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Investigation of the Frequency of Functional Gastrointestinal Diseases and Related Factors in Turkish Infants

Türk Süt Çocuklarında Fonksiyonel Gastrointestinal Hastalıkların Sıklığının ve İlişkili Faktörlerin İncelenmesi

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ABSTRACT

Objective: In this study was to evaluate the frequency of functional gastrointestinal disorders (FGIDs) including functional constipation, functional diarrhea and infantile colic, and the relationship between these diseases and nutritional practices.

Material and Methods: The study included 400 patients (4–24 months old) that applied to the pediatric health and diseases outpatient clinic or emergency clinic between 15 February 2019 and 31 May 2019. Patients without chronic diseases and who did not receive vitamin or appetite-enhancing medications other than vitamin D and iron were included in the study. The socio-demographic and nutritional characteristics of the patients were evaluated through a questionnaire. Patients suspected of having infantile colic, functional diarrhea and functional constipation were evaluated with the ROME-IV diagnostic criteria.

Results: Among 400 patients, 24.2% (n = 97) had infantile colic, 5.8% (n = 23) had functional constipation, and 2.5% (n = 10) had functional diarrhea. In those with infantile colic or functional constipation, cesarean delivery rate was found to be higher than those without (p = 0.008 and p = 0.032, respectively). The frequency of infantile colic was found to be lower in recipients of vitamin D prophylaxis (p = 0.032), and vitamin D use frequency was lower in those with functional constipation (p = 0.001).

Conclusion: In our study, infantile colic was the most common FGID seen in infants, while functional constipation was the second. A higher rate of carbohydrate-rich nutrition was identified in patients with functional diarrhea.

Key Words: Infantile colic, functional constipation, functional diarrhea, Rome criteria

ÖZ

Amaç: Bu çalışmada süt çocuklarında fonksiyonel gastrointestinal hastalıklardan (FGİH) fonksiyonel kabızlık, fonksiyonel ishal ve infantil kolik sıklığı ve bu hastalıkların beslenme alışkanlıkları ile ilişkisinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Çalışmaya, çocuk sağlığı ve hastalıkları polikliniğine ve acil polikliniğine 15 Şubat 2019 ile 31 Mayıs 2019 tarihleri arasında başvuran 4–24 aylık 400 hasta dahil edildi. Çalışmaya bilinen kronik hastalığı olmayan, D vitamini ve demir profilaksisi dışında vitamin veya iştah arttırıcı ilaç desteği almayan hastalar dahil edildi. Anket form aracılığıyla hastaların sosyo-demografik özellikleri ve beslenme özellikleri sorgulandı. İnfantil kolik, fonksiyonel ishal ve fonksiyonel kabızlık açısından şüpheli bulunan hastalar ROME-IV tanı ölçütlerine göre değerlendirildi.

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Conflict of Interest / *Çıkar Çatışması*: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics Committee Approval / *Etik Kurul Onayı*: This study was approved by the Istanbul Research and Training Hospital Ethics Committee for Clinical Studies (15 February 2019, 2019/1696). The family of each patient were informed about the purpose and content of the study, and an informed consent form was obtained from the families that volunteered to participate in the study.

Contribution of the Authors / Yazarların katkısı*: GULSEN N:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the res-ponsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spel-ling and grammar, Providing personnel, environment, financial support tools that are vital for the study, Biological materials, taking responsibility of the referred patients. ***SUNNETCI EConstructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the res-ponsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Providing personnel, environment, financial support tools that are vital for the study, Biological materials, taking responsibility of the referred patients.

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Bulgular: Çalışmaya dahil edilen 400 hastanın %24.2 (n=97)'sinde infantil kolik, %5.8 (n=23)'inde fonksiyonel kabızlık, %2.5 (n=10)'inde fonksiyonel ishal olduğu belirlenmiştir. İnfantil koliği olan ve fonksiyonel kabızlığı olan grupta sezaryen ile doğum oranının fazla olduğu saptandı (sırasıyla, p=0.008, p=0.032). D vitamini profilaksisini düzenli kullanan hastalarda infantil kolik görülme sıklığının daha az olduğu saptanırken (p=0.032), fonksiyonel kabızlığı olanlarda D vitamini kullanımı daha düşük bulundu (p=0.001).

Sonuç: Çalışmamızda, infantil kolik süt çocuklarında görülen en sık FGİH olarak bulundu, ikinci sırada ise fonksiyonel kabızlık vardı. Fonksiyonel ishal ve fonksiyonel kabızlık olan hastalarda karbonhidrattan zengin beslenme oranının yüksek olduğu tespit edildi.

Anahtar Sözcükler: İnfantil Kolik, Fonksiyonel Konstipasyon, Fonksiyonel İshal, Roma Kriterleri

INTRODUCTION

Functional gastrointestinal diseases (FGIDs) are chronic or recurrent gastrointestinal symptoms that cannot be explained by known biochemical or structural abnormalities (1). The Rome diagnostic criteria used to define these diseases were first created in 1990, and initially implemented only for adults. Later, the criteria were revised and the ROME IV criteria were released in 2016. The ROME IV criteria distinctly defines FGIDs in younger children (newborns / infants) and older children (children / adolescents) (2). There are a total of 7 diseases that have been defined in the newborn and early childhood (toddler) category. These are: infant regurgitation, infant rumination syndrome, cyclic vomiting syndrome, infantile colic, functional diarrhea, functional constipation and infant dyschezia (2, 3).

The etiology of FGIDs are multifactorial and include brain-gut interactions, genetic predisposition, and environmental factors (diet etc.) (4, 5). Multiple FGIDs are more common in infants who are breast fed for a relatively short time (6). Children with cow milk allergy are also in the risk group for FGIDs (7). In addition, various dietary factors, such as excessive feeding, excessive juice consumption, and high carbohydrate (fructose) or sorbitol intake, are known to play an important role in the pathophysiology of functional diarrhea (8). Although the frequency of FGIDs was mentioned in a few studies conducted in our country, there were no studies evaluating the relationship between nutritional status and FGIDs in the infancy according to the ROME IV criteria (9-11).

The aim of this study was to investigate the frequency of FGIDs, including constipation, functional diarrhea and infantile colic, and to determine the relationships between FGIDs and nutritional habits.

MATERIALS and METHODS

The study included 400 patients (4–24 months old) that had applied to the Pediatrics outpatient and Emergency clinics of our Hospital between 15 February 2019 and 31 May 2019.

This study was approved by the Istanbul Research and Training Hospital Ethics Committee for Clinical Studies (15 February 2019, 2019/1696). The family of each patient were informed about the purpose and content of the study, and an informed consent form was obtained from the families that volunteered to participate in the study.

Patients that were aged between 4–24 months who did not have any known chronic disease and did not take vitamins or appetite-enhancing medication supplements (fish oil preparations, zinc supplement or multivitamin etc.) other than vitamin D and iron prophylaxis were included in the study.

Children with any chronic diseases, those younger than 4 months and those older than 24 months, infants that were given nutritional supplements other than vitamin D and iron supplements (fish oil preparations, zinc supplements or multivitamins, etc.) were not included in the final study group. Additionally, among patients with diarrhea or constipation, patients with chronic recurrent episodes and warning signs were excluded from the study.

The height, weight and head circumference measurements of all infants were measured and recorded. Z-scores of weight-for-age, height-for-age, head circumference-for-age were calculated by WHO Anthro software.

Variables such as age, socio-demographic characteristics, the route of delivery, birth history, age of parents and their occupation, smoking and alcohol use, education levels, socioeconomic levels were determined with a standard questionnaire. At the same time, we also questioned the nutritional status of the patient, the duration of breastfeeding (duration with only breastfeeding and duration after introducing complementary food), the use of formula milk and additional food types, supplementary diet characteristics, and current dietary content. In addition, the exact use of vitamin D and iron preparations were also recorded. Any drug usage except for vitamin D, iron, and antibiotics were identified as "current drug usage".

Patients suspected of having infantile colic, functional diarrhea and functional constipation were evaluated according to the ROME-IV diagnostic criteria. All patients were retrospectively questioned about their crying and fussing attacks for infantile colic. Patients with complaints of diarrhea and recurrent attacks without warning signs and symptoms were evaluated according to the ROME diagnostic criteria prepared for functional diarrhea. Patients who suffered from constipation without any conclusive symptoms for other causes were also evaluated according to the ROME diagnostic criteria for functional constipation. After identifying patients with functional constipation, infantile colic and functional diarrhea, the characteristics and nutritional habits of all patients were evaluated and compared. The current nutritional status of patients and their consumption of relevant food types were recorded. Therefore, while collecting the

data, no time limitation was specified and the diet list was not evaluated by a nutritionist.

Statistical Analysis

All statistical analyses were performed by using the SPSS version 22.0 statistics software. Mean (standard deviation), median (min-max), frequency and ratio values were used for descriptive statistics. The suitability of quantitative variables to normal distribution was measured by the Kolmogorov Smirnov test with Lilliefors correction. Non-normally distributed quantitative independent data was analyzed with the Mann Whitney U test. Chi-square tests were used in the analysis of qualitative independent data. When Chi-square test conditions were not met, the Fischer Exact test was used. $p<0.05$ values were accepted to show statistical significance.

RESULTS

The mean age of the 400 infants in the study was 11.54± 5.43 months (min. 4 months- max. 23 months). Out of 400 patients, 48.8% (n=195) were female. Mean birth weight was 3244±530 grams and mean birth height was 50.25±3.30 cm. Three hundred and seventy-five (93.2%) of the infants participating in the study were born at term, and 47.8% were born via spontaneous vaginal delivery. Overall, 62.8% of the patients were receiving vitamin D supplements and 47.8% of them were receiving iron supplement (Table I).

Table I: Main characteristics of the infants.

	n (%)
Gender	
Male	205 (51.2%)
Female	195 (48.8%)
Gestation Week	
Term	375 (93.8%)
Preterm	25 (6.2%)
Delivery Types	
Spontaneous vaginal birth	191 (47.8%)
Cesarean section	209 (52.2%)
Vitamin D Usage Status	
Yes	251 (62.8%)
No	149 (37.2%)
Iron Usage Status	
Yes	191 (47.8%)
No	209 (52.2%)
Antibiotic Usage Status	
Yes	288 (72.0%)
No	112 (28.0%)
Any medication	
Yes	85 (21.3%)
No	315 (78.7%)
Exclusive Breast milk	40 (10.0%)
Breast milk + Formula milk	9 (2.3%)
Breast milk + Formula milk + Complementary food	49 (12.3%)
Breast milk + Complementary food	197 (49.3%)
Formula milk + Complementary food	41 (10.3%)
Exclusive Formula milk	3 (0.8%)
Complementary food only	61 (15.3%)

The mean age of the mothers was 29.33±4.98 years, while the mean age of the fathers was 33.15±5.2 years. With regard to educational status of parents, 32.3% of the mothers and 29.3% of the fathers were primary school graduates. 68% of the families' monthly income was between 1500-3000 TL and 26% of them had an income over 3000 TL. 8.5% of the mothers smoked and had continued to smoke during pregnancy (Table II). It was found that 36% of the parents received training concerning complementary nutrition. Considering the nutritional status at the time of admission, it was found that 10% of the patients were exclusively breastfed, while 49.3% received additional food with breast milk.

The mean duration of exclusive breastfeeding was 2 months. During complementary feeding, all parents (100%) included fruits and vegetables into the diet, 85.4% used starchy foods such as potatoes, rice, pasta, oatmeal, and 75% used baby biscuits.

The mean age of initiating complementary food was 6 months. It was determined that 54.2% of the patients started complementary food with yoghurt.

Table II: Main characteristics of the parents.

Maternal age (years)	29.3 ± 5.0
Father's age (years)	33.2 ± 5.2
Maternal education status	
Illiterate	28 (7.9%)
Primary school	129 (32.3%)
Middle School	84 (21.0%)
High school	99 (24.8%)
University	60 (15.0%)
Father's education status	
Illiterate	7 (1.8%)
Primary school	117 (29.3%)
Middle School	100 (25.0%)
High school	116 (29.0%)
University	60 (15.0%)
Families' monthly income	
No income	3 (0.8%)
<1500 TL	21 (5.3%)
1500-3000 TL	272 (68.0%)
>3000 TL	104 (26.0%)
Maternal smoking status	
While pregnant and still smoking	
Smoking during pregnancy but not now	34 (8.5%)
Non-smoking during pregnancy but	3 (0.8%)
smoking now	19 (4.8%)
Smoking and quitting before pregnancy	7 (1.8%)
Never smoked	337 (84.3)

TL: *Turkish Lira, Data are given as mean ± standard deviation for continuous variables, frequency (percentage) for categorical variables.*

Table III: Distribution of characteristics according to infantile colic.

	Infantile Colic (+) (n=97)	Infantile Colic (-) (n=303)	p
Age	12.5±5.6	11.2±5.4	0.066
Maternal parity	2.3±1.5	2.4±1.5	0.600
Gender (Male)	53 (54.6%)	152 (50.2%)	0.433
Gestational week (Term)	91 (93.8%)	284 (93.7%)	0.976
Delivery type (Vaginal)	35 (36.1%)	156 (51.5%)	0.008
Consanguineous marriage	20 (20.6%)	75 (24.8%)	0.405
Vitamin D usage	52 (53.6%)	199 (65.7%)	0.032
Iron usage	37 (38.1%)	154 (50.8%)	0.030
Antibiotic usage	76 (78.4%)	212 (70.0%)	0.109
Any medication	19 (19.6%)	66 (21.8%)	0.646

Data are given as mean ± standard deviation for continuous variables, frequency (percentage) for categorical variables

Table IV: Distribution of characteristics according to functional constipation.

	Functional Constipation (+) (n=23)	Functional Constipation (-) (n=377)	p
Age	13.5 ± 5.6	11.4 ± 5.4	0.069
Maternal parity	2.6 ± 1.4	2.4 ± 1.5	0.039
Gender (Male)	12 (52.0%)	193 (52.0%)	0.927
Gestational week (Term)	23 (100%)	352 (93%)	0.083
Delivery type (Vaginal)	6 (26.1%)	185 (49.1%)	0.032
Consanguineous marriage	5 (21.7%)	90 (23.7%)	0.815
Vitamin D usage	7 (30.4%)	244 (64.7%)	0.001
Iron usage	4 (17.4%)	187 (49.6%)	0.003
Antibiotic usage	19 (82.6%)	269 (71.4%)	0.243
Any medication	4 (17.4%)	81 (21.5%)	0.641
Parental complementary nutrition education	7 (30.4%)	137 (36.3%)	0.567

Data are given as mean ± standard deviation for continuous variables, frequency (percentage) for categorical variables

According to ROME-IV criteria, 24.2% (n=97) of 400 patients included in the study had infantile colic, 5.8% (n=23) of them had functional constipation, and 2.5% (n=10) of them had functional diarrhea.

The data of the patients with infantile colic were compared with the non-colic group. There were no statistically significant differences between the groups in terms of birth weight, birth height, and the weight, height and head circumference at admission (respectively p=0.567, p=0.640, p=0.281, p=0.717 and p=0.515). The frequency of cesarean delivery was found to be high in those with infantile colic (p=0.008). It was found that the incidence of infantile colic was lower in patients using vitamin D prophylaxis regularly (p=0.032), patients with infantile colic were not complying with regular use of iron prophylaxis (p =0.030) (Table III).

There were no relationships between the presence / absence of infantile colic and the following parameters of patients and families: age, educational status, income status, profession, smoking status, and nutritional status (p > 0.05 for each). When food types were analyzed, we found that 89.7% of the patients with colic were receiving starchy foods and 96% of them were receiving fruits and vegetables. Similarly, 86.6% of the patients with no colic were fed with starchy food and 99.3% of them were fed with fruits and vegetables. The age of complementary food initiation was 5.5 months in both groups.

In patients with functional constipation, the technique of breastfeeding was natural breastfeeding in 87.5%, and bottled breast milk in 12.5%; whereas, in those without functional constipation, 98.7% were breastfeeding and 1.3% were feeding bottled breast milk. No significant difference was found in terms of gender in patients with and without functional constipation (p =0.927). Cesarean delivery frequency was significantly higher in patients with functional constipation (p=0.032). In patients with functional constipation, the use of Vitamin D and iron preparations was at a significantly lower frequency (p=0.001, p=0.003). There was no statistically significant difference between the groups in terms of antibiotic use and drug use status (p=0.243, p=0.641) (Table IV).

Table V: Distribution of characteristics according to functional diarrhea.

	Functional Diarrhea (+) (n=10)	Functional Diarrhea (-) (n=390)	p
Age	13.9±5.5	11.5±5.4	0.148
Maternal parity	2.5±1.1	2.4±1.5	0.474
Gender (Male)	4 (40.0%)	201 (51.5%)	0.471
Gestational week (Term)	8 (80.0%)	367 (94.1%)	0.124
Delivery type (Vaginal)	6 (60.0%)	185 (47.4%)	0.432
Consanguineous marriage	3 (30.0%)	92 (23.6%)	0.638
Vitamin D usage	5 (50.0%)	246 (63.1%)	0.398
Iron usage	3 (30.0%)	188 (48.2%)	0.255
Antibiotic usage	9 (90.0%)	279 (71.5%)	0.199
Any medication	1 (10.0%)	84 (21.5%)	0.378
Parental complementary nutrition education	1 (10.0%)	143 (36.7%)	0.083

Data are given as mean ± standard deviation for continuous variables, frequency (percentage) for categorical variables.

While there was no significant difference found in terms of the age of the mother between groups, the age of the father was found to be significantly higher in those with functional constipation (p=0.063, p=0.009). No significant difference was found between the groups in terms of other characteristics (p >0.05 for each). Considering the nutritional status of the group with functional constipation, 4.3% had only breast milk, 52.2% had breast milk and complementary food; whereas, in those without functional constipation, 10.3% had received only breast milk and 49.1% had received breast milk and complementary food.

When those with and without functional diarrhea were compared, no statistically significant difference was found between the groups in terms of delivery type, gender, use of vitamin D prophylaxis, use of iron preparations, antibiotic use, and current drug use status (p>0.05) (Table V).

There was no significant difference found between the two groups in terms of parents' age, educational status, income status, profession, and smoking (p>0.05 for each). In children with functional diarrhea, 85.7% were receiving natural breastfeeding, 14.3% were receiving bottled milk. In those without functional diarrhea, 96.9% were breastfeeding naturally and 3.1% were feeding with bottled breast milk. Considering nutritional status, 10% of the functional diarrhea group received only breast milk, 50% of them received breast milk and complementary food; whereas, 10% of the group without functional diarrhea received only breast milk, 49.2% of them received breast milk and supplementary food. When the nutritional groups were examined, all the patients with functional diarrhea were found to have received starchy foods, fruits and vegetables, 88.8% of them received meat and derivative products. On the other hand, 85.3% of the patients without functional diarrhea were fed with starchy foods and 97.6% of them received fruits and vegetables.

DISCUSSION

In this study, we aimed to investigate the frequency of infantile colic, functional constipation and functional diarrhea in infancy, which were evaluated according to the ROME IV criteria, and the relationship of these diseases with nutritional habits.

Among the 400 children included in our study, 24.2% (n=97) had infantile colic, 5.8% (n=21) had functional constipation, and 3% (n=10) had functional diarrhea. In a survey study conducted by Liu W. et al. (12), 5030 children between 0-24 months were evaluated with the ROME-III criteria, and functional constipation rate was found to be 13.7%, functional diarrhea frequency was 12.3%, and infantile colic frequency was 1.4%. In the study conducted by Van Tilburg et al. (13), it was reported that the frequency of functional constipation was 4.7%, the frequency of functional diarrhea was 2.4%, and infantile colic frequency was 5.9% according to the ROME-III diagnostic criteria. The use of ROME-IV criteria demonstrated a somewhat higher frequency of FGIDs as reported by Robin and colleagues: the frequency of infantile colic was 5.2% and functional constipation frequency was 12.1%; however, interestingly, functional diarrhea was not observed (14). It is apparent that there are large differences in the frequency of FGIDs including our study. These differences are most probably due to the differences in nutritional habits, breastfeeding and approach to child care in different cultures and countries. These results suggest that childcare characteristics and appropriate nutrition are closely associated with the development of FGIDs (15).

In our study, no significant gender distribution differences were found between cases with and without infantile colic, functional constipation, and functional diarrhea. There are studies reporting large variations with age in FGID frequency; but there are also studies reporting similar results to our study in terms of gender (16-19). Furthermore, the narrow age range

in our study may have limited the detection of differences in this regard. Similar to previous studies in the literature, it is apparent that very large cohorts must be analyzed to delineate factors associated with FGIDs.

In our study, the mean age of the mothers of the patients with infantile colic was higher than the mothers of non-colic patients. Supporting the result in our study, Krause et al. (20) found that infantile colic is more common in the children of older mothers. This was suggested to be associated with higher levels of anxiousness among elderly mothers (20). Conversely, according to a study conducted by Kaymaz et al. (18), it was reported that there was no significant difference in the mean age of the mothers of patients with and without infantile colic.

In our study, cesarean delivery frequency in patients with infantile colic was found to be significantly higher than that of non-colic patients. Similar to our study, there are studies reporting higher rates of cesarean delivery in patients with infantile colic (18, 21). However, in a study conducted by Alagöz et al. (22) in Turkey, it was reported that there was no significant difference among those with and without infantile colic in terms of delivery type. In general, it is stated that there is no strong evidence that cesarean delivery is a risk factor for infantile colic (23).

In our study, there was no difference found in the use of vitamin D and iron preparations between the patients with and without functional diarrhea, whereas the use of vitamin D and iron preparations was significantly less frequent in patients with functional constipation. It is well known that parents may stop using iron supplements due concerns about constipation (24). This situation may be the reason of lesser frequency of iron supplement use. However, a strong relationship between vitamin D deficiency and functional constipation has been reported in a previous study (25). In addition, it was found that diet characteristics were significantly associated with functional constipation and diarrhea (26). We observed that, in patients with functional diarrhea, nutrition rich in starch, fat and sugar, were more common. Similarly, in patients with functional constipation, the frequency of carbohydrate and starchy products was higher than those without constipation. In a study conducted by Erhun et al. (27), it was stated that carbohydrate intake is relatively higher in patients with functional constipation, and fiber-poor diet was found to increase idiopathic chronic constipation. In general, it has been stated that low fiber nutrition and decreased fluid intake increase the risk of functional constipation (28).

There are a number of studies reporting varying levels of FGID frequency in children; furthermore, the relationships between these diseases and nutritional characteristics are also up for debate, as studies report very different findings. Cultural and communal nutritional habits, demographic variability, genetic factors, environmental and social effects may all be associated with these significant differences between studies.

Limitations

The fact that we have evaluated the frequency of FGIDs and their relationships with nutrition in the period of infancy based on ROME IV criteria, is the main strength of our study. However, as nutritional properties are based on survey data, the results are bound to parent reports, and thus may potentially have some degree of bias.

CONCLUSION

It was found that the most common FGIDs in our study were infantile colic followed by functional constipation. In cases with infantile colic and functional constipation, we found higher frequency of cesarean delivery and lower vitamin D intake (with supplements). A high rate of carbohydrate-rich nutrition was determined in patients with functional diarrhea. In these cases, the frequency of using bottled breast milk was also higher. Finally, it was also concluded that the reduction of the frequency of functional constipation can be achieved by utilizing normal vaginal delivery when possible.

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