# Association Between Obesity/Overweight and Functional Gastrointestinal Disorders in Children

*†Renato Tambucci, ‡§Paolo Quitadamo, *Michela Ambrosi, †Paola De Angelis, †Giulia Angelino, ||Stefano Stagi, *Albero Verrotti, ‡Annamaria Staiano, and ¶Giovanni Farello

## ABSTRACT

**Objective:** Although emerging data indicate that obese/overweight children are more likely to develop functional gastrointestinal disorders (FGIDs) than normal-weight peers, contrasting results have been reported. The present observational, case-control study aimed at estimating the prevalence of FGIDs in obese/overweight children compared to normal-weight peers.

**Methods:** Consecutive obese and overweight children aged 4 to 18 years attending the obesity outpatient clinic were enrolled as study cases. Normal-weight children were enrolled as comparison group. All the enrolled patients received a thorough health examination from both a pediatric endocrinologist and gastroenterologist. Moreover, they were asked to fill out the Rome III questionnaire for the diagnosis of FGIDs. Data were analyzed to compare the prevalence of FGIDs between cases and controls.

**Results:** Throughout the study period we enrolled 103 cases and 115 controls. No significant age and sex differences were found between the 2 groups. FGIDs were significantly more prevalent in obese/overweight compared to normal-weight children (47.57% vs 17.39%; $P < 0.0001$). Increased prevalence was observed for functional constipation (18.44% vs 7.82%; $P = 0.025$), functional dyspepsia (23.33% vs 6.95%; $P = 0.001$), and irritable bowel syndrome (10.67% vs 2.60%; $P = 0.024$), whereas no difference was observed for functional abdominal pain (1.94% vs 2.60%; $P = 1.00$).

**Conclusions:** Our data suggest that there is a link between excess body fat and FGIDs in children. This finding may offer a model of patients in which the effects of food and nutritional substances, the gut microbial environment, and psychosocial factors are fitting well with the emerging biopsychosocial conceptual model for FGIDs.

**Key Words:** biopsychosocial model, functional constipation, functional dyspepsia, irritable bowel syndrome

(*JPGN* 2019;68: 517–520)

**What Is Known**

- Over the last decades the prevalence of obesity among children and adolescents has increased dramatically.
- Obesity-related comorbidities include a wide variety of severe chronic diseases that may involve almost all organs and systems and may have significant long-term detrimental effects on both health and life expectancy.

**What Is New**

- The presents study reports an increased prevalence of functional gastrointestinal disorders in obese children and adolescents.
- This finding may support the emerging conceptual view of biopsychological model, in which food and nutritional substances, microbial environment, and psychosocial factors play an important role in the pathogenesis of functional gastrointestinal disorders.

Over the last 4 decades the prevalence of obesity among children has increased dramatically and, coincidentally, the well-established comorbidities have become a major health challenge, associated to a significant increase in healthcare costs (1). Obesity-related comorbidities include a wide variety of severe chronic diseases that may involve almost all organs and may have significant long-term detrimental effects on both health and life expectancy. It has been estimated that a high body mass index (BMI) accounted for about 4 million deaths and 120 million disability-adjusted life-years worldwide in year 2015 (1).

Pediatric obesity predicts adult obesity. Indeed, approximately 20% of the obese infants will become obese children, 40% of the obese children will become obese teenagers, and 80% of obese teens will inevitably become obese adults (1). In addition to the potentially life-threatening diseases, such as type 2 diabetes mellitus syndrome, cardiovascular disease, and nonalcoholic fatty liver disease, obese children are more likely to develop psychological and behavioral disorders (2). Moreover, emerging data indicate that obesity is also associated with functional gastrointestinal disorders (FGIDs) (3,4). FGIDs are common disorders in children of all ages and include a range of chronic or recurrent gastrointestinal symptoms that cannot be explained by structural or biochemical abnormalities (5). The pathogenesis of FGIDs remains elusive and is likely multifactorial. Assuming that obesity and FGIDs are mechanistically linked, studying its relationship may

Received July 2, 2018; accepted October 31, 2018.

From the *Pediatric Unit, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, the †Digestive Endoscopy and Surgery Unit, Bambino Gesù Children's Hospital-IRCCS, Rome, the ‡Department of Translational Medical Science, Section of Pediatrics, University Federico II, the §Department of Pediatrics, A.O.R.N. Santobono-Pausilipon, Naples, the ||Health Sciences Department, University of Florence, Anna Meyer Children's University Hospital, Florence, and the ¶Pediatric Unit, Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy.

Address correspondence and reprint requests to Renato Tambucci, MD, Pediatric Unit, University of L'Aquila, San Salvatore Hospital, University of L'Aquila, Via Lorenzo Natali 1, 67100, L'Aquila, Italy (e-mail: renato.tambucci@gmail.com, renato.tambucci@opbg.net).

The authors report no conflicts of interest.



DOI: 10.1097/MPG.0000000000002208

TABLE 1. Demographic and auxological characteristics

| | Obese/overweight | Normal weight | *P* |
|---|---|---|---|
| Number of children | 103* | 115 | |
| Male/female | 52/51 | 55/60 | 0.7862 |
| Age, y, median (range) | 10.50 (4.2–17.9) | 10.90 (4.1–17.6) | 0.7946 |
| Height, cm; mean ± SD | 143.8 ± 14.01 | 139.0 ± 18.32 | 0.7946 |
| Weight, kg; mean ± SD | 56.84 ± 16.19 | 36.64 ± 13.93 | **<0.0001** |
| BMI, kg/m$^2$; mean ± SD | 26.30 ± 3.16 | 17.47 ± 2.93 | **<0.0001** |
| BMI SDS, mean ± SD | 1.90 ± 0.40 | − 0.35 ± 0.94 | **<0.0001** |

BMI = body mass index, SD = standard deviation, SDS = standard deviation score, y = year.
*Thirty-six (31.57%) children were overweight (BMI >85th ≤ 95th percentile), 78 (68.42%) were obese (BMI >95th percentile).

provide insights into the pathophysiology of FGIDs. To date, few studies have been carried out to explore the association between excess body weight and FGIDs in children and most of them suffer from drawbacks such as retrospective study design, lack of control population, or unclear diagnostic criteria.

The primary aim of the present observational, case-control study was to determine whether obese/overweight children and adolescents have a greater prevalence of FGIDs than healthy normal-weight peers. Secondary aims were to summarize the existing data on the association between obesity and FGIDs in children and to discuss the possible role of pathophysiological mechanisms that might link these 2 common conditions.

## METHODS

Overweight and obese children aged 4 to 18 years were consecutively recruited from those attending the obesity outpatient clinic from January 2016 to July 2017 at the Department of Pediatrics of the San Salvatore Hospital in L'Aquila, Italy. According to the Center for Disease Control and Prevention definitions, overweight is defined as a BMI at or above the 85th percentile and lower than the 95th percentile. Obesity is defined as a BMI at or above the 95th percentile (6). Normal-weight children defined as having a BMI between the 5th and the 85th percentile were enrolled as comparison group (6). Controls were consecutively recruited from children attending immunization clinic or the emergency department for a minor injury. Systemic and infectious diseases; previous surgery; genetic, metabolic, neurodevelopmental, and immune disorders; and cardiac, hepatic, or renal diseases were considered exclusion criteria for both cases and controls.

Demographic and past medical history data were obtained at baseline. All patients underwent auxological examination by experienced pediatric endocrinologists. Height was measured in the standing position by using a Harpenden stadiometer (Holtain, London, UK). Weight was measured to 0.1 kg with an electronic stand-on scale. BMI was calculated by dividing weight (in kg) by height squared (in m). Data on BMI were converted into standard deviation scores according to the Italian reference values (7). Afterwards, children were evaluated by pediatric gastroenterologists to identify the possible presence of FGIDs, according to the Rome III criteria (5). All children were interviewed using the Italian version of the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version (8). Children older than 10 years were interviewed directly, whereas parents or caregivers of children younger than 10 were asked to fulfill the questionnaire on behalf of the patient.

The study was conducted in accordance with the Helsinki Declaration, and ethical approval was obtained by the Ethics Committee of the University of L'Aquila. All the patients and/or their parents or caregivers agreed to participate and signed an informed consent.

GraphPad Prism software version 5.0 was used for the statistical analyses. Continuous variables were compared using Student *t* test. Chi-squared test or Fisher exact test were used, where appropriate, to analyze categorical variables. Ordinal variables were evaluated using the nonparametric Wilcoxon test. A *P* value <0.05 was considered statistically significant.

## RESULTS

A total of 114 obese/overweight children were screened throughout the study period. Among them, 11 were excluded due to concurrent diseases (3 gastroesophageal reflux disease, 2 celiac disease, 2 autism spectrum disorder, 2 previous bowel surgery, 1 growth hormone deficiency, 1 congenital heart defect). Out of the remaining 103 children, 33 of 103 (32%) were overweight and 70 of 103 (68%) were obese. One hundred fifteen normal-weight children were enrolled as comparison group (62 from the immunization service and 53 from the emergency department). Baseline demographic and auxological characteristics of both groups are summarized in Table 1. No significant differences between them were found as far as sex and age are concerned.

As detailed in Table 2, obese/overweight children were significantly more likely to have at least one FGID as compared with normal-weight children (47.57% vs 17.39%, respectively).

## DISCUSSION

Our data support the hypothesis that FGIDs are associated with excessive body weight in children. FGIDs include a combination of chronic or recurrent gastrointestinal age-dependent disorders not explained by known biochemical or structural abnormalities (9).

A complete understanding of the pathophysiology of FGIDs remains elusive (9,10). FGIDs are a multifactorial condition and several pathophysiological mechanisms appear to contribute to

TABLE 2. Prevalence of functional gastrointestinal disorders

| | Obese/overweight | Normal weight | Odds ratio (95% confidence interval) | *P* |
|---|---|---|---|---|
| FGIDs, n (%) | 49 (47.57)* | 20 (17.39)† | 4.31 (2.32–7.99) | **<0.0001** |
| FC, n (%) | 19 (18.44) | 9 (7.82) | 2.66 (1.14–6.19) | **0.0251** |
| FD, n (%) | 23 (22.33) | 8 (6.95) | 3.84 (1.63–9.04) | **0.0016** |
| IBS, n (%) | 11 (10.67) | 3 (2.60) | 4.46 (1.20–16.48) | **0.0240** |
| FAP, n (%) | 2 (1.94) | 3 (2.60) | 0.73 (0.12–4.51) | 1.000 |

FAP = functional abdominal pain, FC = functional constipation, FD = functional dyspepsia, FGIDs = functional gastrointestinal disorders, IBS = irritable bowel syndrome. Bold values are those with statistical significance.
*Six obese/overweight children were suffering from both FC and FD.
†Three normal weight children were suffering from both FC and FD.

them, including altered motility, visceral hyperalgesia, brain-gut disturbances, genetic and environmental factors, and psychosocial upsets (10).

Studying the relationship between FGIDs and other conditions may help to better identify their complex biology and possibly optimize the therapeutic approaches. Although recent emerging epidemiological data in both adult and pediatric populations suggest that obesity may predispose to develop FGIDs, the relationship between obesity and FGIDs is currently a matter of debate (3,11).

## Association Between Functional Gastrointestinal Disorders and Obesity: Previous Data

A pediatric review published a few years ago found that obese and overweight children had a higher prevalence of FGIDs than normal-weight children (12). Indeed, almost half of the obese/overweight children had at least 1 FGID. Despite the limited number of publications, the heterogeneity in study designs, and the differences in diagnostic criteria and recruitment settings, the authors concluded that functional abdominal pain syndrome, irritable bowel syndrome (IBS), and functional constipation (FC) were significantly related to excess body weight.

Our results indicate a higher prevalence of FC in obese/overweight children than nonobese peers (19% and 9%, respectively). The first report suggesting a significant association between FC and obesity in children was published by Fishman et al in 2004. The study lacked a control population, but the authors concluded that the prevalence of FC in their cohort of obese children was higher than the historical prevalence observed in the general pediatric population (13). Over the following years, other studies analyzed the prevalence of obesity/overweight in children with FC, reporting a significantly higher prevalence compared with the control healthy population (12,14–16).

In contrast with the above-mentioned studies, 2 large population-based studies found no association between FC (according to the Rome III criteria) and childhood overweight or obesity (17,18). Intrinsic selection bias arising from population-based sampling methods, especially when the relationship between highly prevalent conditions is explored, may explain these inconsistent results.

Finally, a recent comprehensive systematic review showed that the current available data could not confirm or refute the association between functional defecation disorders and overweight/obesity because the results are conflicting across the studies. Moreover, the authors found that only 1 study was rated to be of good quality, whereas most studies were rated to be of fair or poor quality, suggesting that the results should have been interpreted with caution (19).

The association between obesity and IBS in children has been reported by 2 pediatric studies (12,16). In 2011 Bonilla et al, however, analyzed 351 children diagnosed with abdominal pain-related FGIDs (functional abdominal pain [FAP], IBS, and functional dyspepsia [FD]) according to the Rome II criteria, reporting no baseline differences in terms of frequency and intensity of symptoms between obese and nonobese children. Nevertheless, at long-term follow-up patients with obesity were more likely to have persistence of abdominal complains, higher intensity, and higher frequency of pain than nonobese patients (20).

Data on the association between FAP and childhood obesity are even less consistent. In a large school-based study Malaty et al (21) found that obese children were more likely to suffer from recurrent abdominal pain compared to nonobese children (33.3% vs 22.5%, respectively). Nevertheless, later on the same above-mentioned studies by Teitelbaum et al, Phatak and Pashankar et al, and Bonilla et al (12,16,20) failed to find any significant association between obesity and FAP in children. Our data on FAP confirm these results, but the low number of patients detected does not allow for definitive conclusions.

Although we found that FD was the most prevalent disorder in our cohort of patients with obesity, data from scientific literature on the relationship between FD and obesity in children are too limited to draw any conclusions (15). A recent study by Jung et al (22) showed that visceral adiposity was associated with an increased risk of FD, suggesting that visceral adiposity may play an important role as a metabolically active organ in the pathogenesis of FD.

## Possible Pathophysiological Link Between Functional Gastrointestinal Disorders and Obesity

Several explanations have been offered to understand how obesity could cause FGIDs. A caloric intake greater than physiologic needs and notably excessive consumption of high glycemic index foods and sugar-containing beverages associated with low-fiber and high-fat diet are considered causal factors for obesity development (23). Recently, increasing attention has been paid to the effects of food on the onset of FGIDs. Consistent evidence supports the notion that diet containing fermentable oligo-, di-, and monosaccharides and polyols may trigger gastrointestinal symptoms in patients with IBS. Conversely, a diet poor in fermentable oligo-, di-, and monosaccharides and polyols offers considerable symptom relief in the majority of patients (24). Dietary habits and lifestyle behaviors predisposing to excessive weight gain have also been linked to FC development in children (25,26). Furthermore, an increased consumption of fatty meal may result in delayed gastric emptying while excessive food intake during a relatively short time may potentially overcome the functional accommodation and emptying of the stomach, leading to the development of dyspeptic symptoms in individuals with obesity (27).

In addition to dietary habits, obesity and FGIDs share a further potential pathophysiological factor that is under increased consideration: the gut microbiota. During the past years, many studies have focused on the role of gut microbiome in the genesis of FGIDs, and the emerging concept of the microbiome-gut-brain axis has been proposed (28–30). Changes in the gut microbiota composition have been implied in the onset and maintenance of FGIDs, but they have been also suggested as an important factor influencing energy metabolism and development of obesity (31–33).

Finally, psychosocial disorders are considered to play an important role in the pathophysiology of both obesity and FGIDs. Several investigators have clearly shown that psychiatric disorders, such as anxiety, depression, and trauma disorders, are highly prevalent in patients with FGIDs (34–36). Moreover, recent evidence suggests that obesity and psychological problems are not separate conditions but share common biological mechanisms (37–39). Therefore, novel insights into the role of psychosocial factors in children with obesity may help to improve individualized approach for FGIDs.

In summary, our data suggest that FGIDs and obesity are associated conditions in children. Compared to previous articles, we acknowledge that the present study has some undeniable strengths. We tried to keep possible biases to a minimum by prospectively enrolling our patients. Moreover, a control group of age- and sex-matched healthy children was enrolled and the diagnosis of FGIDs was made according to the standardized Rome III criteria by using validated questionnaires for children.

We are also aware that our study has some drawbacks, mainly bound to the study design. Results arise from a single

''snapshot'' of a population sample, in which exposure (obesity) and outcome (FGIDs) have been determined simultaneously. Therefore, it is not possible to determine whether the reported association implies a causality relationship or it is the mere consequence of the high prevalence of both conditions. Moreover, children were enrolled in a tertiary care setting, and thus being perhaps poorly representative of the entire population. Finally, our study lacked a psychological assessment and did not provide information on symptom severity. Understanding if FGIDs are even more severe (and more frequent) in children with obesity could represent a further field to be explored in the future.

Our study may establish a solid basis for further researches about obesity and FGIDs in children. In the emerging conceptual view of the biopsychological model, food and nutritional substances, gut microbial environment, and psychosocial factors play an important role in the pathogenesis of FGIDs. The high prevalence of FGIDs in children with obesity may support this model. Further studies are needed for a more exact and detailed definition of this model, and for the establishment of causal relationships.

## REFERENCES


1. Afshin A, Forouzanfar MH, Reitsma MB, et al., GBD 2015 Obesity Collaborators. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med* 2017;377:13–27.
2. Gibson LY, Allen KL, Davis E, et al. The psychosocial burden of childhood overweight and obesity: evidence for persisting difficulties in boys and girls. *Eur J Pediatr* 2017;176:925–33.
3. Ho W, Spiegel BM. The relationship between obesity and functional gastrointestinal disorders: causation, association, or neither? *Gastroenterol Hepatol (N Y)* 2008;4:572–8.
4. Phatak UP, Pashankar DS. Obesity and gastrointestinal disorders in children. *J Pediatr Gastroenterol Nutr* 2015;60:441–5.
5. Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2006;130:1527–37.
6. Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion. Defining Childhood Obesity: BMI for Children and Teens. *https://www.cdc.gov/obesity/childhood/defining.html*. Published October 20, 2016. Accessed October 28, 2018.
7. Cacciari E, Milani S, Balsamo A, et al. Italian cross-sectional growth charts for height, weight and BMI (2 to 20 yr). *J Endocrinol Invest* 2006;29:581–93.
8. Buonavolontà R, Boccia G, Turco R, et al. Pediatric functional gastrointestinal disorders: a questionnaire on pediatric gastrointestinal symptoms based on Rome III criteria. *Minerva Pediatr* 2009;61:67–91.
9. Hyams JS, Di Lorenzo C, Saps M, et al. Functional disorders: children and adolescents. *Gastroenterology* 2016; pii: S0016-5085(16)00181-5.
10. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. *Gastroenterology* 2016; pii: S0016-5085(16)00223-7.
11. Eslick GD. Gastrointestinal symptoms and obesity: a meta-analysis. *Obes Rev* 2012;13:469–79.
12. Phatak UP, Pashankar DS. Prevalence of functional gastrointestinal disorders in obese and overweight children. *Int J Obes (Lond)* 2014;38:1324–7.
13. Fishman L, Lenders C, Fortunato C, et al. Increased prevalence of constipation and fecal soiling in a population of obese children. *J Pediatr* 2004;145:253–4.
14. Pashankar DS, Loening-Baucke V. Increased prevalence of obesity in children with functional constipation evaluated in an academic medical center. *Pediatrics* 2005;116:e377–80.
15. Misra S, Lee A, Gensel K. Chronic constipation in overweight children. *J Parenter Enteral Nutr* 2006;30:81–4.
16. Teitelbaum JE, Sinha P, Micale M, et al. Obesity is related to multiple functional abdominal diseases. *J Pediatr* 2009;154:444–6.
17. Costa ML, Oliveira JN, Tahan S, et al. Overweight and constipation in adolescents. *BMC Gastroenterol* 2011;11:40.
18. Koppen IJ, Velasco-Benítez CA, Benninga MA, et al. Is there an association between functional constipation and excessive bodyweight in children? *J Pediatr* 2016;171:178.e1–82.e1.
19. Koppen IJ, Kuizenga-Wessel S, Saps M, et al. Functional defecation disorders and excessive body weight: a systematic review. *Pediatrics* 2016;138:pii: e20161417.
20. Bonilla S, Wang D, Saps M. Obesity predicts persistence of pain in children with functional gastrointestinal disorders. *Int J Obes (Lond)* 2011;35:517–21.
21. Malaty HM, Abudayyeh S, Fraley K, et al. Recurrent abdominal pain in school children: effect of obesity and diet. *Acta Paediatr* 2007;96:572–6.
22. Jung JG, Yang JN, Lee CG, et al. Visceral adiposity is associated with an increased risk of functional dyspepsia. *J Gastroenterol Hepatol* 2016;31:567–74.
23. Taber DR, Chriqui JF, Powell L, et al. Association between state laws governing school meal nutrition content and student weight status: implications for new USDA school meal standards. *JAMA Pediatr* 2013;167:513–9.
24. Shepherd SJ, Lomer MC, Gibson PR. Short-chain carbohydrates and functional gastrointestinal disorders. *Am J Gastroenterol* 2013;108:707–17.
25. Tabbers MM, Benninga MA. Constipation in children: fibre and probiotics. *BMJ Clin Evid* 2015;2015:pii: 0303.
26. Chien LY, Liou YM, Chang P. Low defaecation frequency in Taiwanese adolescents: association with dietary intake, physical activity and sedentary behaviour. *J Paediatr Child Health* 2011;47:381–6.
27. Quitadamo P, Zenzeri L, Mozzillo E, et al. Gastric emptying time, esophageal pH-impedance parameters, quality of life and gastrointestinal comorbidity in obese children and adolescents. *J Pediatr* 2018;194:94–9.
28. Mayer EA, Savidge T, Shulman RJ. Brain-gut microbiome interactions and functional bowel disorders. *Gastroenterology* 2014;146:1500–12.
29. Pigrau M, Rodiño-Janeiro BK, Casado-Bedmar M, et al. The joint power of sex and stress to modulate brain-gut-microbiota axis and intestinal barrier homeostasis: implications for irritable bowel syndrome. *Neurogastroenterol Motil* 2016;28:463–86.
30. Zhu L, Liu W, Alkhouri R, et al. Structural changes in the gut microbiome of constipated patients. *Physiol Genomics* 2014;46:679–86.
31. Turnbaugh PJ, Hamady M, Yatsunenko T, et al. A core gut microbiome in obese and lean twins. *Nature* 2009;457:480–4.
32. Kalliomäki M, Collado MC, Salminen S, et al. Early differences in fecal microbiota composition in children may predict overweight. *Am J Clin Nutr* 2008;87:534–8.
33. Tilg H, Adolph TE. Influence of the human intestinal microbiome on obesity and metabolic dysfunction. *Curr Opin Pediatr* 2015;27:496–501.
34. Yacob D, Di Lorenzo C, Bridge JA, et al. Prevalence of pain-predominant functional gastrointestinal disorders and somatic symptoms in patients with anxiety or depressive disorders. *J Pediatr* 2016;163:767–70.
35. Wouters MM, Boeckxstaens GE. Is there a causal link between psychological disorders and functional gastrointestinal disorders? *Expert Rev Gastroenterol Hepatol* 2016;10:5–8.
36. Vu J, Kushnir V, Cassell B, et al. The impact of psychiatric and extraintestinal comorbidity on quality of life and bowel symptom burden in functional gastrointestinal disorders. *Neurogastroenterol Motil* 2014;26:1323–32.
37. Markey CN, August KJ, Bailey LC, et al. The pivotal role of psychology in a comprehensive theory of obesity. *Health Psychol Open* 2016;3:2055102916634365.
38. Simon GE, Von Korff M, Saunders K, et al. Association between obesity and psychiatric disorders in the US adult population. *Arch Gen Psychiatry* 2006;63:824–30.
39. Dinan TG, Quigley EM, Ahmed SM, et al. Hypothalamic-pituitary-gut axis dysregulation in irritable bowel syndrome: plasma cytokines as a potential biomarker? *Gastroenterology* 2006;130:304–11.