

Coexistence of functional gastrointestinal disorders in Latin American infants and preschoolers

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Abstract

Introduction: Coexistence of functional gastrointestinal disorders (FGID) in infants and preschool children has been described, but there is little literature on the main types of FGID coexistence or their characteristics. **Objective:** This study describes the prevalence and possible associations of FGID coexistence among Latin American infants and preschool children. **Methodology:** This is a prevalence study of infants and preschool children conducted in Colombia, Ecuador, Nicaragua and Panama. Children included were outpatients and emergency patients who were identified according to the Rome III Criteria in Spanish as suffering from regurgitation, rumination syndrome, cyclic vomiting syndrome, colic, functional diarrhea, functional constipation and/or dyspepsia. Age, sex and origin of patients were registered. Statistical analyses included Student's T test, chi squared test, Fisher's exact test, univariate analysis, multivariate analysis and calculation of odds ratios and 95% confidence intervals with $p < 0.05$ set as significant. **Results:** Two thousand four hundred and seventeen children were included. Their age range was 2.4 months to 19.8 months of age, and 51.3% were male. The proportion of patients with a diagnosis of at least one FGID was 35.7%. FGID coexistence was found in 3.6% of the patients. The most frequent combination was rumination syndrome plus functional constipation. There were predominances of males, infants and Colombian children in the total sample. **Conclusion:** The most commonly coexisting FGIDs in this group of Latin America infants and preschool children were infant rumination syndrome and functional constipation which were found together most frequently among boys who were under 24 months old.

Keywords

Infants, pre-school, prevalence, gastrointestinal diseases.

INTRODUCTION

According to the Rome IV criteria, functional gastrointestinal disorders (FGIDs) in infants and preschoolers are defined as a diverse and variable combination of recurrent or chronic gastrointestinal symptoms that are not attributable to other medical conditions after adequate medical evaluation. (1) Globally, the prevalence of FGIDs defined by the Rome III criteria ranges between 27.1% and 38.0% in children between 0 and 4 years old. (2) Recently, Robin et al. described a Rome IV prevalence of 24.7% in children

under 3 years of age in the United States. (3) Prevalences between 11.6% and 47.8% have been described for these FGIDs in Latin America, according to the Rome III criteria in Spanish. Prevalence varied by place with 47.8% among hospitalized patients, 38.2% in a pediatric emergency department, 26.6% in a private hospital outpatient clinic and 11.6% in an outpatient clinic for growth and development of healthy children. (4)

Although coexistence of FGIDs has been described, there is little literature on primary coexisting FGIDs (c-FGIDs) or the characteristics of this group of children. School chil-

dren and adolescents have been found to have an 8.4% prevalence of c-FGIDs, primarily coexistence being irritable bowel syndrome and functional abdominal pain which occurs predominantly in girls. (5) Study of FGIDs coexistence will provide a better understanding of the pathophysiology and pathogenesis of the biopsychosocial model of FGIDs in this age group from the genetic, nutritional, environmental, psychosocial, cultural, socioeconomic and infectious points of view. This will allow better definition of its epidemiology, symptoms, comorbidities and effects on health related quality of life of infants and preschoolers.

The objective of this work is to describe prevalence of c-FGIDs and possible risk factors in Latin American infants and preschoolers.

MATERIALS AND METHOD

This is a descriptive, non-experimental, observational, cross-sectional study of prevalence carried out between May 1 and October 31, 2015 using the database of Functional International Digestive Epidemiological Research Survey Group (FINDERS). It was performed by a transnational research group made up of members of the Latin American Society of Pediatric Gastroenterology, Hepatology and Nutrition (SLAGHNP).

Standard data collection methods were used in all participating countries: Colombia, Ecuador, Nicaragua and Panama. Parents who signed informed consent for children under 4 years of age or the recipients were interviewed at hospitals and at outpatient clinics for development of healthy children in Colombia, Nicaragua and Panama, and at an emergency office in Ecuador. Sociodemographic variables recorded included age, sex and country of origin. Children with known histories of organic gastrointestinal disorders such as gastroesophageal reflux disease, cow's milk protein allergy, Hirschsprung's disease, cerebral palsy, vesicoureteral reflux, seizure syndrome, and heart disease were excluded. The Rome III questionnaire for pediatric gastrointestinal symptoms for infants and preschoolers (QPGS-III), which has been validated and tested in Spanish, was used to identify FGIDs. (6) According to the guidelines for Scoring Instructions for Infant/Toddler Report Form for the Rome III Diagnostic Questionnaire on Pediatric Gastrointestinal Symptoms for Infants and Toddlers, the FGIDs identified were infant colic (0-4 months), infant dyschezia (0-5 months), infant regurgitation (0-12 months), infant rumination syndrome (0-24 months), cyclic vomiting syndrome (0-48 months), functional diarrhea (0-48 months) and functional constipation (0-48 months). (7) For the purposes of this study and to allow comparisons of these results with the Rome IV criteria, all possible overlaps were taken into account. (1)

Infants between 0 and 24 months of age and preschoolers between 2 and 4 years were studied. C-FGID was defined as the presence of two or more FGIDs in the same child. The study was approved by the Ethics Committee of the Universidad del Valle de Cali in Colombia.

Given the possibility of transcription errors, 10% of the data were reviewed and then compared with the original forms. Statistical analysis using Stata 15 (StataCorp, College Station, TX) included the two-tailed Student's *t*, chi-square test and Fisher's exact test. Univariate and multivariate analyses were performed for possible c-FGID risk factors, Odds Ratios were calculated between the exposure variable of interest (sex, age, origin) and the effect variable (presence or absence of c-FGID). *p* < 0.05 was considered statistically significant.

RESULTS

We analyzed 2,417 children aged 2.4 ± 19.8 months (range 1 to 48): 1694 from Colombia, 322 from Ecuador, 203 from Nicaragua, and 198 from Panama. Of the total, 67.1% were infants between 1 and 24 months, and 51.3% were male sex. Some type of FGID was diagnosed in 35.7% of these children with functional constipation (19.7%) most prevalent across all age groups followed by infant rumination syndrome (7.2%) among infants and cyclic vomiting syndrome (4.0%) among preschoolers. Data are shown in Table 1.

Table 2 shows coexistence of FGIDs in individual children in the total sample of 2,417 Latin American children. Of the total sample without regard to age, 3.7% had overlapping FGIDs (3.3% with 2 FGIDs and 0.4% with 3 FGIDs). Of the total sample infants, 3.5% were infants with overlapping FGIDs while 0.2% of the total sample were preschoolers with overlapping FGIDs. The most common double overlaps were between infant rumination syndrome and functional constipation (1.0%), and the only triple overlap was among regurgitation, dyschezia, and functional constipation (0.1%).

Possible associations are shown in Table 3. There was a predominance of the male gender (OR 1.84; 95% CI: 1.134 to 3.02; *p* = 0.0083), of infants (OR 10.52; 95% CI: 3.88 to 39.87; *p* 0.0000) and of children from Colombia (OR 6.85; 95% CI: 1.78 to 58.37; *p* 0.0021) when there more than one FGID in the same child.

DISCUSSION

Prevalence of FGIDs in infants and preschoolers

In these 4 Latin American countries, the prevalence of FGIDs by the Rome III criteria in Spanish was 35.7%. This is lower than that described by Rouster et al. of 52.0% for the United States and lower than those reported by Chogle

Table 1. General characteristics of Latin American infants and preschoolers (N = 2,417)

	Latin America	Colombia	Ecuador	Nicaragua	Panamá
Total	2417	1694	322	203	198
Age (months) (X SD)	19.8 (15.0)	19.5 (15.3)	20.9 (13.7)	13.9 (8.9)	26.6 (16.2)
Infant (1-12 months) (n%)	1621 (67.1)	1153 (68.1)	203 (63.0)	186 (91.6)	79 (39.9)
Preschool (13-48 months) (n%)	796 (32.9)	541 (31.9)	119 (37.0)	17 (8.4)	119 (60.1)
Sex (n%)					
Female	1179 (48.8)	825 (48.7)	149 (46.3)	107 (52.7)	98 (49.5)
Male	1238 (51.2)	869 (51.3)	173 (53.7)	96 (47.3)	100 (50.5)
FGID (n%)					
Absent	1555 (64.3)	1008 (59.5)	218 (67.7)	176 (86.7)	153 (77.3)
Present	862 (35.7)	686 (40.5)	104 (32.3)	27 (13.3)	45 (22.7)
Infant regurgitation (n%) ***	89 (3.7)	57 (3.4)	10 (3.1)	16 (7.9)	6 (3.0)
Infant Rumination Syndrome (n%) **	117 (4.8)	110 (6.5)	1 (0.3)	4 (2.0)	2 (1.0)
Cyclic vomiting syndrome (n%) *	81 (3.4)	78 (4.6)	2 (0.6)	1 (0.5)	0 (0.0)
Infant colic (n%) *****	41 (1.7)	38 (2.2)	0 (0.0)	0 (0.0)	3 (1.5)
Functional diarrhea (n%)	24 (1.0)	22 (1.3)	0 (0.0)	2 (1.0)	0 (0.0)
Functional constipation (n%) *	475 (19.7)	354 (20.9)	87 (27.0)	3 (1.5)	31 (15.7)
Infant dyschezia (n%) ****	35 (1.5)	27 (1.6)	4 (1.2)	1 (0.5)	3 (1.5)

SD: standard deviation; FGID: functional gastrointestinal disorder; X: average.

* 0-48 months; ** 0-24 months; *** 0-12 months; **** 0-5 months; ***** 0-4 months.

Table 2. Coexistence of functional gastrointestinal disorders in Latin American infants and preschoolers (N = 2,417)

	Latin America	Colombia	Ecuador	Nicaragua	Panamá
Total	2417	1694	322	203	198
Without FGIDs	1555 (64.3)	1008 (59.5)	218 (67.7)	176 (86.7)	153 (77.3)
With FGIDs	862 (35.7)	686 (40.5)	104 (32.3)	27 (13.3)	45 (22.7)
Without overlap	774 (32.0)	604 (35.7)	102 (31.7)	25 (12.3)	43 (21.7)
With overlap	88 (3.7)	82 (4.8)	2 (0.6)	2 (1.0)	2 (1.0)
With 2 FGIDs	79 (3.3)	75 (4.3)	1 (0.3)	2 (1.0)	1 (0.5)
IRS-FC	25 (1.0)	24 (1.4)	0 (0.0)	0 (0.0)	1 (0.5)
REG-COL	11 (0.5)	11 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
CVS-FC	10 (0.4)	10 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
IRS-COL	5 (0.2)	5 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
REG-IRS	3 (0.1)	2 (0.1)	0 (0.0)	1 (0.5)	0 (0.0)
IRS-FD	2 (0.08)	1 (0.06)	0 (0.0)	1 (0.5)	0 (0.0)
REG-DISC	1 (0.04)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
With 3 FGIDs	9 (0.4)	7 (0.5)	1 (0.3)	0 (0.0)	1 (0.5)
REG-DISC-FC	2 (0.08)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.5)

COL: infant colic; FD: functional diarrhea; DISC: infant dyschezia; FC: functional constipation; REG: infant regurgitation; IRS: infant rumination syndrome; CVS: cyclic vomiting syndrome; FGIDs: functional gastrointestinal disorders.

et al. of 40.0% and 40.5% in Latin American countries, but it is higher than the results of van Tilburg et al. of 27.1% in the United States. (8-11) Vandenplas et al. found that for medical experts worldwide the most likely prevalences are

regurgitation (30.0%), colic (20.0%) and functional constipation (15.0%). (12) In this study, the most common FGID in infants was infant rumination syndrome. This differs from the findings of van Tilburg et al. and Rouster

Table 3. Possible risk factors in Latin American infants and preschoolers with coexistence of functional gastrointestinal disorders (N = 862)

	2 or more FGIDs		OR	95% CI	P
	No	Yes			
	774 (89.8)	88 (10.2)			
Age groups					
Preschool	259	4	1.00		
Infant	515	84	10.52	3.88-39.87	0.0000
Sex					
Female	388	31	1.00		
Male	386	57	1.84	1.14-3.02	0.0083
Country					
Ecuador	102	2	1.00		
Colombia	604	82	6.85	1.78-58.37	0.0021
Nicaragua	25	2	4.04	0.27-57.43	0.1432
Panamá	43	2	2.34	0.16-33.16	0.3878

FGIDs: functional gastrointestinal disorders.

Table 4. Comparison of prevalence in infants and preschoolers with coexistence of functional gastrointestinal disorders (N = 2,417)

	Velasco N = 2417	van Tilburg ¹⁰ N = 264	Chogle ⁹ N = 1183	Rouster ⁷ N = 332
2 FGIDs	9.2%	12.6%	4.6%	13.0%
3 or more FGIDs	1.0%	8.6%	0.4%	5.0%

FGIDs: functional gastrointestinal disorders.

et al. in the United States where regurgitation was most frequent. It also differs from the findings of Chogle et al. that the most common FGID in Latin American countries, where was infant colic. (9, 10)

The most common FGIDs in preschoolers in the 4 Latin American countries we studied was constipation as has been found in the United States and other Latin American countries. (8-11) Recently, Robin et al. described a Rome IV FGID prevalence of 24.7% in the United States. Regurgitation was the most frequent in infants while constipation was most frequent for preschoolers. (3) The variability of these prevalences depends on the regions in which the studies are conducted, and genetic, nutritional, environmental, psychosocial, cultural, socioeconomic and infectious factors typical of each country are involved.

Coexistence

The Rome IV criteria for infants and preschoolers do not discuss the issue of FGID coexistence in one patient. This

contrasts with the criteria for schoolchildren and adolescents for whom studies have shown that there may be coexistence of more than one functional abdominal pain disorder in one individual patient. However, those studies do not report their characteristics. (5, 13, 14) This study found that the prevalence of one child presenting two FGIDs was 9.2% while the prevalence of one child presenting three or more FGIDs was 1.0%, as shown in Table 4. Rouster et al., Chogle et al., and van Tilburg et al. have reported prevalence ranges for presentation of 2, or 3 or more FGIDs in the same child of 5.0% to 13.0%, 0.4% to 4.6%, and 8.6% to 12.6%, respectively. (8, 10, 11)

Few studies describe which FGIDs coexist. In this study, the most frequently occurring combination of two FGIDs was infant rumination syndrome and functional constipation. The most frequent coexistence of three FGIDs was regurgitation, infant dyschezia and functional constipation. The study by Vandenplas et al. does not detail coexistence of specific FGIDs, but it does analyze coexistence of clinical symptoms such as flatulence, abdominal distension, constipation, diarrhea, regurgitation and colic. That study found that the most frequent combinations were colic with abdominal distension and colic with regurgitation. (12)

This study found no cases of coexistence of infant dyschezia and functional constipation, but Kramer et al. reported Rome III prevalences for infant dyschezia of 3.9% at one month of age, 0.9% at three months of age, and 0.9% at 9 months of age. Four of the children in that study had coexisting infant dyschezia and functional constipation. (15) Robin et al. have described a 9.6% Rome IV rate of FGID coexistence. (3)

Associations

Robin et al. and van Tilburg et al. found no statistical differences in gender or race, and in contrast to our study, they found that more boys were affected than girls between 0 and 2 years of age. (3, 11)

The strengths of this study include its large sample size and the fact that it was conducted private and public outpatient clinics, hospitals and emergency rooms in several Spanish-speaking Latin American countries. A single methodology, that proposed by FINDERS, was used in all countries to allow comparison.

Among the limitations of the study is the possibility that the results cannot be generalized throughout Latin America even though it includes cities from several countries. In addition, we did not perform a systematic evaluation or anamnesis of the children surveyed, and simultaneous medical diagnoses could have existed that are not described in the study. Also, other possible risk factors other than

sociodemographic factors were not included which may explain the biopsychosocial model of this entity.

In the future, multicenter intercultural epidemiological studies with large sample sizes according to the Rome IV criteria are needed to determine FGIDs' impacts on quality of life. Research on the pathophysiology and genetic, metabolic and neurophysiological characterizations of most FGIDs are also needed since their pathophysiology is poorly understood. (1)

In conclusion, there is a low prevalence of c-FGIDs among infants and preschoolers in Latin America, with a predominance in males and in infants under 24 months. Infant rumination syndrome and functional constipation are the most frequent presentations. This invites future studies to deepen our understanding of FGID coexistence in this age group.

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