

# Functional constipation in the first-year-old onset at the first visit to a specialized clinic elicits a delay in referrals, the worst symptoms, and the excessive use of rectal laxatives

## Abstract

**Purpose:** To assess and compares sociodemographic, clinical, anthropometric, and treatment characteristics in two subgroups of children with FC: 1) with onset in the first 12 months old and 2) with onset after 13 months old.

**Methods:** Observational, retrospective cohort study, including consecutive cases of children/adolescents for initial evaluation of constipation. Data were collected in a pre-designed standard protocol, and the parents answered all the questions during the first visit. Inclusion criteria: age between 01 month to 15 years of age, with a diagnosis of FC defined according to the Rome Criteria III and Rome IV criteria. Exclusion criteria: constipation of organic etiology; other chronic health problems such as neurological, genetic, mental/psychiatric disorders or growth and development disorders. The stool form was evaluated according to Bristol Stool Form Scale. Two experienced pediatric gastroenterologists determined the patients' final diagnoses of FC. Approval was obtained from the ethics committee.

**Results:** Five hundred and four children were identified with constipation at their initial visit. Thirty-two were excluded based on the inclusion and exclusion criteria. The remaining 472 children (225 with onset within the first 12 months and 247 after 13 months) were included. There was a long time to first visit in those with onset in the first 12 months of life. There is no difference in BMI/age scores between the two groups. FC onset in the first 12 months has more scybalous stools, painful defecation, bloody stools, a lower proportion with bowel toilet training, and bladder control. In FC starting in the first 12 months of life, only half of the children (55%) were treated with laxatives, and an entire group used rectal treatment.

**Conclusion:** FC is a common Functional Gastrointestinal Disorder affecting infants during the first months of life. The primary inadequate treatment and referral delay implies worsening symptoms, chronicity, and non-implementing North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines.

**Keywords:** constipation, infant, children, rome criteria, laxatives, defecation disorders

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**Abbreviations:** FC, functional constipation; SUS, Brazilian public health system; PEG, polyethylene glycol; IQR, interquartile range

## Introduction

Defecation disorders are among the ten most common problems in general pediatric practice.<sup>1</sup> Prevalence of Functional Constipation (FC) in infants and toddlers varies between studies and ranges from 5% to 27%, and in toddlers is reported to be higher than in infants,<sup>2,3</sup> with the median age of onset of 2.3 years.<sup>4</sup>

In a multicentre study in Brazil, the prevalence of FC in infants treated in private pediatric practice was 7.6%.<sup>5</sup> Thus, FC represents a critical workload in a specialized clinic.<sup>6</sup>

In children with FC before age 4, a long-term follow-up found that 63% had recovered, and the rate was higher in those younger than two years at initial evaluation.<sup>7</sup> Another follow-up study of children in the first year of life demonstrated that 69% had recovered after six months, and relapse occurred in 15% within three years. Additionally, duration <3 Months before referral was significantly correlated with

a better outcome, suggesting that early therapeutic intervention may beneficially contribute to the resolution of constipation.<sup>8</sup>

Vandenplas et al.<sup>9</sup> evaluated the opinion of 15 international experts on the long-term consequences of functional gastrointestinal symptoms in children younger than 12 months. The prevalence of FC was 15%, and good quality data are lacking in assessing these children. In the FC under treatment, only 50% of the children improve and remain without medication after 6 to 12 months,<sup>10,11</sup> around 25% maintain the symptoms until adulthood,<sup>12</sup> and the patient's Health-Related Quality of Life is impaired.<sup>13,14</sup>

Accordingly, a study analyzing the clinical and therapeutic presentation of children with FC in the first 12 months of life could contribute to a better understanding and approach to this disorder.

## Aims

To assess and compares sociodemographic, clinical, anthropometric, and treatment characteristics in two subgroups of children with FC: 1) with onset in the first 12 months old and 2) with onset after 13 months old.

## Methods

### Study design and study population

The study was an observational, single-center, retrospective cohort study, including consecutive cases of children/adolescents referred from the Brazilian Public Health System (SUS) for initial evaluation of constipation attended at a single Pediatric Gastroenterology Outpatient Clinic. Patient data were collected in a pre-designed standard protocol, and the parents answered all the questions during the first pediatric clinic visit. All data were stored in a database of Excel spreadsheets (Microsoft, Redmond, Washington). Pediatric gastroenterologists manage patients. Inclusion criteria: age between 01 months to 15 years of age, with a diagnosis of FC defined according to the Rome Criteria III<sup>15,16</sup> between January 2015 to August 2016. and from September 2016 to December 2018, according to the Rome IV criteria.<sup>17,18</sup>

Exclusion criteria: constipation of organic etiology; or associated with chronic health problems such as neurological, genetic, mental/psychiatric disorders or growth and development disorders. The stool form was evaluated using the Brazilian version of the Bristol Stool Form Scale.<sup>19</sup> The patients' final diagnoses of FC were determined after four months of follow-up by two experienced pediatric gastroenterologists (MAC, NCM). Approval was obtained from the ethics committee of our institution (CAAE 90158218.0.0000.5411).

### Statistical analysis

Statistical analysis was performed using GraphPad Prism version 7.00 for Windows (GraphPad Software, San Diego, CA). The Kolmogorov-Smirnov test was used to verify whether the variables had a normal distribution and to define the tests between parametric

and non-parametric. Categorical variables are presented as counts (n) and percentages (%) and analyzed using Fisher's exact test. Continuous variables were expressed as Median and Interquartile Range (25-75) and the comparison between groups using the Mann-Whitney test. Statistical tests were two-tailed, and the significance level was  $p < 0.05$ .

## Results

Five hundred and four children were identified with constipation at their initial visit. Thirty-two were excluded based on the inclusion and exclusion criteria and insufficient documentation for an FC diagnosis (i.e., the clinic record did not characterize constipation in terms of the Rome III-IV criteria). Thus, the remaining 472 children, 225 with onset within the first 12 months and 247 after 13 months, were included. Table 1 presents the baseline characteristics. There was a long time to first visit in those with onset in the first 12 months of life. Parents have a good education, and the mother is the primary informant. The family lives in a house with few rooms and a crowding index of 0.8. There is no difference in BMI/age scores between the two groups.

Table 2 presents that FC onset in the first 12 months has more scybalous stools, painful defecation, bloody stools, a lower proportion with bowel toilet training, and bladder control. There was no statistically significant difference in the proportion of fecal incontinence, vomiting, anorexia, and abdominal pain associated with FC. Table 3 compares treatment with laxatives before and after the first consultation at the specialized clinic. In FC starting in the first 12 months of life, only half of the children (55%) were treated with laxatives, and an entire group used rectal treatment. No difference between Sodium Picosulfate and Polyethylene Glycol (PEG 3350) laxatives was prescribed at the specialized clinic.

**Table 1** Comparison of children's baselines characteristics according to the age of functional constipation onset

	≤12 months old n=225 (48%)	≥13 months old n=247 (52%)	p<
	Median (IQR)		
Sex: Female (%)	43	42	ns
First-born child (%)	64	42	ns
Age at the first visit, mo	76 (43-108)	90 (65-120)	0.0001
Age of constipation onset, mo	3 (3-7)	44 (26-72)	0.0001
Time to first visit, mo	68 (32-103)	40 (18-64)	0.0001
Age of mothers, years	32 (28 - 36)	34 (29 - 39)	ns
Age of fathers, years	35 (31 - 42)	36 (32 - 43)	ns
Mothers' schooling	12 (9 - 12)	12 (9 - 12)	ns
Fathers' schooling	10 (9- 12)	10 (6 - 12)	ns
Respondent (mother) (%)	84	83	ns
Number of rooms	5 (4 - 6)	5 (4 - 6)	ns
Number of people at home	4 (3 - 4)	4 (3 - 4)	ns
Number of children at home	2 (1-2)	2 (1-2)	ns
Crowding index (person/room)	0.8 (0.6 -1)	0.8 (0.6 -1)	ns
z score Bowel Mass Index /Age	0.2 (-0.5 - 1.2)	0.6 (-0.35-1.8)	ns

IQR, interquartile range; ns, no significant

**Table 2** Comparison of the children's clinical characteristics according to the age of functional constipation onset

	≤12 months old n=225 (%)	≥13 months old n=247 (%)	p<
Defecation frequency xx/week*	2 (1-3)	2 (1-7)	ns
Scibalous	53	32	0.0002
Large feces	48	56	ns
Hard bowel movement	50	51	ns
Straining on defecation	89	82	ns
Painful defecation	76	61	0,001
Blood in stool	46	30	0.0004
Fecal incontinence >1/week	44	52	ns
Bristol stool form scale*	2(1-2)	2(1-2)	ns
Vomiting	10	8	ns
Anorexia	15	13	ns
Abdominal pain	63	61	ns
Bowel toilet trained	76	93	0.0003
Bladder control	80	96	0.0001
Noturnal enuresis	12	9	ns

\*Median and IQR (Interquartile Range); ns =no significant

**Table 3** Comparison of treatment with laxatives before and after the first consultation according to the age of functional constipation onset

	≤12 months old n=225 (%)	≥13 months old n=247 (%)	p<
<b>Treatment before the first visit</b>			
Laxatives (all prescribed)	55	72	ns
Liquid paraffin	19	15	ns
Rectal laxatives (glycerin suppository)	54	5	0.0001
<b>Treatments indicated in the first visit</b>			
Laxatives (all prescribed)	79	92	0.0007
Sodium picosulfate	71	79	ns
Polyethylene glycol (PEG 3350)	21	18	ns
Lactulose	1	1	ns
Liquid paraffin	30	35	ns

ns =no significant

## Discussion

The current observational, retrospective cohort study investigates the clinical and therapeutic approach of two groups of FC. In summary, there was a delay in referrals, scybalous stools, anal pain, bloody stools, and a significant proportion of rectal laxative treatment for the group ≤ 12 months before the first visit to a specialized clinic. In the current study, a substantial proportion (48%) of FC was initiated in the first year, with more severe clinical characteristics, denoting a significant workload and the need for specialized care. Two studies described that 16% to 40% of infants with FC develop symptoms during the first six months of life.<sup>7,20</sup> In the current study, the median and Interquartile Range of onset of FC for the subgroup <=12 months were (3 3-7 months). Possibly corresponding with the change from

breast milk to formula feeding or the introduction of solids foods as a trigger for the onset of FC.<sup>21</sup>

Although standard definitions and criteria have been formulated to describe FC, these are only sometimes used in research and clinical practice. In this study, the diagnosis of FC is efficiently completed by history, physical examination, as an established protocol, and according to the Rome III- IV criteria, with no testing necessary. Indeed, these criteria established uniformity in the definition of FC, which enables comparison analysis.

So, adequate diagnoses will enable choosing the appropriate treatment, which is expected to improve the clinical outcomes of these patients. Our data showed that children with late onset of FC search for a specialized clinic sooner than children with an earlier onset—

consequently, long delays to the first visit proportionate undertreatment in primary care, like excess rectal laxatives. Delays in treatment with prolonged symptoms may worsen the prognosis for long-term resolution and exposure to potentially noxious medical testing and intervention. In the current study, many infants received ineffective therapeutic interventions. Therefore, it is imperative to recognize that an educational program must educate medical primary care clinicians about effective treatment options according to published procedures and avoid the consequences of poorly treated constipation.<sup>22-25</sup>

A distinguishing study reported painful defecation and hard stools in 43 and 92% of infants and young children, respectively.<sup>26</sup> Indeed, a history of painful or hard bowel movements may encourage the child to retain their stools to avoid this unpleasant experience. This can lead to a vicious cycle, where voluntary stool retention leads to increased water absorption from the feces, with hard stools and painful defecation.<sup>7,27</sup> Reducing fear and making the parents understand the underlying pathophysiological mechanisms is essential. The goal of treating FC is to restore a regular defecation pattern.

Non-pharmacological treatment includes parental education, reassurance, and regular dietary advice with sufficient dietary fiber. One study found that half of the physicians recommended a dietary intervention for FC.<sup>28</sup> However, nutritional advice may not be sufficient for infants, and laxatives may be required as the first-line treatment. In the present study, not surprisingly, only half of children with constipation onset before 12 months old has received laxative as therapy.

This study does have some limitations. First, include a sample of children seen in tertiary care visits. Thus, the results may not represent the entire Pediatric population and cannot be generalized. Secondly, the questionnaire did not include the relationship between neonatal factors to evaluate the risk for the development of FC, such as prematurity, antibiotic treatment, cesarean delivery, formula feeding, and hospital stay. The strengths include a large sample size, data obtained using protocols specially developed for the study, and standardized diagnosis methods, such as the Rome Criteria and the Bristol stool form scale.

## Conclusion

In conclusion, this current study demonstrates that FC is a common Functional Gastrointestinal Disorder affecting infants during the first months of life. The primary inadequate treatment and referral delay implies worsening symptoms, chronicity, and non-implementing North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines.

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## Authors' contributions

Mary de Assis Carvalho contributed to the conception of the work, analysis, and interpretation of the data, drafted the initial manuscript, and revised the article critically; Juliana Tedesco Dias collected the data and drafted the initial manuscript. Andrea Catherine Quiroz Gamarra, Cristian E. Moreno Sandoval, and José Hermann Avendaño Caraballo performed the collection of the data and interpretation of the data. Nilton Carlos Machado contributed to the conception of the work, analysis, and interpretation of the data, drafted the initial manuscript, and revised it critically.

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## Conflicts of interest

The authors declare no conflict of interest.

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