A Population-Based Study on the Epidemiology of Functional Gastrointestinal Disorders in Young Children

Ashish Chogle, MD, MPH[1], Carlos A. Velasco-Benitez, MD[2], Ilan J. Koppen, MD[3], Jairo E. Moreno, MD[4], Carmen R. Ramírez Hernández, MD[5], and Miguel Saps, MD[6]

Objective To perform a population-based study with Rome III criteria to describe the prevalence of functional gastrointestinal disorders (FGIDs) in children in Colombia.

Study design We conducted a multicity cross-sectional study to investigate the epidemiology of FGIDs in children 0-48 months of age using the Rome III criteria in Colombia. Children with organic medical diseases were excluded. Parents provided demographic information and completed the Spanish version of the Questionnaire on Pediatric Gastrointestinal Symptoms for Infants & Toddlers.

Results Parents of 1231 subjects completed the questionnaires; 48 children were excluded due to presence of organic diseases and being older than 48 months of age. Four hundred eighty children (40.5%) were diagnosed with at least 1 FGID according to the Rome III diagnostic criteria (49% female, median 12 months). Functional constipation was the most commonly diagnosed disorder in infants (up to 12 months of age) and children of ages 13-48 months (16.1% and 26.8%, respectively). Analysis revealed that the prevalence of FGID was significantly greater in children who were the only child in the family ($P = .003$), children who were first-born ($P = .007$), and children with divorced or separated parents. ($P = .001$).

Conclusions FGIDs are common in children younger than 4 years of age. Functional constipation and infant colic were the most common FGIDs in infants (up to 12 months of age), and functional constipation and rumination were the most common FGIDs in children 13-48 months of age. *(J Pediatr 2016;179:139-43).*

Functional gastrointestinal disorders (FGIDs) are common in children and adults.[1,2] Studies from the US,[1,3-5] Germany,[6] United Kingdom,[7] China,[8] Sri Lanka,[9] El Salvador,[1] Panama,[10] Ecuador,[11] and Colombia[12] have found a high prevalence of FGIDs in school-age children (range, 20%-29%). The prevalence in infants and toddlers largely is unknown. An international group of physicians, nutritionists, and educators who were surveyed on their perceived prevalence of FGIDs estimated that up to 30% of infants younger than 12 months had a FGID.[1] The survey found a great range of prevalence of FGIDs and heterogeneity in methods and definitions. Only 2 studies have used the Rome III criteria to diagnose FGIDs in infants and toddlers. None of these studies has been conducted in Latin America. A prospective study conducted in Italy and a large, cross sectional study in the US have investigated the prevalence of FGIDs in this age group by using the Rome III criteria.[1,2] The latter study found that 27% of infants/toddlers met criteria for at least 1 FGID.

Infection patterns and health care delivery vary by region. The use of antibiotics in the first 2 years of life,[3] intestinal and extraintestinal infections,[4] gastrointestinal allergies,[5] diet, breastfeeding time period, and early adverse life events[6] are likely to differ among countries. Ethnic differences, culture, parental beliefs, and coping abilities may affect the prevalence of FGIDs and the way the family and society relates to them. The Rome criteria are based on the report of clinical signs and symptoms, which at very young age are dependent exclusively on information provided by parents. Some of the criteria rely on the parents' interpretation of nonverbal child's behavior (painless or painful stools) and stool consistency (hard or unformed stools) and size (large diameter stools) that may vary by culture and the parents' own experience. Parental perception of illness and fears also are likely to vary by culture. The presence of FGIDs at early stages of life may have long-term consequences and influence the child's sick role in the family, perception of vulnerability, the family dynamics, parental quality of life, and health care use.[7]

The relevance of the aforementioned factors and their impact on the child and family life underscore the need for large studies that use standardized diagnostic criteria in children of different regions and ethnicity. Using the Rome III criteria, we conducted a multicity study to investigate the epidemiology of FGIDs in infants, toddlers, and children younger than 4 years of age in Colombia. Because of the dearth of data on the epidemiology of FGIDs in young children and the

FGID	Functional gastrointestinal disorder
QPGS-III IT	The Rome III Functional Gastrointestinal Disorders Questionnaire for Infants and Toddlers

From the [1]Division of Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Orange County, Orange, CA; [2]Department of Pediatrics, Universidad del Valle, Cali, Colombia; [3]Department of Pediatric Gastroenterology, Hepatology, and Nutrition, Nationwide Children's Hospital, Columbus, OH; [4]Clinica Reina Sofía, Grupo de Clínicas Colsanitas, Bogotá, Colombia; [5]Hospital Regional María Inmaculada, Florencia, Colombia; and [6]Department of Pediatric Gastroenterology, Hepatology, and Nutrition, Nationwide Children's Hospital, Columbus, OH

The authors declare no conflicts of interest.

http://dx.doi.org10.1016/j.jpeds.2016.08.095

potential long-term implications of FGIDs, our study has the potential to fill an important void in the literature and help understand the pathogenesis of FGIDs in children.

Methods

We performed a cross-sectional study in children 0-48 months of age presenting for a well-child visit at primary care clinics in Colombia. Colombia (northwest of South America) is the third-most populous country (48 million inhabitants) in Latin America, after Brazil and Mexico. The study was conducted in 4 geographically dispersed cities of various sizes; 2 large cities, Bogotá (population 6 840 116; Department of Cundinamarca) and Cali (population 2 119 908; Department of Valle del Cauca) and 2 small cities, Florencia (population 143 871; Department of Caquetá) and San Andrés de Sotavento (population 63 147; Department of Córdoba). Colombia is an ethnically and culturally diverse country, with its people descending from the original native inhabitants, Spanish colonists, Africans slaves, and immigrants from Europe and the Middle East. The climate in Colombia is varied but mostly tropical and isothermic as the result of its proximity to the equator. All the cities included in the study have a tropical-subtropical climate. These factors may be important at the time of comparing results of studies from different countries.

The Rome III Functional Gastrointestinal Disorders Questionnaire for Infants and Toddlers (QPGS-III IT) is a validated tool to diagnose FGIDs according to the Rome III criteria.[7] The questionnaire is only available in the English language. To conduct this study, first, the QPGS-III IT was translated into Spanish (QPGS-III IT-Spanish) and adapted to the local language by 3 bilingual physicians of the Functional International Digestive Epidemiological Research Survey. The Spanish version subsequently underwent reverse translation and was assessed for fidelity by comparison of the original English version of the QPGS-III IT with the translated version. Focus groups of mothers attending primary care clinics confirmed their understanding of the terms of the questionnaire.

Local nurses at primary care clinics invited all consecutive parents of children 1-48 months of age of both sexes (age group of infant/toddler version of the Rome III criteria) arriving for well child visits to participate in an epidemiologic study. Consenting parents received an explanation on the definitions and symptoms of FGIDs before completing the QPGS-III IT-Spanish. Parents/caregivers provided information regarding medical history and the sociodemographic (age, sex) and familial (family structure and size, family history of gastrointestinal disorders) variables of the participants. Subjects with organic medical diseases and those more than 48 months of age were excluded. The institutional review board and Human Subjects Committee of Universidad del Valle of Cali, Colombia, approved the study. The Rome III criteria are included in the **Appendix** (available at www.jpeds.com).

Statistical Analyses

Prevalence data were pooled from the 4 cities for the initial analysis. We evaluated group comparisons by using a 2-sample *t* test and χ^2 test as appropriate. To evaluate possible risk factors for FGIDs, univariate analysis with OR calculation and logistic regression analysis were performed between each of the exposure variables of interest: the sociodemographic variables (age, sex), the familial variables (family structure and size, family history of gastrointestinal disorders), and the effect variable (presence or absence of FGIDs). *P* values of less than .05 were considered statistically significant.

Results

Parents/caregivers of 1620 children were invited to participate. Of these, 1530 (94.4%) agreed to be included in the study. Parents of 1231 children (75.9%) completed the questionnaires. Twenty-four children (1.5%) were excluded from the study due to presence of organic disease (cow milk protein allergy, bronchopulmonary dysplasia, organic constipation, lactose intolerance, laryngomalacia, gastroesophageal reflux disease). Another 24 children (1.5%) were excluded due to being more than 48 months of age (wrongly included). A total of 1183 children (73%) were included in the study. (**Figure**; available at www.jpeds.com). There was no significant difference in age or sex between the children who participated in the study and those who were excluded from the study.

Participants had a mean age of 19.3 months ± 15.3 SD (median 15 months, range 1-48 months) and 585 (49.5%) were female participants (**Table I**); 527 children of ages 1-12 months, 276 children of ages 13-24 months, 186 children of ages 25-36 months, and 194 children of ages 37-48 months of age. Four hundred eighty children (40.5%) fulfilled the Rome III

Table I. Sociodemographic and familial variables in the study population

Age	
Age range	1-48 mo
Mean ± SD	19.3 ± 15.3 mo
Median age	15 mo
Sex	
Female	585 (49.4%)
Male	598 (50.6%)
Cities	
Cali	616 (52.1%)
Florencia	330 (27.9%)
Sotavento	119 (10.1%)
Bogotá	118 (10.0%)
Parents separated/divorced	
No	768 (64.9%)
Yes	415 (35.1%)
Only child	
No	597 (50.5%)
Yes	586 (49.5%)
First-born child	
No	564 (47.7%)
Yes	619 (52.3%)
Family history of FGIDs	
No	1174 (99.2%)
Yes	9 (0.8%)
Previous history of diarrhea	
No	1036 (87.6%)
Yes	147 (12.4%)

Table II. Prevalence of FGIDs in infants and toddlers (1-48 mo of age) from Colombia

	Age group, mo	Total children in the age groups	Diagnosed with FGID	%
Total	1-48	1183	480	40.6
Regurgitation	1-12	527	42	8.0
Rumination	1-12	527	38	7.2
	13-48	656	18	2.7
Cyclic vomiting	1-12	527	20	3.8
syndrome	13-48	656	40	6.1
Colic	1-4	259	27	10.4
Functional	1-12	527	10	1.9
diarrhea	13-48	656	3	0.5
Dyschezia	1-5	308	10	3.2
Functional	1-12	527	85	16.1
constipation	13-48	656	176	26.8

criteria for at least 1 FGID, of whom 235 (49%) were female participants. Functional constipation was the most commonly diagnosed disorder in infants (up to 12 months of age) and children of ages 13-48 months (16.1% and 26.8%, respectively) (**Table II**). There was an overlap between FGID diagnoses in 5% of children. Of the children diagnosed with FGIDs, 95% children qualified for 1 FGID diagnosis, 4.6% for 2, and 0.4% for 3 FGID diagnoses.

The sociodemographic, familial, clinical, and environmental variables of children with and without FGIDs were compared (**Tables III** and **IV**). Multiple regression analysis revealed that the prevalence of FGIDs was significantly greater in children who were the only child in the family ($P = .003$), children who were first-born ($P = .007$), and children with divorced or separated parents. ($P = .001$). Having a family history of FGIDs did not influence the prevalence in children ($P = .8$).

Discussion

We surveyed the parents of children younger than 4 years of age presenting to primary care clinics for well child visits in 4 Colombian cities. We found that 40.5% of studied children fulfilled the Rome III criteria for at least 1 of the FGID diagnoses. In a study conducted in 320 mothers in the US, van Tilburg et al[2] found that 27% of US children younger than 3 years of age had FGIDs. Functional constipation was found to be more prevalent in Colombian infants (16.1% vs 4.7%) than their US counterparts. The reason for this difference in functional constipation is unclear. Dietary factors or parental interpretation of the stool characteristics could explain these differences. Studies conducted in school-age children (8-18 years) of the same cities as this study found a lower prevalence of functional constipation (11.9%) than the prevalence obtained in children of ages 1-4 years (26.8%) in the current study.[8] Koppen et al[9] assessed parental perception of stool consistency compared with the Bristol Stool Form Scale. Their data were collected from the same mothers/caregivers who were recruited for our study. There was only fair agreement between the Bristol Stool Form Scale and parental report of stool consistency We cannot rule out that the subjective nature of some of the Rome III criteria for functional constipation (painful stools, large diameter stools) could be interpreted differently by parents of different countries and cultures what could at least partially explain the differences in prevalence among studies.

The prevalence of infant dyschezia found in the current study (1 month, 5.7%; 2-5 months, 2.5%) also was greater than the prevalence found in a national study of health care doctors in the Netherlands (1 month, 3.9%; 3 months 0.9%).[10] Rates of infantile colic have been reported previously to be between 3% and 28% worldwide.[11] We found a 10.4% prevalence rate of colic. van Tilburg et al[2] found a lower prevalence of infant colic (5.9%) using the QPGS-III IT. Similarly to functional constipation, the differences in interpretation between mothers/caregivers in the US and Colombia of the criterion "straining and crying before successful passage of soft stools" could explain the difference in prevalence. Obtaining accurate data on the prevalence of infant colic is important because colic has been considered a risk factor for developing FGIDs later in life[13] and thus the use of preventative measures potentially could decrease FGIDs in older children.[12]

Studies on infant regurgitation have shown a wide range of prevalence. A population-based study from Italy has found a low prevalence (7%) of infant regurgitation that is comparable with our data.[14] The study relied on pediatricians as reporters of the child symptoms. van Tilburg et al[2] have found a greater prevalence of regurgitation (25.9%) in US infants. The reason the existence of such a high difference between children in Colombia and the US is unknown. Because the main positive criterion for the diagnosis of regurgitation is the presence of regurgitation 2 or more times per day, we cannot exclude that differences in feeding techniques or focused attention to the number of regurgitation episodes could explain this high difference in prevalence.

Other than the study of van Tilburg et al,[2] the prevalence of cyclic vomiting, functional diarrhea, and rumination syndrome has not been studied in this age group because of a previous lack of standardized questionnaires. Our data showed

Table III. Relationship between the presence of FGIDs and sociodemographic, familial, and clinical variables in infants and children from Colombia

		OR	95% CI	*P* value
Age	1-12 mo	1		
	13-48 mo	0.98	0.97-0.99	.000
Sex	Female	1		
	Male	1.03	0.81-1.31	.77
Separated/divorced parents	No	1		
	Yes	1.5	1.16-1.94	.002
Only child	No	1		
	Yes	1.42	1.12-1.81	.0028
First born child	No	1		
	Yes	1.38	1.08-1.75	.0068
Family history of FGIDs	No	1		
	Yes	1.17	0.23-5.47	.81
Previous history of diarrhea	No	1		
	Yes	1.30	0.9-1.87	.13

Table IV. Relationship between the individual FGIDs and sociodemographic, familial, and clinical variables in infants and children from Colombia

	Regurgitation		Rumination		Colic		Constipation		Dyschezia		Functional diarrhea		CVS	
	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value
Separated/divorced parents														
No	1.00		1.00		1.00		1.00		1.00		1.00		1	
Yes	0.29	<.01*	0.51	.54	0.94	.92	2.24	<.01*	1.13	.80	0.84	.67	1.07	.79
Only child														
No	1.00		n/a		1.00		1.00		1.00		1.00		1	
Yes	0.57	.09			0.82	.68	2.46	<.01*	3.01	.02*	0.59	.17	1.09	.73
First-born child														
No	1.00		1.00		1.00		1.00		1.00		1.00		1	
Yes	0.60	.12	0.78	.25	0.81	.65	1.95	<.01*	2.93	.02*	0.59	.16	1.29	.33
Family history of FGIDs														
No	n/a		n/a		n/a		1.00		n/a		1.00		n/a	
Yes							2.61	.32			4.28	.14		
Previous history of diarrhea														
No	1.00		1.00		1.00		1.00		n/a		1.00		1	
Yes	0.39	.19	1.74	.61	1.27	.82	0.79	.52			0.42	.23	2.5	<.01*

CVS, cyclic vomiting syndrome; *n/a*, not available.
*Statistically significant.

that approximately 0.5%-7% of studied children are afflicted with these FGIDs. Except for functional diarrhea and regurgitation, the prevalence of all other FGIDs was greater in Colombian infants and toddlers than the US children. It is unclear whether differences in parent's recruitment methods could explain some of the variation in prevalence between both studies. van Tilburg study[2] used internet based recruitment while we recruited consecutive parents from primary care visits.

The analysis of the possible association of FGIDs with predisposing risk factors revealed some interesting findings. Similarly to van Tilburg et al,[2] we did not find sex predominance in FGIDs (51% male and 49% female participants, $P = .77$). These results are in line with other studies by our group conducted in older Colombian children that also have found a similar prevalence of FGIDs in both sexes. Although an adult meta-analysis has shown a female predominance in irritable bowel syndrome,[15] the sex data in children are mixed, and the time of transition from a pediatric sex pattern to adult pattern is still unknown. Moreover, the meta-analysis on the relation between sex and IBS in adults did not show sex predominance in Latin America as oppose to the US and Europe.[15] It has been reported previously that functional abdominal pain and constipation in older children and adolescents are more common in members of the same families.[16,17] We did not find an association between family history and increased prevalence of FGIDs except in the case of functional constipation. The US study on FGIDs in infants and toddlers also found that parents of children who had hard stools had hard stools themselves.[2] Our study in older children in Colombia did not find FGIDs to be more common in families with parents who had FGIDs.[18] The prevalence of FGIDs was greater in children who were the only child in the family, children who were first-born, and children with divorced or separated parents (**Table IV**). Studies by Functional International Digestive Epidemiological Research Survey in school-age children in Colombia[18] and other Latin American countries[19] also showed that children with divorced or separated parents also had a greater prevalence of FGIDs. Early domestic adversities such as divorced or separated parents could trigger onset of FGIDs in children.[20] In our study, there was a greater prevalence of regurgitation and constipation in children with divorced or separated parents. Constipation and dyschezia were more common in the only child in the family and first-born child. Greater prevalence of FGIDs in an only child and first-born child could potentially be explained by a heightened attention (attention bias) to the symptoms of the only child in the house.

Some of the strengths of our study include the use of validated questionnaires that were specially translated to local language by the use of standardized methods for this study, the large sample size, and the multicity sites that enhanced the diversity and external validity of our sample. Limitations of our study include the selection of a sample of children who were being seen in primary care offices for well child visits that may not be representative of the entire pediatric community in Colombia. Also, given the ethnic, dietary, and environmental differences, these conclusions may not be extrapolated to other countries in the region. There could be a potential selection bias with mothers of symptomatic children visiting primary care providers more often than mothers of asymptomatic children. We cannot exclude that the educational intervention on FGIDs given before the completion of the study could have resulted in parents over-reporting the child's symptoms; however, at the time of design of the study and although we were cognizant of this potential risk, we preferred this option to the possibility of parents misreporting symptoms because of a lack of understanding. The diagnosis of functional constipation was based on a questionnaire, and a physical examination (including digital rectal examination) was not done to diagnose the condition. If a physical examination was done, it could have resulted in more children fulfilling the Rome III criteria for functional constipation. Performing a physical

examination with a digital rectal examination in all the enrolled children without a medical indication and for research purposes only would be ethically inappropriate. We would like to emphasize that the questionnaire that we have used is only a screening tool. A complete evaluation by a physician is always necessary to diagnose FGIDs. Our questionnaire did not include questions about the age of toilet training and the occurrence of fecal incontinence after acquiring toileting skills. This omission, along with lack of a comprehensive physical examination by the physicians, may have resulted in underestimation of the actual prevalence of functional constipation especially in the older children in our study.

In conclusion, the current findings suggest that FGIDs are common in children younger than 4 years of age in Colombia. Functional constipation and infant colic were the most common FGIDs in infants, and functional constipation and rumination were the most common FGIDs in children 1-4 years of age. We found greater prevalence rates of FGIDs than a study from the US that used similar questionnaires and diagnostic criteria; however, the US sample consisted of individuals who participated in previous online panels, whereas the mothers/caregivers in our study were recruited at the clinic visit. Large prospective longitudinal studies are needed to determine whether FGIDs in infants and toddlers persist into childhood, adolescence, and adulthood. Further studies in children of different countries will be important to further elucidate the role of the different bio-psycho-social factors in the pathogenesis of FGIDs. ■

Submitted for publication Apr 14, 2016; last revision received Jul 5, 2016; accepted Aug 26, 2016

Reprint requests: Ashish Chogle, MD, MPH, Division of Pediatric Gastroenterology, Hepatology, & Nutrition, Children's Hospital of Orange County, 1201 W La Veta Ave, Orange, CA 92868.

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Appendix. Rome III diagnostic criteria for FGIDs: infant/toddler

Infant regurgitation
Diagnostic criteria must include both of the following in otherwise-healthy infants 3 wk to 12 mo of age:
1. Regurgitation 2 or more times per day for 3 or more weeks
2. No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing

Infant rumination syndrome
Diagnostic criteria must include all of the following for at least 3 mo:
1. Repetitive contractions of the abdominal muscles, diaphragm, and tongue
2. Regurgitation of gastric content into the mouth, which is either expectorated or rechewed and reswallowed
3. Three or more of the following:
   a. Onset between 3 and 8 mo
   b. Does not respond to management for gastroesophageal reflux disease, or to anticholinergic drugs, hand restraints, formula changes, and gavage or gastrostomy feedings
   c. Unaccompanied by signs of nausea or distress
   d. Does not occur during sleep and when the infant is interacting with individuals in the environment

Cyclic vomiting syndrome
Diagnostic criteria must include both of the following:
1. Two or more periods of intense nausea and unremitting vomiting or retching lasting hours to days
2. Return to usual state of health lasting weeks to months

Infant colic
Diagnostic criteria must include all of the following in infants from birth to 4 mo of age:
1. Paroxysms of irritability, fussing or crying that starts and stops without obvious cause
2. Episodes lasting 3 or more h/d and occurring at least 3 d/wk for at least 1 wk
3. No failure to thrive

Functional diarrhea
Diagnostic criteria must include all of the following:
1. Daily painless, recurrent passage of three or more large, unformed stools
2. Symptoms that last more than 4 wk
3. Onset of symptoms that begins between 6 and 36 mo of age
4. Passage of stools that occurs during waking hours
5. There is no failure-to-thrive if caloric intake is adequate

Infant dyschezia
Diagnostic criteria must include both of the following in an infant younger than 6 mo of age
1. At least 10 min of straining and crying before successful passage of soft stools
2. No other health problems

Functional constipation
Diagnostic criteria must include one month of at least 2 of the following in infants up to 4 years of age:
1. Two or fewer defecations per week
2. At least 1 episode/week of incontinence after the acquisition of toileting skills
3. History of excessive stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large diameter stools that may obstruct the toilet

Accompanying symptoms may include irritability, decreased appetite, and/or early satiety. The accompanying symptoms disappear immediately following passage of a large stool.

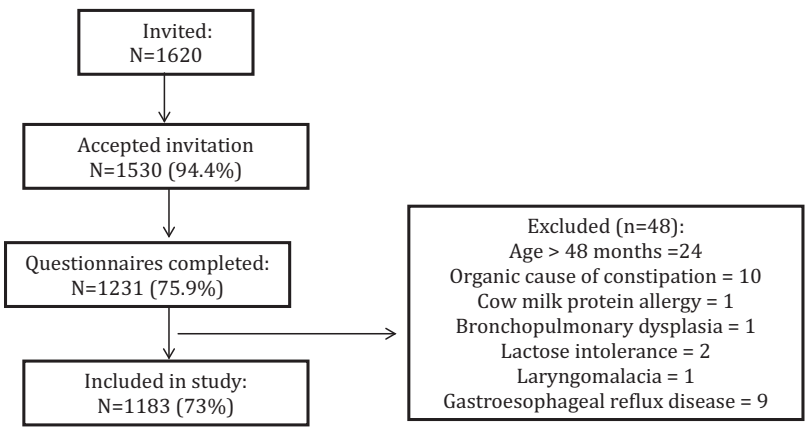

Figure. Flow diagram of subject recruitment and inclusion.