

Dietary habits in Greek children with functional constipation based on Rome III criteria: a school-based, cross-sectional multivariate analysis

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Abstract

Background Functional constipation (FC) is the most common gastrointestinal disorder of childhood and has a multifactorial etiology. We aimed to assess dietary habits in Greek children with FC compared to the general population (control group, CG).

Methods This was a subgroup analysis of a school-based, cross-sectional study carried out in children 6-18 years of age, between January and June 2014, using the Rome III criteria for the diagnosis of FC. Dietary parameters, as well as socioeconomic and demographic data and their association with the likelihood of FC, were analyzed through multivariate logistic regression analysis and expressed as odds ratios (OR).

Results A total of 1439 children (1218 CG, 221 FC) were included in the analysis. The final model showed that consumption of fiber was the only dietary parameter significantly related to FC; higher frequency of consumption was inversely related to the likelihood of FC (OR: 0.98, 95% CI: 0.96, 0.99, P=0.048). Significant socioeconomic confounders with a positive association with FC were: parental educational level, victimization, physical activity and number of adults at home.

Conclusions Increased frequency of fiber consumption is significantly associated with higher odds of FC irrespective of socioeconomic background and lifestyle parameters. Interventional studies are required to validate these cross-sectional observations.

Keywords Constipation, diet, population study, children, ROME-III

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Introduction

Functional constipation (FC) is the most common functional gastrointestinal disorder (FGID) in childhood, with a reported prevalence ranging from below 1% to up to 32%, depending on the reference population and the definition used [1]. The longstanding nature of the

condition has a significant psychological impact on the family and poses a substantial economic burden for health systems, accounting for up to 25% of visits to a pediatric gastroenterologist in the United States (US) and comprising one of the 10 most common problems encountered by general pediatricians [2]. A study in the US on the cost of FC concluded that constipated children’s mean annual cost to the health system was 3 times greater compared to healthy control group (CG) [3].

Understanding the etiological basis is essential in order to apply preventive measures for such a common and costly condition. Several hypotheses have been proposed in relation to the etiology of pediatric FC, including genetics, behavior, intestinal microbiota, brain-gut axis, and diet. In most cases univariate analyses have been implemented, focusing on one parameter [4]. In this study we aimed to assess dietary habits in a large population of children diagnosed with FC according to the Rome III criteria and to evaluate differences compared to non-constipated controls,

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through a multivariate analysis taking into account several confounding factors.

Patients and methods

The current study was a subgroup analysis of a cross-sectional, school-based study [5] carried out by the 1st Department of Pediatrics of the National and Kapodistrian University of Athens, Greece, between January and June 2014, after receiving ethical approval by the Ethics Committee of the Ministry of Education (approval reference Id:305/25-05-2012). Written informed consent was sought and was signed by the parents or legal guardians of all participating children.

The methodological procedures have been described in detail previously [5]. In short, parents of children from schools (primary schools: 6-11-year-olds, gymnasiums: 12-14-year-olds, and lyceums: 15-17-year-olds) across the country were invited to participate via a letter and those consenting were included in the analysis. Two groups were formed: children with FC and CG. Children fulfilling the criteria for other FGIDs were excluded. The study sample was a sub-population of a national study on the prevalence of FGIDs in Greek children. Therefore, no sample-size calculation was applied for the present analysis, but all eligible children were included. Demographic, socioeconomic, clinical and dietary data were provided by the parents of children younger than 12 years, or directly by older children.

Rome III questionnaire

The official Greek translation of the Rome III questionnaire (QPGS-RIII) was utilized.

Demographic/socioeconomic information

The following data were recorded: geographic data (urban/rural, mainland/islands, main urban centers/elsewhere); sex; age; parental country of origin (both parents Greek, one parent Greek and both parents non-Greek); paternal and maternal educational level (primary school, gymnasium, lyceum, higher degree); family's economic status (poor, average, good); number of adults at home; number of children at home; family size (2-3 persons, 4-5 persons, 6-8 persons); parental presence at home (single-parent families or not); TV exposure (≤ 1 h per day, 1-3 h per day, >3 h per day); victim of bullying at school (yes/no); presence of a person with a severe health problem at home (yes/no); and level of physical exercise (none, 1-3 days per week, 4-7 days per week). For simplicity, paternal and maternal educational level (primary school=0, gymnasium=1, lyceum=2, higher degree=3) were combined (by aggregating the respective scores) to form a new variable, the combined parental educational level, which ranged from 0-6 and was treated as continuous for the purposes of the analysis.

Dietary information

The questionnaire used in this study is a modified version of a frequency-based questionnaire of dietary habits published previously [6]. Details on the structure and administration of the final form of the questionnaire have been published before from our group in a study assessing dietary habits in abdominal pain-related functional gastrointestinal disorders [7]. In brief, the dietary parameters of interest in the present analysis were: dairy, meat, fish, fiber, junk food, and non-lactose simple carbohydrates. The following information was requested from the participants: occasions of fruit consumption per week (in any form); servings of fresh juice per week; fizzy drinks (cups or cans) per week; occasions of sweet consumption per week; occasions of savory snack consumption per week; servings of milk per week; occasions of cheese consumption per week; servings of yoghurt per week; of the 14 meals per week how many include vegetables/legumes; of the 14 meals per week how many include salad; of the 14 meals per week how many include meat; of the 14 meals per week how many include fish; of the 14 meals per week how many include fast food, exclusively; in how many of the 14 meals per week is additional fast food consumed after the meal.

Dietary variables were organized into the following groups: fiber includes fruits, vegetables and salads; dairy includes milk, cheese and yoghurt; meat includes consumption of red or white meat; fish includes servings of any fish; junk food includes fast food and savory snacks; and non-lactose simple carbohydrates include fruits, juice, sweets and fizzy drinks. In all cases, frequencies and not actual quantities were assessed. A detailed description of the questionnaire and grouping of variables is provided in Table 1.

Statistical analysis

Continuous data are presented using mean \pm standard deviation (SD) and median (interquartile range), while categorical variables are described using absolute (n) and relative (%) frequencies. Continuous parameters were compared using the Student's *t*-test or the Mann-Whitney *U* test in the case of skewed distributions. The relations between categorical variables were assessed using Fisher's exact test. In 2 previous studies in the same population [5,7], we showed that the socioeconomic and demographic background is related to the likelihood of any FGID, as well as abdominal pain-related FGID. In the present analysis, we initially used a stepwise logistic regression approach, incorporating all socioeconomic and demographic variables, to identify probable confounders. The statistically significant parameters derived from the first model were used as confounders in the second multivariate regression analysis, where we assessed the correlation of dietary habits with the likelihood of FC, which was the main aim of this study. Again, a stepwise, backwards procedure was applied, starting from the full model. For logistic regression analysis, results are reported as odds ratios (OR) and 95% confidence

intervals (95%CI). The cutoff point for establishing statistical significance was set at $P=0.05$. The analysis was carried out using Stata 11.0 MP software (StataCorp, TX).

Table 1 Food-frequency questionnaire and grouping of data

Question	Group
Occasions of fruit consumption per week (in any form)	Fiber, non-lactose simple carbohydrates
Servings of fresh juice per week	Non-lactose simple carbohydrates
Fizzy drinks (cups or cans) per week	Non-lactose simple carbohydrates
Occasions of sweet consumption per week	Non-lactose simple carbohydrates
Occasions of savory ^a snack consumption per week	Junk food
Servings of milk per week	Dairy
Occasions of cheese consumption per week	Dairy
Servings of yoghurt per week	Dairy
Out of the 14 meals per week, how many include vegetables/legumes?	Fiber
Out of the 14 meals per week, how many include salad?	Fiber
Out of the 14 meals per week, how many include meat? ^b	Meat
Out of the 14 meals per week, how many include fish?	Fish
Out of the 14 meals per week, how many include fast food ^c , exclusively?	Junk food
In how many of the 14 meals per week is additional fast food ^c consumed after the meal?	Junk food

^aChips, crisps, pastries, salty biscuits; ^bwhite or red meat; ^cpizza, burgers, hot-dog, Greek pita-bread with kebab (and other type of meat products), sandwiches from kiosks and takeaway shops ("submarine" type)

Table 2 Demographic factors in the study population and associations with FC

Demographic characteristic, n (%)	Total (n=1439)	FC (n=221)	Controls (n=1218)	P-value*
Group				0.455
Primary school (6-12 years)	377 (26.2%)	53 (24.0%)	324 (26.6%)	
High school (gymnasium & lyceum, 12-18 years)	1062 (73.8%)	168 (76.0%)	894 (73.4%)	
Main urban centers				<0.001
Athens & Thessaloniki	788 (54.8%)	96 (43.4%)	692 (56.9%)	
Elsewhere	650 (45.2%)	125 (56.6%)	525 (43.1%)	
Urban vs. rural				0.003
Rural	459 (31.9%)	90 (40.7)	369 (30.3%)	
Urban	979 (68.1%)	131 (59.3%)	848 (69.7%)	
Islands vs. mainland Greece				0.005
Mainland Greece	1190 (82.7%)	168 (76.0%)	1022 (84.0%)	
Islands	248 (17.3%)	53 (24.0%)	195 (16.0%)	

*Fisher's exact test

FC, functional constipation

Results

Associations of FC with socioeconomic and demographic characteristics

Two thousand five hundred questionnaires were distributed, and informed consent was not provided for 842 children (33.7% negative response). Of the remaining 1658 children, complete dietary data were available for 1439 (1218 CG, 221 FC). Participants with missing dietary data were not included in the analysis. Age and sex were comparable between the 2 groups (age, FC vs. CG: 13.0 ± 2.7 vs. 12.8 ± 2.8 , $P=0.27$; sex, females, FC vs. CG: 50.7% vs. 50.2%, $P=0.94$). Detailed demographic and socioeconomic data are presented in Tables 2 and 3, respectively, along with bivariate associations with FC.

When a multiple, backwards, stepwise, logistic regression analysis was applied, starting from a full model with all socioeconomic and demographic data, the following parameters were significant in the final equation: physical activity (4-7 days per week vs. none, OR 0.53, 95%CI 0.36-0.77, $P=0.001$), bullying (yes vs. no, OR 1.69, 95%CI 1.08-2.65, $P=0.022$), TV exposure (>3 h per day vs. ≤ 1 h, OR 1.88, 95%CI 1.11-3.18, $P=0.019$), parental educational level (OR 0.87, 95%CI 0.78-0.95, $P=0.005$), area of residence (main urban centers Athens/Thessaloniki vs. elsewhere, OR 0.66, 95%CI 0.48-0.91, $P=0.011$), and number of adults at home (4 vs. 2, OR 2.42, 95%CI 1.37-4.30, $P=0.002$).

Associations of FC with dietary habits

Table 4 illustrates the associations between dietary parameters and the likelihood of FC. In this unadjusted, bivariate analysis, significant associations with FC were found for fiber, non-lactose simple carbohydrates and junk food.

Finally, a second multiple, backwards, stepwise, logistic regression analysis on the probability of FC was performed. We started from a full model including all dietary variables and the set of significant socioeconomic/demographic parameters

Table 3 Socioeconomic factors [3 (A) categorical variables, 3 (B) continuous variables] in the study population and associations with FC

3 (A)	Total (n=1439)	FC* (n=221)	Controls (n=1218)	P-value*
Paternal educational level				<0.001
Primary school	69 (4.8%)	17 (7.7%)	52 (4.3%)	
Gymnasium	219 (15.2%)	47 (21.3%)	172 (14.1%)	
Lyceum	565 (39.3%)	92 (41.6%)	473 (38.9%)	
University	585 (40.7%)	65 (29.4%)	520 (42.7%)	
Maternal educational level				<0.001
Primary school	69 (4.8%)	17 (7.7%)	52 (4.3%)	
Gymnasium	118 (8.2%)	31 (14.0%)	87 (7.1%)	
Lyceum	585 (40.7%)	92 (41.6%)	493 (40.5%)	
University	666 (46.3%)	81 (36.7%)	585 (48.1%)	
Family's economic status				0.749
Good	553 (38.4%)	83 (37.6%)	470 (38.6%)	
Average	803 (55.8%)	123 (55.7%)	680 (55.8%)	
Poor	83 (5.8%)	15 (6.8%)	68 (5.6%)	
Number of adults at home				0.001
1	95 (6.6%)	18 (8.1%)	77 (6.3%)	
2	1171 (81.4%)	164 (74.2%)	1007 (82.7%)	
3	110 (7.6%)	18 (8.1%)	92 (7.6%)	
4	60 (4.2%)	21 (9.6%)	42 (3.4%)	
Family size (persons at home)				0.002
2-3 persons	243 (16.9%)	40 (18.1%)	203 (16.7%)	
4-5 persons	1021 (71.0%)	139 (62.9%)	882 (72.5%)	
6-8 persons	174 (12.1%)	42 (19.0%)	132 (10.9%)	
Parental presence at home				0.508
Single parent	120 (8.3%)	21 (9.5%)	99 (8.1%)	
Both parents	1319 (91.7%)	200 (90.5%)	1119 (91.9%)	
Days of physical exercise per week				0.002
None	236 (16.4%)	42 (19.0%)	194 (15.9%)	
1-3 days	807 (56.1%)	139 (62.9%)	668 (54.9%)	
4-7 days	395 (27.5%)	40 (18.1%)	355 (29.2%)	
Television exposure (h per day)				<0.001
≤1	525 (36.5%)	60 (27.2%)	465 (38.2%)	
1-3	835 (58.0%)	138 (62.4%)	697 (57.2%)	
>3	79 (5.5%)	23 (10.4%)	56 (4.6%)	
Victim of "bullying" at school				0.025
No	1300 (90.3%)	190 (86.0%)	1110 (91.1%)	
Yes	139 (9.7%)	31 (14.0%)	108 (8.9%)	
Person at home with a severe health problem				0.111
No	1340 (93.1%)	200 (90.5%)	1140 (93.6%)	
Yes	99 (6.9%)	21 (9.5%)	78 (6.4%)	

3 (B)

Variable	Total (n=1439) mean ± SD, median (IQR)	FC (n=221) mean ± SD, median (IQR)	Controls (n=1218) mean ± SD, median (IQR)	P-value**
Number of children at home	2.2±0.9, 2 (2, 3)	2.4±1.0, 2 (2, 3)	2.2±0.9, 2 (2, 2)	0.015
Parental combined educational level	4.4±1.5, 5 (4, 6)	4.0±1.6, 4 (3, 5)	4.5±1.4, 5 (4, 6)	<0.001

*Fisher's exact test

**Mann-Whitney test

The parental combined educational level is a 0-6 scale resulting from summing the maternal and paternal educational level: primary school: 0, gymnasium: 1, lyceum: 2, higher degree: 3

FC, functional constipation; SD, standard deviation; IQR, interquartile range

that resulted from the first model. In the final, reduced model, parental educational level, victimization, physical activity and number of adults at home retained their statistical significance.

In relation to dietary variables only fiber was statistically significant. Consumption of fiber had an inverse relation to the likelihood of FC (OR 0.98, 95%CI 0.96-0.99, P=0.048).

Table 4 Distribution of dietary parameters in the study population and comparisons between children with FC and controls

Dietary variable*	Total mean \pm SD, median (IQR)	FC mean \pm SD, median (IQR)	Controls mean \pm SD, median (IQR)	P-value†
Fiber	18.1 \pm 9.1, 17 (11, 24)	16.5 \pm 9.0, 15 (10, 22)	18.4 \pm 9.1, 17 (11, 24)	0.005
Dairy	16.5 \pm 8.0, 16 (11, 21)	15.9 \pm 10.1, 15 (10, 20)	16.5 \pm 7.5, 16 (11, 21)	0.30
Non-lactose simple carbohydrates	13.5 \pm 7.6, 15 (11, 21)	15.2 \pm 8.9, 13 (10, 18)	13.1 \pm 7.3, 12 (8, 16)	0.001
Junk food	8.1 \pm 5.6, 7 (5, 10)	9.5 \pm 5.9, 8 (6, 12)	7.8 \pm 5.5, 7 (4, 10)	<0.001
Meat	5.0 \pm 2.7, 4 (3, 6)	5.2 \pm 3.1, 4 (3, 7)	5.0 \pm 2.7, 4 (3, 6)	0.30
Fish	2.0 \pm 1.8, 2 (1, 2)	2.1 \pm 2.1, 2 (1, 3)	2.0 \pm 1.7, 2 (1, 2)	0.55

*Servings per week. †Student's t-test

FC, functional constipation; SD, standard deviation; IQR, interquartile range

Twenty-seven children with FC also fulfilled the criteria for an abdominal-pain related FGID. In a previous study [7] we have shown that abdominal-pain related FGIDs are significantly associated with junk food and fish consumption. In order to detect whether the coexistence of abdominal pain-related FGIDs would confound the observed associations, the multivariate logistic regression analysis was repeated including only the 194 children with FC and without a diagnosis of abdominal pain-related FGIDs. The results remained practically unchanged regarding the direction of the estimated correlations.

Discussion

In the present study, we assessed the relation between dietary habits and the likelihood of FC in a large, school-based sample of Greek children, based on the Rome III criteria. We observed that a lower intake of fiber was the sole factor associated with a higher probability of FC, irrespective of socioeconomic and demographic background, which have been shown to correlate significantly with FGIDs.

In general, most of the hypothesized mechanisms in pediatric FC involve, as the final step, a withholding behavior attributed to underlying, longstanding fear of a painful defecation. This is triggered by hard, occasionally bulky, dehydrated stools, and repetitive postponement perpetuates a vicious cycle of pain, fear and avoidance. Different theories exist regarding what might systematically lead to this sequence of events. Prolonged colonic transit time, dietary factors (primarily low residue), changes in intestinal microbiota, even genetic predisposition have been implicated [2].

A uniformly accepted definition for fiber does not exist, and various different methods of characterization have been used. In all cases, the common denominator is that "dietary fiber is a group of carbohydrate polymers, oligomers and lignin that escape digestion in the small intestine and reach the colon intact, where they are partially or completely fermented by the gut microbiota" [8,9]. Fiber is probably the most extensively investigated dietary factor in pediatric and adult FC. In general, most observational studies have

shown an inverse relation between consumption of fiber and likelihood of constipation, similar to our results. Depending on the design of each study, fiber intake may have been assessed either indirectly (through food frequency questionnaires, as consumption of fiber-containing foods) [10-12], or directly, after quantification through a 24- or 72-h dietary record form [13-15]. Furthermore, it has been shown that adherence to dietary patterns rich in vegetables/fruits/whole-wheat grains, such as the Mediterranean diet, is inversely related to FGIDs and specifically FC in Greek children [16]. Based on observational results, clinical trials have been conducted in constipated children, aiming to assess fiber as a possible treatment. Several meta-analyses [17-19] have tried to summarize the results of the clinical trials. The most recent [20], which included all available data, concluded that fiber may be beneficial in improving evacuation frequency. All systematic reviews acknowledge the significant heterogeneity of the included trials in terms of constipation definition, method/dose/type of fiber supplementation and outcomes of interest. A 2014 decision analysis article [21] assessed the financial impact of increased fiber consumption and the subsequent reduction in the prevalence of constipation and related utilization of health resources. The estimated annual reduction in constipation-related cost in the entire US adult population, would exceed 2 billion dollars if 50% of the US adult population reached the recommended daily consumption of fiber.

The beneficial effect of fiber in FC has been attributed to 2 factors. First, fiber, particularly low-fermentable and non-fermentable, acts as a bulking agent by increasing luminal water content [22]. Hydrated, bulky, soft stools promote normal motility of the colon [23] and reduce the probability of a painful, unpleasant feeling during the defecation by the young child, therefore preventing a withholding behavior. Second, in recent years, dietary fiber has been recognized as a major modifying factor of the gut microbiome. Modern modalities such as next-generation sequencing demonstrated intestinal dysbiosis in constipated adults [24,25]. Most data have shown an altered balance, with reduced presence of *Bifidobacterium* and *Lactobacillus* genera and increased abundance of *Bacteroidetes* and *Enterobacteriaceae* [26,27]. In pediatric populations similar studies are scarce. In otherwise healthy children with FC, 2 studies [28,29] found significant increases

in clostridia and bifidobacteria in FC, whereas another study in obese children with FC [30] demonstrated significantly smaller *Prevotella* populations and larger numbers of several genera of firmicutes.

It is mainly experimental data from animal studies that have provided insight into the physiological link between intestinal microbiota and FC. Current evidence suggests that a microbiome imbalance results in dysregulation of intestinal physiology in many aspects, including sensory, motor, immune and vascular functions [22]. A characteristic finding is that the bacterial endotoxin lipopolysaccharide is able to influence intestinal motility by prolonging gastric emptying time and causing sphincter dysfunction [31]. The short chain fatty acids (SCFAs) produced by some gut microbes induce the release of GLP-1 and polypeptide YY and stimulate the enteric cholinergic reflex [32,33]. A different mode of action for SCFAs includes the induction of 5-hydroxytryptamine release, thus accelerating colonic transit [34]. It is evident that gut microbiota have multiple potential roles in intestinal health through complex physiologic mechanisms at the cellular and molecular level, which remain largely unknown.

There is no universally endorsed recommendation of daily fiber intake for children. A widely used “rule of thumb” is the age (in years) plus 5-10 g [35]. A prospective study in constipated children identified that at least 10 g of daily dietary fiber for younger children (3-7 years) and at least 15 g of daily dietary fiber for older children (8-14 years) are the recommended cutoffs to relieve constipation [36]. The most recent (2014) guidelines of the European and North American Societies of Pediatric Gastroenterology Hepatology and Nutrition do not recommend extra fiber supplementation in children with FC [37].

The main strength of this study is its large sample size, which provided increased power to detect statistically significant associations via multivariate models that effectively eliminated the confounding effect of socioeconomic variables. The main limitation was the cross-sectional nature of the survey and the use of Rome III (instead of the currently available Rome IV) criteria. When the present study was being conducted the Rome IV version was not yet available. Studies comparing the performance of Rome III vs. Rome IV have shown relatively good agreement, despite the changes in the FC criteria [38]. In addition, the study could be subject to response bias; a social desirability effect may have shaped participants’ answers. Moreover, participants’ dietary habits were not interpreted in the form of total caloric intake or a summary of consumed food quantities, and no grouping of children based on their exact nutritional intake was performed. The use of weighed food diaries, instead of food frequency questionnaires, would have provided information on whether the upper limits of recommended daily allowances for dairy products were exceeded or those for fiber intake were not reached in children with FC.

In conclusion, the present study demonstrated a significant association between fiber and the likelihood of FC in school-aged children, independently of socioeconomic background. The amount and type of fiber that provide the maximum beneficial effect remain to be determined in future studies.

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Summary Box

What is already known:

- Functional constipation (FC) is a common condition of unknown, multifactorial etiology
- Diet as a contributing factor has been investigated with inconclusive results
- Diet-related prevention strategies are not feasible because of the lack of specific aims

What the new findings are:

- Fiber-containing food, when assessed simultaneously with other dietary parameters, is the sole factor associated with FC
- Dietary habits should be assessed in the context of socioeconomic and lifestyle risk factors, such as physical activity, bullying, parental educational level and number of adults at home, which are significantly and independently associated with a higher likelihood of FC

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