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ORIGINAL ARTICLE

The frequency of and factors affecting functional gastrointestinal disorders in infants that presented to tertiary care hospitals

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Abstract

This study aimed to determine the prevalence of infantile functional gastrointestinal disorders (FGIDs) based on Rome IV diagnostic criteria, and to determine the associated patient demographic and nutritional characteristics. A total of 2383 infants aged 1–12 months which were evaluated by 28 general pediatricians and pediatric gastroenterologists on the same day at nine tertiary care hospitals around Istanbul, Turkey, between November 2017 and March 2018, were included in the study. Patients included consulted the pediatric outpatient clinics because of any complaints, but not for vaccines and/or routine well child follow-ups as this is not part of the activities in the tertiary care hospitals. The patients were diagnosed with FGIDs based on Rome IV diagnostic criteria. The patients were divided into a FGID group and non-FGID group, and anthropometric measurements, physical examination findings, nutritional status, risk factors, and symptoms related to FGIDs were evaluated using questionnaires. Among the 2383 infants included, 837 (35.1%) had ≥1 FGIDs, of which 260 (31%) had already presented to hospital with symptoms of FGIDs and 577 (69%) presented to hospital with other symptoms, but were diagnosed with FGIDs by a pediatrician. Infant colic (19.2%), infant regurgitation (13.4%), and infant dyschezia (9.8%) were the most common FGIDs. One FGID was present in 76%, and ≥2 FGIDs were diagnosed in 24%. The frequency of early supplementary feeding was higher in the infants in the FGID group aged ≤6 months than in the non-FGID group ($P = 0.039$).

Conclusion: FGIDs occur quite common in infants. Since early diversification was associated with the presence of FGIDs, nutritional guidance and intervention should be part of the first-line treatment. Only 31% of the infants diagnosed with a FGID were presented because of symptoms indicating a FGID.

Keywords Infant colic · Infant regurgitation · Dyschezia · Functional constipation · Functional diarrhea · Rome IV criteria · Functional gastrointestinal disorder

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What is Known:
- *The functional gastrointestinal disorders (FGIDs) are a very common disorder and affect almost half of all infants.*
- *In infants, the frequency of FGIDs increases with mistakes made in feeding. When FGIDs are diagnosed in infants, nutritional support should be the first-line treatment.*

What is New:
- *This study shows that only a third of children presented to hospital because of the symptoms of FGIDs, but pediatricians were able to make the diagnosis in suspected infants after appropriate evaluation.*
- *The early starting of complementary feeding (<6 months) is a risk factor for the development of FGIDs.*

Introduction

Functional gastrointestinal disorders (FGIDs) are characterized by a variable combination of age-related, chronic, and recurrent symptoms that cannot be attributed to structural or biochemical abnormalities. Usually the symptoms tend to improve as an infant grows and develops [1]. It remains unknown if FGIDs accompany physiological development or are caused by impaired behavioral responses to internal-external stimuli [2]. Since children cannot report symptoms in a reliable or reproducible way before the age of 8 years, FGIDs are diagnosed according to physical examination and history information provided by the care givers. Various definitions, classifications, and diagnostic criteria have been developed for FGIDs, including the Rome III criteria published in 2006 [3]. Many subsequent studies on infantile FGIDs and the fact that Rome III criteria are based on experience without evidence led to the development of updated and more objective diagnostic criteria such as Rome IV (1). Studies based on Rome III criteria show that ≥1 FGIDs are observed in approximately 50% of infants, especially infantile colic, regurgitation, and constipation [4]. Sometimes only 1 FGID occurs in an infant, whereas other times ≥2 can occur. In cases of ≥2 FGIDs, the negative effects on quality of life are more severe [5].

It is never recommended to cease breastfeeding because of the presence of a FGID in an infant as FGIDs also commonly occur in infants that are formula fed. Determining the factors affecting FGIDs in breastfed infants will provide very useful information for reducing the symptoms [6, 7]. The present study aimed to determine the prevalence of infantile FGIDs based on Rome IV diagnostic criteria, and to determine the associated patient demographic and nutritional characteristics.

Methods

Study design and cohort

There were 15,940 outpatients aged <18 years that were evaluated by 28 pediatricians and pediatric gastroenterologists at nine tertiary hospitals around Istanbul, Turkey, between November 2017 and March 2018. These consisted of patients who applied to pediatric outpatient clinics because of any complaints (not for vaccines and/or routine well child follow-ups). Patients admitted to the pediatric emergency department were not included in the study. Among these patients, there were 2416 infants aged 1–12 months, of which 2383 infants were included in the study after excluding those with a known chronic disease and those receiving treatment for any other organic disease. All infants were examined at presentation by a pediatrician and the diagnosis of FGIDs according to Rome IV criteria [1] was confirmed by a pediatric gastroenterologist on the same day. The study lasted 5 months. During this period, children who were admitted to the hospital were examined by a general pediatrician and a pediatric gastroenterologist on the same day.

Study design

All patients aged 1–12 months that met the inclusion criteria and presented to hospital for any reason were included in the study. In some of the patients, the cause for presentation was symptoms of FGIDs (constipation, vomiting, excessive crying, etc.), whereas in others, it was symptoms of other diseases (cough, runny nose, ear pain, feeding problems, etc.). Whether presenting with symptoms of FGIDs or other symptoms, all infants were evaluated for the presence of criteria fulfilling Rome IV criteria for a FGID. Independent of the reason for the presentation at the outpatient clinic, the presence of absence of a FGID according to the Rome IV criteria at the moment of presentation or in the past was evaluated in each infant. The Cow Milk Symptom Score (CoMiSS®) was also determined in all infants, in order to eliminate the likelihood of cow milk allergy [8]. If the CoMiSS was ≥12 in infants with accompanying allergy findings, these were excluded because of the suspicion of allergy as diagnosis. Pediatricians examined each patient thoroughly. In addition to the primary cause of presentation, each patient was evaluated for FGIDs according to ROME IV criteria. Pediatricians collected data on the demographic and socioeconomic characteristics of the parents, as well as patient gender, birth weight, birth order, delivery method, breastfeeding status and duration, vitamins and medications used, and diet. Nutrition patterns in all infants were documented in detail, including breastfeeding, formula feeding, transition to supplementary feeding, and nutritional

contents. Data were also collected concerning feeding. Two-stage questionnaire forms were used. First of all, the questions in the study forms we created were asked one by one to the parents caring for the patient, and the answers received were filled in by the doctors who examined the patient. In the second stage, the ROME IV family questionnaires were distributed to the families and they were asked to answer and hand over them. All data were recorded in previously created follow-up files.

Anthropometric measurements

Weight, height, and length were measured using methods previously described by the World Health Organization (WHO) [9]. All scales and stadiometers were calibrated at each site before the study commenced. Measurements were performed using the same standardized Conformité Européene-marked scales and stadiometers (freely digital scale with stadiometer, Desis-M 101 B scale with stadiometer, and Seca 201 circumference measuring tape) at the nine study hospitals to ensure that all centers adhered to the same standards.

Statistical analysis

Descriptive statistics were used for continuous variables (mean ± SD, median, and range). The significance of correlations between categorical variables was determined using the chi-square test. For 2 × 2 categorical variable comparisons, in cases where the expected result was <5 in >20% of cells based on the chi-square test Fisher's exact test was used instead. The compliance of continuous variables to normal distribution was determined via the Shapiro-Wilk test. Comparison of 2 independent and normally distributed continuous variables was made with Student's *t* test, and comparison of 2 variables that were independent and not compatible with normal distribution was performed using the Mann-Whitney *U* test. The level of statistical significance was set at $P = 0.05$. Data were analyzed using IBM SPSS Statistics for Windows v.20.0 (IBM Corp., Armonk, NY, USA).

Results

Among the 2383 patients, 837 (35.1%) had ≥1 FGIDs, of which 260 (31%) had already presented with symptoms of FGIDs and were previously diagnosed with a FGID, and 577 (69%) presented to hospital because of other symptoms, but when evaluated by a pediatrician, they were diagnosed with a FGID. The most common symptoms of a FGID at presentation were vomiting (52.7%), crying (44.6%), abdominal bloating (30.4%), and constipation (29.6%). In the FGID group, the female/male ratio was 1:1.08, mean age was 3.6 ± 2.8 months, versus a female/male ratio of 1:1.09 and mean of 5.6 ± 3.3 months in the non-FGID group. Mean age was lower, the number of patients with a history of preterm delivery was higher, and the frequency of probiotic use was higher in the FGID group than in the non-FGID group ($P < 0.001$, $P < 0.001$, and $P = 0.005$, respectively). The incidence of exclusive breastfeeding during the first 6 months in the non-FGID group was 40.2%, versus 24.8% in the FGID group ($P < 0.001$). The demographic characteristics of the patients in both groups are presented in Table 1.

Infantile colic was the most frequent FGID (19.2%), followed by regurgitation (13.4%), and dyschezia (9.8%). Functional constipation was only present in 4.7% and functional diarrhea in 0.8%. Infant rumination syndrome (0.7%) and cyclic vomiting syndrome (0.5%) were rare. The majority of infants with a FGIDs were diagnosed with just one FGID (n = 636 [76%]), but 24% (n = 201 [24%]) has ≥ 2 FGIDs. Infantile colic was the most common single FGID (n = 214 [8.9%]), followed by regurgitation (n = 187 [7.8%]), dyschezia (n = 110 [4.6%]), and constipation (n = 95 [4.0%]), respectively. Functional constipation and diarrhea was the most common combination of FGIDs (n = 57 [2.3%]), followed by constipation and regurgitation (n = 52 [2.2%]), and regurgitation combined with diarrhea (n = 39 [1.6%]), respectively (Table 2).

In all, 20.9% of patients with combined FGIDs were born pre-term, whereas 13.4% of those with just 1 FGID were born pre-term; the difference was significant ($P < 0.001$). In addition, the age at onset of complaints was younger and a family history of atopy history was more common in the patients with ≥2 FGIDs ($P < 0.001$ and $P = 0.02$, respectively). Comparison of the demographic data in the patients with 1 FGID and ≥2 FGIDs is presented in Table 3. While 17 of 127 (13.4%) cases with FGIDs were born at 35–37 weeks of gestation, 62 (48.8%) were born at 30–35th gestational week and 48 (37.8%) <30 weeks of gestation. In the non-FGID group, 64/150 (42.7%) premature babies were born at the 35–37th gestational week, 58 (38.7%) at the 30–35th week, and 28 (18.7%) at <30 weeks. When both groups were compared, the ratio according to age between both groups was statistically significant (P <0.001).

The frequency of regurgitation, infantile colic, and dyschezia was significantly higher in the pre-term patients than in the full term patients ($P = 0.016$, $P = 0.025$, and $P < 0.001$ respectively).

Evaluation of complementary feeding time and content

FGIDs were reported in 678/1547 (43.8%) children before the age of 6 months. The incidence of starting early

Table 1 Demographic characteristics in the FGID and non-FGID groups

	Total	FGID group	Non-FGID group	*P*
n (%)	2383 (100)	837 (35.1)	1546 (64.9)	
Gender, *n* (%)				
Female	1138 (47.8)	401 (47.9)	737(47.7)	0.384
Male	1245(52.2)	436 (52.1)	809 (52.3)	
Mean age (months)				
Mean ± SD	4.9 ± 3.3	3.6 ± 2.8	5.6 ± 3.3	<0.001
Median (range)	4.0 (1.0–12.0)	2.5 (1.0–12.0)	5.2 (1.0–12.0)	
Timing of birth				
Full term	2106 (88.4)	710 (84.8)	1393 (98.9)	<0.001
Pre-term	277 (11.6)	127 (15.2)	150 (1.1)	
Delivery method				
Cesarean	1379 (57.9)	495 (67.2)	884 (57.2)	0.355
Vaginal	1004 (42.1)	342 (32.8)	662 (42.8)	
Birth weight, g	3180	3200	3120	0.871
Med (min–max)	(540–3780)	(650–3780)	(540–3650)	
Consanguineous marriage				
Yes	404 (16.9)	121 (14.5)	283 (18.3)	0.019
No	1979 (83.1)	716 (85.5)	1263 (81.7)	
Regular vaccination				
Yes	2282 (95.7)	807 (96.4)	1475 (95.4)	0.287
No	101 (4.3)	30 (3.6)	71 (4.6)	
Probiotics usage				
Yes	143 (6.0)	66 (7.9)	77 (5.0)	0.005
No	2240 (94.0)	771 (82.1)	1469 (95.0)	
Family history of atopy				
Yes	414 (17.4)	131 (15.6)	283 (18.3)	0.113
No	1969 (82.6)	706 (84.4)	1263 (81.7)	
Only mother's milk*				
Yes	829 (34.8)	208 (24.8)	621 (40.2)	<0.001
No	1554 (65.2)	629 (75.2)	925 (59.8)	

*Those who are exclusively breastfed for the first 6 months

complementary feeding in the FGID group was 5.3%, compared to 2.3% in the non-FGID group ($P = 0.002$). Among the 836 patients aged >6 months, 159 (19%) had a FGID. Complementary feeding was started in 45/113 (39.8%) patients with functional constipation before the age of 6 months, whereas only 423/2270 (18.6%) patients without constipation started complementary feeding before the age of 6 months ($P < 0.001$).

Complementary feeding in the FGID group primarily consisted of cereal, rice, pudding, and fruit juice, versus vegetables, fruits, meat, and yogurt in the non-FGID group ($P < 0.001$) (Table 4).

Table 2 The prevalence and distribution of FGID in the FGID group

	Type	*n*	%
Single FGID	Infant colic	214	8.9
	Infant regurgitation	187	7.8
	Infant dyschezia	110	4.6
	Functional constipation	95	4.0
2 FGIDs	Infant colic/dyschezia	57	2.3
	Infant colic/regurgitation	52	2.2
	Infant regurgitation/ dyschezia	39	1.6
≥3 FGIDs	Infant colic/regurgitation/ dyschezia	22	0.9

Evaluation of anthropometric measurements

The mean weight-for-length/height (WFL/H) *z*-score, which is an indicator of acute malnutrition, was 0.2 ± 1.8 in the FGID group and 0.2 ± 1.8 non-FGID group; the difference was not significant ($P = 0.155$). The mean WFL *z*-score was 0.2 ± 1.8 in the single FGID group and 0.1 ± 1.7 multiple FGID group; the difference was not significant ($P = 0.525$). There were not any significant differences in length-for-age (LFA) between the FGID group and non-FGID group, or between

Table 3 The demographic characteristics of the patients with single FGID and ≥2 FGIDs

	FGID g	Single FGID	≥2 FGIDs	*P*
n (%)	837 (100)	636 (76.0)	201 (24.0)	
Gender, *n* (%)				
Female	401 (47.9)	304 (47.8)	97 (48.3)	0.909
Male	436 (52.1)	332 (52.2)	104 (51.7)	
Age at onset of complaints (months)				
Mean ± SD	1.7 ± 2.1; 780	2.7 ± 3.0; 1591	1.0 ± 1.0; 188	<0.001
Timing of Birth				
Full term	710 (84.8)	551 (86.6)	159 (79.1)	<0.001
Pre-term	127 (15.2)	85 (13.4)	42 (20.9)	
Delivery method				
Cesarean	495 (59.1)	371 (58.3)	124 (61.7)	0.355
Vaginal	342 (40.9)	265 (41.7)	77 (38.3)	
Consanguineous marriage				
Yes	121 (14.5)	90 (14.2)	31 (15.4)	1.00
No	716 (85.5)	546 (85.8)	170 (84.6)	
Family history of atopy				
Yes	131 (15.7)	89 (14.0)	42 (20.9)	0.020
No	706 (84.3)	547 (86.0)	159 (79.1)	
Only mother's milk*				
Yes	208 (24.8)	159 (25.0)	49 (24.3)	0.306
No	629 (75.2)	477 (75.0)	152 (75.7)	

*Those that were exclusively breastfed for <6 months and those that were exclusively breastfed for >6 months

the patients with 1 FGID and ≥2 FGIDs (P = 0.206 and P = 0.236, respectively). No significant data were found in any FGID subgroups in terms of z-score < –2; however, the mean z-score was significantly lower in the patients with regurgitation than those without regurgitation (P = 0.001) (Table 5).

Discussion

The present study included infants aged 1–12 months that presented to pediatric outpatient clinics at tertiary care hospitals for any reason. Infants needing vaccinations or routine follow-up at clinics for healthy babies are not part of the activities in these hospitals. As a consequence, the incidence of FGIDs may be underestimated due to the design of our study. General pediatricians primarily investigated the presence of FGIDs according to ROME IV criteria. Pediatric gastroenterologists also evaluated the patients that were diagnosed with FGID by general pediatricians; 837/2383 (35.1%) s had a confirmed diagnoses of a FGID. Among these cases, 260 (31%) had presented to hospital due to symptoms of FGIDs which were confirmed as a FGID, while 577 (69%) presented to the hospital because of other symptoms and FGIDs were diagnosed when evaluated by a pediatrician. Van Tilburg et al. [10] reported that t 27% of infants aged 0–3 months had FGIDs and the most common FGID was IR, based on Rome III criteria. An European study using ROME IV diagnostic criteria that included 1698 infants aged 0–12 months noted that the frequency of FGIDs was 24.7% and that regurgitation was the most common FGID (13.8%) [11]. Although the frequency of FGIDs in the present study did not differ significantly from that in these earlier studies, it was slightly higher.

Table 4 Complementary feeding according to food group

n (%)	FGID group *n* = 159	Non-FGID group *n* = 677
Grains and rice	70 (44.0)	84 (12.4)
Pudding and fruit juice	51 (32.1)	138 (20.4)
Vegetables and fruits	25 (15.7)	213 (31.5)
Meat and yogurt	13 (8.2)	242 (35.7)
P	<0.001	

The design of the present study that was conducted in tertiary care hospitals is likely to contribute to the observed differences. Only 31% of the present study's patients were presented because of symptoms indicating FGIDs, suggesting that regardless of the reason for presentation, all infants should be evaluated for FGIDs.

According to literature, 30–67% of infants present with functional regurgitation, 5–20% have infantile colic, 3–27% have constipation, 6–7% have functional diarrhea, 3.4% have chronic vomiting syndrome, 2.4% have dyschezia, and 1.9% have rumination syndrome [4, 11–13]. In the present study, the most common FGID was colic (19.2%), followed by regurgitation (13.4%), dyschezia (9.8%), constipation (4.7%), diarrhea (0.8%), rumination (0.7%), and cyclic vomiting (0.5%). FGIDs associated with intense crying, such as colic and dyschezia, account for more consultations than other FGIDs. In the present study, the higher frequency of colic and dyschezia was attributed to this than when performed in a tertiary hospital. The frequency of infant dyschezia in the present study was much higher (9.8%) than in other studies. As is known, the upper age limit for the diagnosis of dyschezia has been increased to 9 months based on ROME IV criteria. Nonetheless, many infants with dyschezia can be mistakenly diagnosed with functional constipation. We think that both the increase in the age limit for diagnosing dyschezia and the fact that the present study was conducted by pediatricians and pediatric gastroenterologists in tertiary care clinics have contributed to the high frequency.

In the present study, the peak age to present with a FGID was 2–4 months; it is known that these diseases are most common during the first 6 months of life [4, 14]. In total,

Table 5 Weight-for-length *z*-score according to FGID diagnoses

Diagnoses, *n* (%)	*z*-score Mean ± SD	*P**	≤ −2 SD *n* (%)	> −2 SD *n* (%)	*P*
Infant regurgitation	−0.1 ± 1.8	0.001	34 (1.4)	286 (12.0)	0.703**
No diagnosis of infant regurgitation	0.3 ± 1.8		205 (8.6)	1858 (78.0)	
Infant colic	0.3 ± 2.0	0.390	32 (1.3)	425 (17.9)	0.05**
No diagnosis of infant colic	0.2 ± 1.8		207 (8.7)	1719 (72.1)	
Functional constipation	0.4 ± 1.8	0.961	8 (0.3)	105 (4.4)	0.217**
No diagnosis of functional constipation	0.2 ± 1.8		231 (9.7)	2039 (85.6)	
Functional diarrhea	−0.1 ± 2.5	0.983	2 (0.1)	16 (0.7)	0.702***
No diagnosis of functional diarrhea	0.2 ± 1.8		237 (9.9)	2128 (89.3)	
Cyclic vomiting syndrome	−0.1 ± 0.9	0.376	2 (0.1)	9 (0.4)	0.306***
No diagnosis of cyclic vomiting syndrome	0.2 ± 1.0		237 (9.9)	2135 (89.6)	
Infant dyschezia	0.1 ± 1.5	0.370	16 (0.7)	218 (9.1)	0.084**
No diagnosis of infant dyschezia	0.2 ± 1.9		223 (9.4)	1926 (80.8)	
Infant rumination syndrome	0.04 ± 1.4	0.506	2 (0.1)	14 (0.6)	0.672***
No diagnosis of infant rumination syndrome	0.2 ± 1.8		237 (9.9)	2130 (89.4)	

*Mann-Whitney *U* test. **Chi-square test. ***Fisher's exact test

35.1% of the infants 1–12 months old presented with a FGID; 43.8% of the infants age 0–6 months had a FGID (mean age: 3.6 ± 2.8 months) and in the non-FGID group, this mean was 5.6 ± 3.3 months ($P < 0.001$). These data are compatible with the literature. Salvatore et al. observed that the frequency of regurgitation was 37.3% in full term infants, versus 45.7% in preterm infants ($P = 0.015$), and the frequency of constipation in full term infants was 41.9%, versus 58.9% in pre-term infants ($P < 0.001$) [15]. In the present study, the frequency of FGIDs was 33.7% in full-term infants, versus 45.8% in preterm infants ($P < 0.001$).

Breast milk is the ideal nutrient for infants and has many beneficial effects on the development of mucosal immunity [16]. In the present study, exclusive breastfeeding during the first 6 months in the non-FGID group was 40.2%, versus 24.8% in the FGID group ($P < 0.001$). Whether the lower rate of breastfeeding is causal for the presence of a FGID, or if breastfeeding was more frequently stopped because of the presence of FGID cannot be deducted from our data. Gastrointestinal disturbances in infants can often cause changes in nutritional regimens, especially cessation of breastfeeding and transition to other foods [17]. We do not know if breastfeeding was stopped because of the presence of GI symptoms or if these infants had never been breastfed. It is very likely that the finding of the higher use of probiotics in the FGID group is more likely to be related to the consequence of the symptoms, and not related to the causality of the symptoms.

FGIDs can present as a single FGID or a combination of different FGIDs. Bellaiche et al. reported that 77.8% of all FGID patients had multiple FGIDs, of which 63% had 2 and 14.7% had ≥3 [5]. In this study, 28.1% of the patients had gas/bloating and colic, 17% had colic and regurgitation, and 8% had gas/bloating and regurgitation. van Tilburg et al. [10] reported that 28.8% of infants had ≥2 FGIDs and 5.2% had ≥3 FGIDs. In the present study, 636 (76%) of 837 patients diagnosed with FGIDs had 1 FGID and 201 (24%) had ≥2 FGIDs. Whereas in Bellaiche et al.'s [5] study the most common combination of FGIDs was gas/bloating and colic (28.1%), in the present study, the most common combination of FGIDs was infantile colic and dyschezia, which we think was because gas/bloating was not treated as a separate FGID in the present study. The most common combination of ≥3 FGIDs in the present study was infantile colic/regurgitation/dyschezia (0.9%), versus 5.2% in Tilburg et al.'s [9] study. A comparison of studies on FGIDs in different countries/regions was shown at Supplementary material.

The intestinal microbiome sequences in infants fed breast milk and formula differ from each other, and dysbiosis increases the frequency of development of other FGIDs, especially in infantile colic [16]. In the present study, the rate of breastfeeding during the first 6 months of life was significantly lower in the FGID group ($P < 0.001$), but there was not a significant difference between the patients with 1 FGID and ≥2 FGIDs ($P = 0.306$).

Salvatore et al. [15] reported there was no difference in the number of FGIDs between pre-term and full-term infants ($P = 0.773$). Our findings are not agreement with the findings from Salavtore et al. In the present study, 20.9% of the patients with ≥2 FGIDs were pre-term, whereas 13.3% of patients with 1 FGID were pre-term ($P < 0.001$).

Food protein allergies are included in the differential diagnosis of FGIDs. Food allergy should also be considered in patients with accompanying symptoms and in patients resistant to the treatment of FGIDs [18]. Jones et al. [19] observed that atopy occurs at a high frequency in patients with FGIDs. In the present

study, in patients with ≥ 2FGIDs, the age at onset of complaints was younger (1.0 ± 1.0 m; n = 188; P<0.001) and a family history of atopy was more common (20.9 %; n= 42; P<002).

Complementary feeding should only be introduced when the gastrointestinal functions are sufficiently mature, which occurs between week 17 and 6 months [20]. If complementary feeding is initiated before this period, the possibility of FGIDs can increase [20]. In the present study, the transition to early complementary feeding in infants aged <6 months was 2.3%, whereas in the FGID group, it was 5.3% (P = 0.002).

The transition to complementary feeding can be accomplished via various food groups that differ according to geographic region (cereals, yoghurt, vegetables, and fruits). In the present study, 159/836 (19%) infants aged >6 months had FGIDs. It was observed that the FGID group primarily was fed cereal, rice, pudding and fruit juice, whereas the non-FGID group was fed primarily vegetables, fruits, meat, and yogurt; the difference was significant (P < 0.001). It is not recommended to use simple sugars or sucrose and fruit juices that contain fiber-free fructose before the age of 1 year [21]. There are studies showing that the frequency of FGIDs decreases in older children fed a low-FODMAP diet (fermentable, oligo-, di-, and mono-saccharides and polyols) [21].

Growth retardation is not part of FGIDs. If WFL or LFA z-scores in infants are ≤ −2, investigations are recommended [22]. In the present study, there was no difference in WFL and LFA z-scores ≤ −2 and >−2 and the presence or absence of FGIDs (P = 0.155 and P = 0.206, respectively). Additionally, there was no growth retardation in the FGID group. When the types of FGIDs were examined separately, there was no differences in the patients with weight-for-age (WFA) and LFA z-scores < −2. Although acute and chronic malnutrition should not be present, especially in cases of regurgitation, the z-score means may be slightly lower provided that they remain within the normal range [23]. In the present study, z-scores were significantly lower in patients with regurgitation than in those without regurgitation (P = 0.001).

A limitation of the present study is that detailed analyses of microbiota according to diet, which is one of the most important factors that can affect the development of FGIDs, could not be investigated. The study was conducted in tertiary care hospitals, which is also a limitation; if the study also included patients from primary health care facilities, data could have been compared, so as to obtain more definitive conclusions.

In conclusion, 31% of the infants with a FGID presented because of different symptoms. Many infants fulfill the diagnostic criteria for a combination of FGIDs. According to our findings, FGIDs are more common in preterm infants, in those that are not breastfed and if complementary feeding with cereal, rice, pudding, and fruit juice started early.

Abbreviations FGID, Functional gastrointestinal disorders; FODMAP, Fermentable, oligo-, di-, and mono-saccharides and polyols; LFA, Length-for-age; WFL/H, Weight-for-length/height; WHO, World Health Organization

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Code availability N/A

Authors' contributions Omer Faruk Beser had primary responsibility for protocol development, enrollment, outcome assessment, preliminary data analysis, and writing the manuscript. Fugen Cullu Cokugras had primary responsibility for protocol development, outcome assessment, and supervised the design and execution of the study. Guzide Dogan, Ozlem Akgun, Murat Elevli, Pinar Yilmazbas, Meric Ocal, Nevzat Aykut Bayrak, Rabia Gonul Sezer, Abdulkadir Bozaykut, Coşkun Celtik, Esra Polat, Nelgin Gerenli, Serdar Bozlak, Hasret Ayyildiz Civan, Neslihan Ozkul Saglam, Sadik Sami Hatipoglu, Gamze Özgürhan, Eda Sunnetci Silistre, Burcu Solmaz, Gunsel Kutluk, Hamide Sevinc Genc, Hasan Onal, Ayse Merve Usta, Nafiye Urganci, Ayse Sahin, Sebahat Cam, Sema Yildirim, and Asilay Yildirim participated in analytical framework for the study and contributed to the patient screening. Yvan Vandenplas supervised the design and execution of the study, performed the final data analyses, and contributed to the writing of the manuscript.

Data availability N/A

Declarations

Ethical approval The study protocol was approved by the University of Health Sciences, Okmeydanı Education and Training Hospital Ethics Committee, and all the parents provided written informed consent. Data were collected in an anonymous way and analyzed and reported only in aggregate form. Given the purely descriptive and retrospective nature of the study, informed consent was waived.

Consent to participate All the parents provided written informed consent.

Consent for publication N/A

Conflict of interest The authors declare no competing interests.

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