations

Strength of recommendation	Code
Highly recommended (If reached $\geq 75\%$ agreement)	A
Recommended (If reached 50–74% agreement)	B
Not recommended (If reached $< 50\%$ agreement)	C

with group discussion, correction, and modification of statements [15]. Some questions were chosen to enter the 2nd round of voting to see if the experts' opinions had changed after the group discussion. The panel consisted mainly of experts from different regions of Saudi Arabia who were working in different healthcare sectors (university, armed forces, Ministry of Health, or private sector hospitals). All members of the panel had clinical experience in the management of FGIDs in children. In addition, most of the panel groups had research experience and publications in the same field of interest (constipation among children).

The voting process was conducted in two stages. After completing the first stage of voting, a virtual meeting was held to modify each statement according to the participants' comments and recommendations. The 2nd round of voting was conducted to reach a final consensus on all the proposed statements. We kept the statements that reached  $> 75\%$  agreement, and those that failed to reach this percentage (even after the 2nd round of voting) were reviewed and discussed by panel experts. Each statement was classified according to the degree of recommendation and quality of evidence using a modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system [16]. We classified the strength of our recommendations into highly recommended, recommended, and not recommended according to the voting percentage. The modified GRADE system is shown in **Table 1** [16].

## RESULTS

The coordinators developed 64 statements for the initial voting rounds. Of these 64 statements, 27 needed further discussion and endorsement. After these two rounds of voting and discussion, 37 statements were eliminated as they did not reach consensus, and the remaining 27 statements were included for final approval. The 2nd round of electronic voting (postadvisory board meetings) contained only 27 statements. After this round of voting, five statements were eliminated owing to a lack of evidence or not reaching panel consensus. The final 22 approved statements were presented along with their corresponding recommendations.

### Rome IV criteria

1. Rome IV criteria are the standard tool for diagnosing constipation, which most pediatricians apply in their daily practice.

*Strength of recommendation: A (total agreement=89%)*

2. Stool consistency and frequency are the core of the Rome IV criteria.

*Strength of recommendation: A (total agreement=78%, partial agreement=11%)*

3. The symptoms of Rome IV criteria are all equally important for the diagnosis of constipation; however, they can be ordered according to their clinical relevancy and frequency.

*Strength of recommendation: A (total agreement=78%)*

FGIDs are common among infants and toddlers worldwide and include different GI tract disorders characterized by recurrent, chronic, and non-specific symptoms that cannot be attributed to any organic or biochemical abnormalities [2]. The Rome IV criteria are considered the gold standard for diagnosing FGIDs. They are recent versions of a series of updates for the original 1994 Rome criteria [17]. According to the Rome IV criteria [13], infants up to 4 years of age must have at least two of the following symptoms for at least one month to be diagnosed with FC: (1) no more than two defecation attempts per week, (2) history of stool retention, (3) history of painful bowel movement, (4) history of a lumpy/large stool, and (5) presence of a bulky fecal mass in the rectum. Additionally, for toilet-trained children, the following criteria may also be applied: (6) one or more episodes of incontinence/week and (7) history of the presence of large bulky stool that may obstruct the toilet [13].

Symptoms defined by the Rome IV criteria are based on stool frequency (as defecation attempts) and consistency (as lumpy stool and fecal mass); therefore, experts agreed that stool frequency and consistency are the most important clinical symptoms to diagnose constipation in infants below 1 year of age. Symptoms of the Rome IV criteria are important for diagnosing FC; however, consensus panel experts believed that they can be ordered according to their clinical relevancy and frequency. Moreover, we confirmed that the presence of a large fecal mass in the rectum and a history of excessive stool retention were the most frequent symptoms in the Rome IV criteria used to diagnose FC in Saudi Arabian toddlers.

### Alarming symptoms and signs

4. Pediatricians should be alert for signs and symptoms that indicate a more serious underlying pathology of infant constipation (red flags).

*Strength of recommendation: A (total agreement=89%)*

5. All alarming signs are indeed important, but not in the same weight.

*Strength of recommendation: A (total agreement=89%)*

6. Normally, most infants (95%) produce their first meconium within 24 hours and 99% within 48 hours after delivery.

*Strength of recommendation: A (total agreement=78%)*

As mentioned before, the diagnosis of FGIDs, including FC, is a diagnosis of exclusion. Alarming symptoms and signs (red flags) that refer to the presence of underlying pathology (organic cause) must be carefully checked before reaching the diagnosis of FGIDs. These warning signs include failure of the newborn to pass the meconium in the first 24 hours after delivery, abdominal distention, bilious vomiting, failure to thrive, bloody or mucoid stool, delayed neurological development, anal or sacral abnormalities, and presence of signs of other organic causes (such as fever or urinary tract infections) [9,18].

The pediatrician should examine every child/infant with constipation for any alarming signs by looking for any anatomic abnormalities, inspecting the child/infant for any anal/sacral abnormalities, performing a total physical examination for failure to thrive, and then looking for anatomic GI problems suggested by abdominal distention and vomiting.

Approximately 95% of newborn infants pass stool in the first 24 hours and 99% in the first 48 hours after delivery [19]. The inability of the newborn to pass stool (meconium) in the first

24 hours is an alarming sign of intestinal anatomic or neurologic obstruction, suggesting Hirschsprung's disease. Usually, failure of the newborn to pass the meconium is associated with rejection of food and vomiting of intestinal contents (bilious) [19]. Neurodevelopmental delay is not always considered an alarming symptom of constipation; however, it is a significant sign for the general health of the infant/child. Some neurodevelopmental disorders, such as autism spectrum disorder, have been associated with FC [20]. The exact pathophysiology of this association is not fully understood; however, constipation has been suggested to occur due to an inadequate response of the child to the defecation urge [20,21].

### Epidemiology of infantile constipation

7. The prevalence of infantile constipation in Saudi Arabia has increased in recent years and it ranges from 5% to 30%.

*Strength of recommendation: B (agreement on 5–10=44%, 10–20=22%, and 20–30=33%)*

The most frequently reported FGIDs among infants in the literature were regurgitation (13.8%), colic (4.2%), dyschezia (4%), and FC (3%) [10]. FC was the highest reported FGID (9.7%) among the toddlers in Europe [10]. The diagnosis of FC in infants is common among pediatricians worldwide. FC has variable prevalence across different regions as shown in **Table 2** [22]. Its prevalence ranges from 10% to 23% in South and North America [22–24], 0.7% to 12% in Europe [10,22], 0.5% to 29.6% in Asia [22,25–27], and 31.4% among African children [12]. In contrast, chronic constipation was reported in 32.2% of Saudi children aged 7–17 years [28].

Of note, FC has a higher prevalence rate in Saudi Arabia and Africa compared with that in Europe and America. FC in Saudi Arabia showed nearly the same prevalence as the surrounding countries such as Egypt, which has a prevalence of 30.4% [29]. This difference in prevalence among different parts of the world may be related to the different compositions of infant formulas, environmental factors, and genetic factors. The panel experts believe that the increasing trend of FC diagnosis in Saudi Arabia is due to following factors:

- a. Increased use of milk formulas.
- b. Poor/wrong formula milk preparation by inexperienced mothers.
- c. Some Saudi mothers continue on exclusive milk/formula for up to 8–9 months without weaning (late introduction of complementary food).
- d. Some mothers introduce food before the infant reaches 4 months of age.
- e. Increasing food allergy prevalence among Saudi infants.
- f. Low rate of breastfeeding among Saudi mothers.

**Table 2.** Prevalence of functional constipation across different parts of the world

Area	Prevalence (%)	Reference
South and North America	10–23	[22–24]
Europe	0.7–12	[10,22]
Asia	0.5–29.6	[22,25–27]
Africa	31.4	[12]
Saudi Arabia	32.2	[28]

### Infantile dyschezia

8. Infantile dyschezia and functional constipation are two distinct functional disorders that can be distinguished by history and usually require a different management plan.

*Strength of recommendation: B (total agreement=67%)*

According to the Rome IV criteria [13], infant dyschezia is defined as “straining and crying of the infant less than 9 months of age for  $\geq 10$  minutes with each attempt to defecate before the successful or unsuccessful passage of soft stool without the presence of any other health problems”. Dyschezia is not a form of constipation because of the presence of normal stool consistency (soft stool) and frequency. In most infants, symptoms of dyschezia begin in their early months of life and usually resolve spontaneously in 3–4 weeks.

The prevalence of dyschezia among infants aged  $< 6$  months has been reported to be 4% in Europe [10], 2.4% in the United States of America [30], and 3.2% in Colombia [24]. Another study from the Netherlands found that 3.9% and 0.9% of infants at 1 and 3 months, respectively, fulfilled the Rome III criteria for infant dyschezia [31]. Experts agreed on the need to conduct a large-scale observational study to reveal the prevalence of infant/child dyschezia in the Saudi community.

### Cow milk allergy

9. Infant constipation should be considered a symptom of cow milk allergy.

*Strength of recommendation: A (total agreement=100%)*

Cow milk allergy (CMA) is an allergic reaction of the infant’s immune system towards one or more milk proteins [32]. This immune-mediated reaction affects different body systems, including digestive, respiratory, and skin, or may even cause a multiple system effect in the form of systemic anaphylaxis [33]. Diagnosis of CMA depends on full history, especially of atopy of parents or siblings and the presence of one or more of the following symptoms [34,35]:

- a. GI tract manifestations including vomiting, diarrhea, regurgitation, colic, constipation, hematochezia, or malnutrition.
- b. Skin manifestations: atopic dermatitis, eczema, or itching.
- c. Respiratory manifestations: frequent cough and wheezes.
- d. General manifestations: irritability or persistent distress.

Constipation alone is not a frequent symptom of CMA [34]. Most CMA cases present with a combination of symptoms in different body organs [32]. Some cases of CMA may be mistaken for lactose intolerance because they share a common presentation; however, immune-mediated reaction is not a part of lactose intolerance pathophysiology [33].

The role of CMA in FC has been widely investigated in the literature. Many studies have shown that constipation occurs because of hypersensitivity to cow milk proteins [36-39]. In a retrospective study conducted on 136 constipated Polish infants less than 3 years of age [40], 99 (72.8%) cases were caused by CMA, and all cases improved after starting the elimination diet.

According to the European Academy of Allergy and Clinical Immunology recommendations [41], most panel experts (56%) agreed that no data are available in the literature describing constipation as a single manifestation of CMA. The panel experts reported variable frequencies of constipation in CMA infants in their clinical practice. Seven experts (78%) reported constipation frequency from 5% to 25%, one expert (11%) reported a frequency from 25% to 50%, and one expert (11%) reported a frequency >50% of CMA cases.

### Bristol and the Brussels infant and toddler stool scales

10. Brussels Infant and Toddler Stool Scale (BITSS) has replaced the Bristol stool scale (BSS) as the favorite tool for diagnosis and follow-up of infants with constipation.

*Strength of recommendation: B (total agreement=56%)*

For years, experts have been trying to develop the best, easiest, and most comprehensive scale to assess infant stool consistency. The stool scale is a substantial tool for a better understanding of gut physiology and assessment of bowel symptoms [42]. These efforts have yielded several valid stool scales in recent years, such as the BSS, Amsterdam Infant Stool Scale (AISS), and BITSS.

The Bristol stool chart is a clinical assessment tool that was developed in 1997 to assess stool consistency and colonic transit time in toilet-trained individuals [43]. It classifies stools into seven types according to their shape and consistency [43]. The stool of infants wearing diapers does not look like the description presented in the Bristol chart. It is not representative of appearance of stool for those below one year of age. In contrast, the AISS is very good because it considers color, consistency, and amount [44]. However, the AISS is not generally used because it is quite complicated. The BSS was developed to describe the intestinal transit time in adults [43]. Since the Bristol scale mainly targeted toilet-trained children, a more comprehensive scale i.e., BITSS was developed in 2019 for non-toilet-trained children [45]. It is a reliable, validated, and comprehensive clinical tool for assessing stool consistency in non-toilet-trained children. Instead of the seven types of stools classified by the Bristol scale, the BITSS categorizes stools into four groups: hard, formed, loose, and watery groups [45]. While the BSS used the term “normal” consistency, the BITSS descriptions are limited to “watery, loose, formed, and hard” and does not use “normal” [43,45]. A trial comparing the BSS and BITSS concluded that BITSS is more sensitive in detecting hard stools [46].

BITSS will soon be available on an artificial intelligence-based mobile application; anyone can take a photo of a diaper containing stool, and the application will check the form of the stool. Experts hope that this app will be a more objective tool for describing stool consistency. The application was based on 3,000 photos. With the advent of the application, parents’ description of the infant stool is no longer required.

### Recommendations of formulas composition and their effects on constipation

11. Purified or distilled water is recommended for infant formula preparation.

*Strength of recommendation: B (total agreement=67%)*

12. Poor formula preparation may be a cause of the infant’s constipation.

*Strength of recommendation: A (total agreement=89%)*

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13. Infant formula that contains Magnesium is recommended for infants with constipation as Magnesium increases stool frequency, decreases stool consistency, and lessens pain related to defecation.

*Strength of recommendation: A (total agreement=89%)*

14. The palm-oil-free formula is recommended for infants with constipation.

*Strength of recommendation: B (total agreement=56%)*

15. Infant formulas that contain protein hydrolysates soften the stool consistency in non-constipated infants.

*Strength of recommendation: B (total agreement=67%)*

The bowel status of infants is substantially controlled by feeding type, especially in the early months after birth [47]. FC has a higher prevalence in formula-fed infants than in breast-fed infants [48]. Experts have explained this high prevalence by the difference in composition between mother's milk and formula milk. For instance, the free palmitic acid present in formula milk may link with the free fatty acids and form an insoluble calcium fatty acid soap, which results in the formation of a hard firm stool [48]. Experts agree that the method of formula preparation may also contribute to the development of constipation among infants. Each infant formula has a specific method of preparation, and the wrong method of preparation may expose the infant to GI problems, poor feeding, or constipation.

Magnesium sulfate has been widely investigated as a treatment option for FC. It was first introduced in 1829 by Sir James Murray and has since been investigated for its pharmacological actions on constipation [49]. It acts as an osmotic laxative by attracting body fluids to be retained in the intestine, which makes the stool soft and easy to excrete [50]. In recent years, magnesium sulfate-rich natural mineral waters have been investigated for their effects on stool frequency and consistency. To the best of our knowledge, only three types of mineral waters have been clinically studied for their efficacy in constipation: Hépar [51,52], Ensinger Schiller Quelle [53], and Donat Mg [54]. The results of clinical trials on these mineral waters have shown better outcomes in terms of stool consistency and frequency compared to low-mineral natural water or tap water.

Milk formula enriched with Mg is highly recommended for infants with constipation. Accumulating evidence has shown that extra Mg in infant formula improves stool consistency and frequency and minimizes pain related to defecation. The novalac Mg-enriched formula demonstrates good outcomes for infantile constipation. It (improved transit) was reported to decrease stool consistency, increase stool frequency, and increase stool weight compared to the strengthened regular formula [55]. A more recent study conducted in the Middle East showed similar results and reported an improvement in stool consistency and frequency in the Mg-rich formula (Novalac formula) group compared with the control group (Similac Comfort) [56]. Moreover, a study by Xinias et al. [57] reported similar outcomes for stool frequency and consistency but using a different Mg-enriched formula.

Infant formulas that contain high levels of Mg have been reported to increase stool frequency, decrease stool consistency i.e., form loose stools, and improve pain related to defecation compared to other formulas [56,57]. Besides being effective, Mg-rich formula is safe,



increases overall parental satisfaction, and improves the quality of life (QoL) of both parents and infants. Furthermore, almost all parents wanted to adhere to the Mg-rich formula one month after formula intake [56].

Palm oil (PO) is the main source of dietary fats, including high levels of saturated fatty acids (mainly palmitic acid), monounsaturated fatty acids, and polyunsaturated fatty acids, in West Africa [58,59]. High-quality PO products contain over 95% triacylglycerol and a very small amount (<0.5%) of free fatty acids [60]. Two large studies, observational and randomized controlled trials (RCT), investigated the effect of PO-containing formulas on stool consistency and frequency in infants [61,62]. In both studies, the authors assessed GI tolerance of the included breastfed healthy full-term infants to the new PO-containing milk formula. Both studies reported a lower stool frequency and a harder stool consistency in infants fed with PO-containing formula than in those fed with non-PO-containing formula [61,62]. Another meta-analysis composed of nine RCTs reported the same results for the PO formula [63]. However, these data are not sufficient to recommend against the use of PO for infant formula, especially since no severe adverse events were reported.

Protein hydrolysate used in hydrolyzed milk formulas is another source of infant nutrition that has been discussed in the literature. Milk formula with hydrolyzed protein has been reported to soften the hard stool and increase stool frequency in nonconstipated infants [64,65].

### The role of prebiotics and probiotics in infantile constipation

16. Infant formulas that contain prebiotics or probiotics are not recommended as a routine therapy for infants with constipation.

*Strength of recommendation: B (total agreement=56%)*

The human body is filled with millions of microorganisms (mostly bacteria), which live mainly in the digestive system. These gut bacteria, also called GI microbiota, are very beneficial as they enhance the immune system [66], decrease the severity of depression and anxiety [67], help in weight loss, protect against obesity [68], and improve the overall health status. Probiotics are living microorganisms (mostly bacteria) found in certain foods or supplements that can improve the health status of the body when administered in adequate amounts [69]. In contrast, prebiotics are non-digestible carbohydrate fibers that act as nutrients for GI microbiota [70].

Normal mother's milk contains a large amount of prebiotics and a small number of probiotics. In contrast, infant formula does not contain the same composition of prebiotics and probiotics; therefore, prebiotics are added to milk formula to make it resemble the mother's milk. In a study conducted by Bongers et al. [47], infants who were fed with milk formula supplemented with prebiotics had a soft stool; however, they did not show any difference in stool frequency compared to the standard formula. Similar results regarding the formation of soft stool in constipated infants were reported in a clinical trial by Ashley et al. [71]. Moreover, using the synbiotic infant formulas, which are a mixture of prebiotics and probiotics, for infants with FC was reported to significantly improve the state of constipation and QoL for both infants and their parents [57]. The outcomes of probiotic use in FC vary significantly according to the probiotic strain used. For instance, the use of *Bifidobacterium longum* and *Lactocaseibacillus rhamnosus* strains was reported to produce soft stool; however, other strains (*Bifidobacterium bifidum* or *Lactocaseibacillus johnsonii*) did not show any significant differences compared to the

control group [72]. The available evidence regarding the use of infant formulas containing prebiotics or synbiotics is insufficient to recommend its use for constipated infants.

Locust bean gum (LBG), a slowly fermented thickening agent, decreases fecal pH and stimulates the development of fecal microbiota [73]. A panel of experts confirmed that bean gum has positive effects on the GI microbiota. This point has been poorly discussed in the literature, and more studies are required to confirm the role of bean gum on the GI microbiota.

### Management of infants with functional constipation

17. Lactulose may not be the best option for childhood constipation because of its side effects as flatulence, abdominal pain, nausea, vomiting, and bloating.  
*Strength of recommendation: A (total agreement=89%)*
18. Rectal treatment is not favorable for infants with constipation; however, it can be used in cases that need acute relief of pain.  
*Strength of recommendation: B (total agreement=67%)*
19. Goat milk formula is not recommended for infants with constipation.  
*Strength of recommendation: A (total agreement=78%)*
20. Dietary treatment is recommended for infants with constipation for up to 6 months.  
*Strength of recommendation: A (total agreement=89%)*
21. Experts stipulate that mothers' milk is the best for infant constipation. Mg and bean gum have roles in constipation treatment. Palm oil and protein composition are less frequently used.  
*Strength of recommendation: A (total agreement=100%)*
22. Pediatricians prefer milk formulas that improve constipation and decrease the frequency of regurgitation (as thickened milk formula).  
*Strength of recommendation: A (total agreement=100%)*

According to the NASPGHAN (North American Society of Pediatric Gastroenterology, Hepatology and Nutrition) and ESPGHAN (European Society of Pediatric Gastroenterology, Hepatology and Nutrition) 2014 guidelines for the treatment of infants with FC [7], normal fiber intake, sufficient fluid intake, and normal physical activity are recommended as first-line nonpharmacological treatments for pediatric constipation. Due to its high biological value, experts encourage mothers to continue breastfeeding infants and toddlers less than two years of age. Polyethylene glycol (PEG) has replaced lactulose as a first-line treatment option in cases of fecal disimpaction owing to the high frequency of side effects reported with lactulose use. PEG has demonstrated better clinical outcomes for stool disimpaction rate and stool frequency in constipated infants when compared to lactulose [74]. Lactulose may not be the best treatment option for childhood constipation because of its side effects such as flatulence, abdominal pain, nausea, vomiting, and bloating [75].

Rectal treatment provides a fast and safe approach for infantile constipation; however, it still carries some medical hazards owing to its invasive nature. Rectal enemas and glycerin suppositories are not frequently used in the treatment of infants with constipation in clinical practice. An African-based large-scale, cross-sectional study found that, among 2,271 constipated infants treated with different types of medications, 854 (37.6%) were treated with

laxative enemas and 775 (34.1%) were treated with oral laxatives [12]. Despite being generally harmless, rectal enemas may cause severe trauma to the rectal mucosa if incorrect insertion occurs. In addition, enemas may aggravate the infant's fear of defecation and cause general discomfort from the therapeutic approach. A retrospective observational study conducted in Britain demonstrated that 97% of the included children treated with PEG reported successful fecal disimpaction compared to only 73% treated with enema and suppositories [76]. Expert panel members express what happens in daily practice as rectal treatment (as a glycerin suppository) is not recommended, except in cases that require acute relief of pain.

Tannock et al. [77] showed that the stool microbiota of infants fed with goat milk resembles that of infants fed with breast milk. Another case series study of 20 constipated infants reported that infants fed with formula goat milk had a lower fat content in the stool, fewer crying attacks, and better stool consistency [78]. However, experts do not recommend goat milk for infants with constipation as data present in the literature on the effect of goat milk on infant constipation are very scarce, and other alternatives are available.

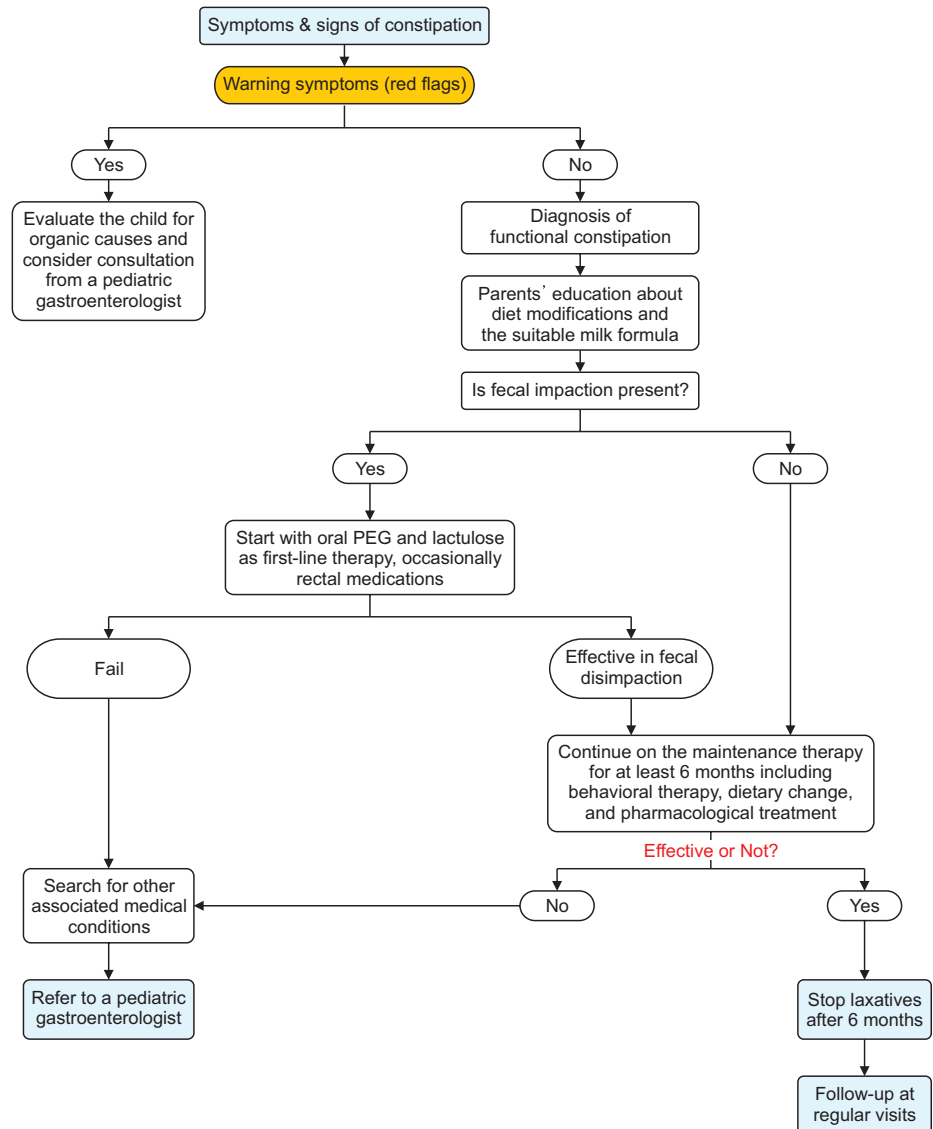
Since most infants (25–50%) present with combined FGID symptoms such as constipation, regurgitation, colic, and gas/bloating [12], pediatricians prefer to prescribe milk formulas adapted for constipation and thickened with LBG, especially in patients with constipation and severe regurgitation, as these formulas improve constipation, decrease regurgitation, and decrease episodes of gas [79,80].

Management recommendations for infants with FC are presented in the management algorithm in **Fig. 1**. Treatment recommendations included initial therapy, maintenance therapy, and follow-up visits. The goal of maintenance therapy is to maintain soft bowel movements one or two times per day. Ensuring stool regularity is an essential part of the treatment plan because rectal impaction can recur and restart the constipation cycle. **Table 3** contains a complete set of the consensus panel statements with the agreement percentage of each statement.

## CONCLUSION

FGIDs are highly prevalent among Saudi infants and children, and the number of diagnosed cases has increased dramatically in the last few years. A large proportion of infants present with combined symptoms of FGIDs, which requires more attention to all parents' complaints. The diagnosis of FC is a diagnosis of exclusion; therefore, physical examination should be focused mainly on finding any alarming signs (red flags). Diagnosing FC is achieved by fulfilling the Rome IV criteria, after which the type of therapeutic intervention should be determined according to the patient's age and health status. Different therapeutic options are available for pediatric patients with FC. Dietary treatment is recommended for infants with constipation for up to six months. When nonpharmacological interventions fail to improve the symptoms of pediatric FC, pharmacological treatment with laxatives is indicated. The treatment is primarily aimed at disimpaction to remove fecal masses. This was achieved through a temporary high-dose of oral PEG or lactulose. Subsequently, maintenance therapy with PEG should be initiated to prevent the re-accumulation of feces. In addition to PEG, several other options may be used, such as Mg-rich formulas or stimulant laxatives.

However, rectal enemas and suppositories are not recommended as a treatment option because of their side effects, except in cases that require acute relief of pain. Moreover, infant



**Fig. 1.** Management algorithm for infants with functional constipation. PEG: polyethylene glycol.

formulas that contain prebiotics or probiotics are not recommended as routine therapy for infants with constipation, while the use of the partially hydrolyzed formula is inconclusive.

These clinical practice recommendations are intended to be adopted by pediatricians and primary care physicians across Saudi Arabia.

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**Table 3.** The full set of experts' consensus statements

Statement	Agreement percentage	Strength of recommendations
1. Rome IV criteria are the standard tool for diagnosing constipation and most pediatricians apply it in their daily practice.	89%	A
2. Stool consistency and frequency are the core of the Rome IV criteria.	78%	A
3. The symptoms of Rome IV criteria are all equally important for the diagnosis of constipation; however, they can be ordered according to their clinical relevancy and frequency.	78%	A
4. Pediatricians should be alert for signs and symptoms that indicate a more serious underlying pathology of infant constipation (red flags).	89%	A
5. All alarming signs are indeed important, but not in the same weight.	89%	A
6. Normally, most infants (95%) produce their first meconium within 24 hours and 99% within 48 hours after delivery.	78%	A
7. The prevalence of infantile constipation in Saudi Arabia is increasing in the last years and it ranges from 5% to 30%.	5–10=44%, 10–20=22%, 20–30=33%	B
8. Infantile dyschezia and functional constipation are two distinct functional disorders that can be distinguished by history and usually require a different management plan.	67%	B
9. Infant constipation should be considered a symptom of cow milk allergy.	100%	A
10. Brussels infant and toddler stool scale (BITSS) has replaced the Bristol stool scale as the favorite tool for diagnosis and follow-up of infants with constipation.	56%	B
11. Purified or distilled water is recommended for infant formula preparation.	67%	B
12. Poor formula preparation may be a cause of the infant's constipation.	89%	A
13. Infant formula that contains Magnesium is recommended for infants with constipation as Magnesium increases stool frequency, decreases stool consistency, and lessens pain related to defecation.	89%	A
14. The palm-oil-free formula is recommended for infants with constipation.	56%	B
15. Infant formulas that contain protein hydrolysates soften the stool consistency in non-constipated infants.	67%	B
16. Infant formulas that contain prebiotics or probiotics are not recommended as a routine therapy for infants with constipation.	56%	B
17. Lactulose maybe not be the best option for childhood constipation because of its side effects as flatulence, abdominal pain, nausea, vomiting, and bloating.	89%	A
18. Rectal treatment is not favorable for infants with constipation; however, it can be used in cases that require acute relief of pain.	67%	B
19. Goat milk formula is not recommended for infants with constipation.	78%	A
20. Dietary treatment is recommended for infants with constipation for up to 6 months.	89%	A
21. Experts stipulate that mothers' milk is the best for infant constipation. Mg and bean gum have roles in constipation treatment. Palm oil and protein composition are less frequently used.	100%	A
22. Pediatricians prefer milk formulas that improve constipation and decrease the frequency of regurgitation (as thickened milk formula).	100%	A

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