Obesity and gastroesophageal reflux disease and gastroesophageal reflux symptoms in children

Hoda M Malaty[1]
J Kennard Fraley[1,2]
Suhaib Abudayyeh[1]
Kenneth W Fairly[1]
Ussama S Javed[1]
Heba Aboul-Fotouh[1]
Nora Mattek[3]
Mark A Gilger[4,5]

[1]Department of Medicine, [2]Children's Nutrition Research Center (CNRC), [4]Department of Pediatrics, [5]Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA; [3]Department of Gastroenterology, Oregon Health and Science University, Portland, OR, USA

Correspondence: Hoda M Malaty
Veterans Affair Medical Center (111D)
2002 Holcombe Blvd. Houston,
TX 77030, USA
Tel +1 713 795 0232
Fax +1 713 790 1040
Email hmalaty@bcm.tmc.edu

Background: The association between body mass index (BMI) and gastroesophageal reflux disease (GERD) has been extensively studied among adults but few studies have examined such association in children. Aims: 1) to determine the relationship between BMI in children and GERD, and 2) to use the National Center for Health Statistics (NCHS) values for BMI as a valid source for comparison.

Methods: We identified two cohorts of children aged between two and 17 years who were seen at Texas Children's Hospital (TCH). The first cohort consisted of children diagnosed with GERD based on upper gastrointestinal endoscopic and histologic evaluation, which was recorded in the Pediatric Endoscopic Database System-Clinical Outcomes Research Initiative (PEDS-CORI) at TCH. A diagnosis of GERD was based on the presence of erosive esophagitis or esophageal ulcers. Endoscopic reports that were incomplete or did not include demographic features, indications for endoscopy, or endoscopic findings were excluded. The second cohort consisted of all children with symptoms due to gastroesophageal reflux (GER) who received outpatient gastrointestinal (GI) consultation at TCH for any 9th revision of the International Statistical Classification of Diseases (ICD-9) code suggestive of GER. There was no overlap between the two cohorts as each child was indexed only once. Children with any comorbid illnesses were excluded.

Measurements: The records for each child namely, age, gender, height, and weight were obtained on the same date as that of the diagnosis. Using the growth curves published by the NCHS, the gender/age specific weight-for-age Z-score (WAZ), and height-for-age Z-score (HAZ) were calculated. BMI was calculated as the weight in kilograms divided by height in meters squared. Children having values greater than the 95th percentile for their age/gender-specific BMI were defined as obese.

Results: In a one-year period (January 2006 to December 2006), a total of 627 children who attended the GI clinic at TCH were identified with GERD symptoms of whom 131 underwent endoscopic examination. The mean age was 9.7 years; 42% were females; 57% were Caucasians; 15% were African Americans, and 28% were Hispanics. Using National Health and Nutrition Examination Survey (NHANES) data obtained from the same period as the the current data as a baseline for comparison, the BMI of children diagnosed with GERD was higher than the BMI reported by NHANES data. The final analysis of test proportion showed an overall proportion of 0.207 for the current study versus NHANES data (0.174). The current study also showed that more boys than girls have BMI greater than 95th percentile (24.7% vs 16.5%, respectively, OR = 1.7, 95% CI = 1.2–2.6, p = 0.04).

Conclusions: Children diagnosed with GERD or those who presented with symptoms of GERD are more likely to be obese. The findings of this study show a possible association between obesity and GERD in children. Further understanding about the co-morbidity between GERD and obesity in children may have important implications on GERD management and treatment in children.

Keywords: gastroesophageal reflux disease, children, body mass index

Introduction

Gastroesophageal reflux disease (GERD) is common in children with major presenting symptoms of heartburn, regurgitation, epigastric pain, and vomiting.[1–3] Furthermore, our recent follow-up study showed that 30% of children who suffered from recurrent abdominal pain had a final diagnosis of GERD.[4] Several studies reported an association between obesity and GERD among adults.[5–7] Other studies have demonstrated a higher prevalence of asthma among obese children and adults.[8–9] Thus, obesity may act as a confounder by increasing the frequency of both diseases. Further, the community-based pilot study showed that 20% of African American and Hispanic children residing in Houston, Texas suffered from undiagnosed recurrent abdominal pain, some of which is likely due to GERD.[10]

Despite continued research on GERD in children, the management of pediatric patients with GERD continues to be a challenge to physicians due to insufficient studies on the risk factors of the disease in children, and symptoms suggestive of GERD are not rare in childhood.[11–12] Untreated GERD in children could be associated with a decrease in quality of life for both the children and their parents and may lead to complications, such as erosive esophagitis, and in rare cases, failure to thrive, esophageal stricture, and apnea.[13–14]

The direct relationship of GERD and childhood obesity has not been extensively explored. The objective of this study is to compare the prevalence of obesity among children diagnosed with GERD and those without these symptoms in the US using the published National Health and Nutrition Examination Survey (NHANES) obesity rates during a similar time period.

Materials and methods

Design

The study is a cross-sectional retrospective study that identified two cohorts of children between the ages of two and 17 years who were seen at Texas Children's Hospital (TCH).

The first cohort of children was identified from the Clinical Outcomes Research Initiative (CORI) that was developed in 1995 as a national registry of endoscopic procedures. Pediatric Endoscopic Database System (PEDS)-CORI, a pediatric component of CORI, was created in November 1999.[15] This cohort of children was identified by using upper endoscopy (EGD) information compiled in PEDS-CORI from a single site at TCH in children between the ages of two and 17 years. Children were identified during the period of January 2006 to December 2006.

Confirmation of GERD

We identified a cohort of children between the ages of 2 and 17 years diagnosed with GERD, based on the findings of upper gastrointestinal endoscopic examination that was recorded in the PEDS-CORI at TCH. These children underwent endoscopic examination and were diagnosed of having GERD based on endoscopic findings and histological reports of erosive esophagitis and/or esophageal ulcers.[15] Endoscopic reports that were incomplete or did not include demographic features, indications for endoscopy, or endoscopic findings were excluded from the analysis.

The second cohort of children was identified through the administrative database at TCH, which contains medical diagnoses obtained at all inpatient and outpatient encounters; these diagnoses were coded according to the 9th revision of the International Classification of Disease, Clinical Modification (ICD-9 CM)[16] and the Current Physician's Terminology (CPT) codes.[17] These children with gastroesophageal reflux (GER) symptoms received outpatient gastrointestinal (GI) consultation at and identified for any ICD-9 code suggestive of GERD (eg, of heartburn, regurgitation, epigastric pain, and vomiting) but did not undergo endoscopic evaluation. This cohort of children was identified between the same periods as the first cohort. Patients between two and 17 years were only included in this cohort.

These children with GER symptoms received outpatient GI consultation and were identified for any ICD-9 code suggestive of GER but did not undergo endoscopic evaluation.

In the two cohorts studied, we excluded patients with cerebral palsy (ICD-9 CM codes 343.0–343.9, 344.0–344.9, and 348.0–348.9), mental retardation (ICD-9 CM codes 317.00–379.00), tracheoesophageal congenital anomalies (ICD-9 CM codes 530.84, 751.1, 750.5, and 750.7), or congenital esophageal stenosis (ICD-9 CM code 750.3). These patients are known to have severe GERD, the mechanisms of which are likely to be different from GERD in children without these comorbid conditions.[18–21] We also excluded children with GERD and asthma because of documented association between asthma and GERD. For patients with multiple entries in the database, only the first was counted.

Measurements

The records for each child with respect to age, gender, height, and weight were measured on the same day on which the diagnosis was made.

All participants in both the cohorts of the current study had waiver of consent approval via the institutional review board of TCH and the Baylor College of Medicine, Houston, Texas.

Statistical analysis

Using the growth standards published by the National Center for Health Statistics (NCHS), we calculated the gender/age specific weight-for-age Z-score (WAZ), height-for-age

Z-score (HAZ) and body mass index (BMI) for-age Z-score. BMI was calculated as the weight in kilograms divided by height in meters squared. Those greater than the 95th percentile for their age/gender-specific BMI were defined as obese. Fisher's exact or Chi-square analyses were performed to measure the differences in the overall prevalence of obesity between the categorical independent variables. Logistic regression with presence of obesity as the binary outcome and all potential risk factors for GERD as independent variables was performed and the crude odds ratios (ORs) and 95% confidence intervals (CI) were calculated for all the study variables. We also calculated means, standard deviations (SD), and CI for HAZ, WAZ, weight-for-height, and BMI-for-age Z scores for all children. The BMI percentile was calculated using the Centers for Disease Control (CDC) (based on NHANES II) standards, which would predict that 5% of a sample taken from a similar population would be above the 95th percentile of BMI. Since obesity rates have been tracking upward since the original NHANES II data were collected, we chose a survey taken at a time comparable to the period when the GERD data were collected for comparison. Analyses were performed using Minitab (Minitab Inc., State College, PA, USA) and SPSS (SPSS lnc., Chicago, IL, USA) statistical software. Statistical significance was assessed by using an α level of 0.05.

Results

During the one-year study period, a total of 627 children attending the GI clinic at TCH were identified with GERD symptoms. Of those, 131 children were diagnosed with GERD after they underwent endoscopic and histological evaluation. The mean age of total children studied was 9.7 years, 42% were females, 57% were Caucasians, 15% were African Americans, and 28% were Hispanics. The comparison of the two cohorts studied is presented in Table 1. There was no significant difference between both cohorts in respect to HAZ, WAZ, or BMI for-age Z-score. However, children who underwent endoscopic examination were older than children who presented only with symptoms of GERD ($p = 0.001$).

Children with BMI $\geq$ 95th percentile for age and gender was 21.4% of the total children examined. There was no difference among children receiving upper gastrointestinal endoscopic examination or those in whom diagnosis was based on GERD symptoms, BMI greater than or equal to 95th percentile being 21.4% and 20.3%, respectively ($p = 0.45$). There was a slight increase in the incidence of obesity in boys with GERD compared to NHANES data, 24.7% versus 16.7%, respectively ($p = 0.003$). This trend was not observed among girls.

Effect of age, gender, and ethnicity on obese children

Although GERD is the primary dependent variable of the current study, we further examined the prevalence of BMI $\geq$ 95th percentile and its association with some of the independent variables, such as age, gender, and ethnicity. The results revealed a greater prevalence of GERD among boys with BMI greater than 95th percentile than girls; 24.7% versus 16.5%, respectively (OR = 1.7, 95% CI = 1.2–2.6, $p = 0.04$). This trend was also seen when each cohort was

Table 1 Means (± SD) Z-scores for the two studied cohorts of children using the CDC standardized age/gender-specific anthropometric measurements

		N	Mean	SD	SEM	95% CI for mean		Minimum	Maximum	Sig.
						Lower bound	Upper bound			
Htage_Z	Cohort-1	496	–0.24	1.58	0.09	–0.42	–0.06	–8.26	4.31	0.883
	Cohort-2	131	–0.22	1.36	0.12	–0.45	0.02	–5.18	6.79	
	Total	627	–0.23	1.51	0.07	–0.38	–0.09	–8.26	6.79	
Wtage_Z	Cohort-1	496	0.09	1.78	0.10	–0.12	0.30	–10.71	4.01	0.584
	Cohort-2	131	0.19	1.69	0.15	–0.10	0.48	–7.55	4.61	
	Total	627	0.12	1.75	0.08	–0.05	0.29	–10.71	4.61	
BMIage_Z	Cohort-1	496	0.35	1.41	0.08	0.18	0.51	–5.93	3.46	0.669
	Cohort-2	131	0.41	1.43	0.12	0.16	0.66	–3.30	5.92	
	Total	627	0.37	1.41	0.07	0.23	0.50	–5.93	5.92	
Age (mos)	Cohort-1	496	121.91	49.65	2.26	117.47	126.34	36.00	227.00	0.000
	Cohort-2	131	144.05	50.89	4.32	135.52	152.58	40.00	217.00	
	Total	627	126.85	50.74	2.03	122.86	130.84	36.00	227.00	

Abbreviations: Htage_Z, height-for-age Z-score; Wtage_Z, weight-for-age Z-score; BMIage_Z, BMI for-age Z-score; Cohort-1, Children with GERD symptoms; Cohort-2, Children with GERD diagnosed by upper endoscopic examination; SD, Standard deviation; SEM, Standard error of mean; CI, confidence interval.

examined independently as boys continued to show a greater prevalence with BMI greater than 95th percentile than girls, but the significant difference disappeared due to the reduced sample size (Table 2). There was no significant difference of BMI $\geq$ 95th percentile between Caucasians, African Americans, and Hispanics, or between younger and older children (Table 2).

Discussion

Several studies have reported an association between obesity and GERD among adult populations;[5–6,22] however very few studies have reported such an observation among children. This is the first such study to show a possible association between obesity and GERD in a large cohort of children while controlling for asthma as a confounder factor. Several important observations have emerged from the study. First, the findings showed that children, especially boys, diagnosed with GERD and/or with GERD symptoms are more likely to be obese than the general population of children. Possibilities for this trend could be due to the fact that both GERD symptoms and childhood obesity share several variables such as behavior problems, anxiety, withdrawal, and low self-esteem that are not directly related to the etiology of both the conditions. Obese children may experience extrinsic gastric compression by the surrounding adipose tissue, leading to an increase in intra-gastric pressure and subsequent relaxation of the lower esophageal sphincter, thus leading to increased esophageal acid exposure.[23–25] Another explanation is that obese children are likely to have higher consumption of food and/or "junk food" compared to nonobese children and this induces heartburn which is considered the major symptom for GERD.[26] It is also likely that GERD symptoms could cause children to withdraw from common childhood activities and responsibilities, including sports and outdoor play. GERD symptoms could be accompanied by a fear, of developing stomach ache every day that could be associated with decreasing physical activity which is related to weight gain.[27–29]

Nevertheless, this finding was consistent among the two cohorts studied; those who were only treated for their symptoms and those underwent endoscopic examination. This observation indicates that the association between GERD and obesity in children does not depend on the severity of the disease but rather on its symptoms, as children who underwent endoscopic evaluation were more likely to have severe or more recurrent symptoms than those did not have endoscopic examination. Our findings are consistent with the results from a Norwegian study, which reported that obesity and asthma were independently associated with GERD symptoms in children.[8]

Although there was no proportional difference between boys and girls in the current study, there was a significant difference in that there was a greater prevalence among boys with BMI $>$ 95th percentile than girls. The reason for this observation is not known but emphasizes the difference of the epidemiology and the risk factors of GERD between adults and children. As for adults, a newly published study found that BMI is positively associated with symptoms of GERD in both normal-weight and overweight women.[30] Another study from Italy confirmed this observation as it reported a higher prevalence of GERD among women than men.[5] It was

Table 2 Effect of gender, ethnicity, and age on the examined children with BMI $>$ 95th percentile (Obese)

Variable	Total children		Children with GERD symptoms		Children with GERD diagnosed by upper endoscopy	
	Prevalence	P value	Prevalence	P value	Prevalence	P value
Gender						
• Boys	24.6%		24.8%		24.4%	
• Girls	16.5%	0.04*	16.3%	0.08	17.2%	0.34
• Total	20.7%		20.3%		21.4%	
Ethnicity						
• Caucasians	21.1%		19.6%		22.6%	
• African-Americans	24.3%	0.67	26.3%	0.63	22.2%	0.96
• Hispanics	19.4%		19.4%		NP	
Age					23.3%	
• 10 years	22.1%	0.70	21.7%	0.55	20.5%	0.82
• 10–17 years	19.3%		18.6%			

Abbreviations: BMI, body mass index; GERD, gastroesophageal reflux disease; NP, no prevalence.

interpreted that females are more prone to have GERD than males due to the female hormonal functions.[31]

The increasing prevalence of obesity among schoolchildren in the US and over the world has been the subject of increasing interest,[20–21] in part because children who are obese show related signs of comorbidity including elevated blood pressure, cholesterol, diabetes mellitus, and many psychological factors.[22–24] Because a single factor may confound many other or different disorders,[26] a better understanding of the comorbidity between GERD and other conditions (eg, obesity) may have important management implications regarding prevention or treatment of GERD in children. For example, observed congruities between the disorders suggesting management already demonstrated to be efficacious for pediatric obesity should also be tested for their effects on GERD. Additional research is needed to further understand the association or the causality between GERD and obesity in children. This could be achieved by conducting longitudinal and follow-up studies on children with both conditions.

The utilization of data such as these for constructing a prospective cohort of children suffering from GERD symptoms has some shortcomings. First, the cross-sectional nature of the data prevented us from making a statement regarding the possibility of causality between GERD and obesity because we do not have an internal comparison group (a non-GERD group). However, the reviewer is correct in that we do not have an internal comparison group (a non-GERD group). However, we believe it would be useful to provide the readers a comparison of the obesity prevalence in these GERD patients with a comparison of the general US population at a similar time period.

Therefore, we used the published NHANES obesity rates from the same period as that of the study for a baseline comparison. Second, we did not have a control group but used the NHANES survey which is a valid comparison for the national BMI. A third limitation is that we used a wide age range (2–17 years) to evaluate the obesity in those with GERD. However, the definition of obesity in the current study is an accepted definition based on CDC guidelines and the use of the NCHS standards which are age- and gender-specific, allows comparisons of children over a wide range of ages. A final limitation of the study is that we did not include children diagnosed with GERD based on pH evaluation only; however, we checked the records for this group of children and this was an extremely small number which would have not influenced the current results or the conclusions of the study.

In summary, the study demonstrated clear evidence of an association between childhood obesity and GERD and its symptoms. Recognition of these results will have important implications for the management of childhood GERD.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Ashorn M, Ruuska T, Karikoski R, Laippala P. The natural course of gastroesophageal reflux disease in children. *Scand J Gastroenterol*. 2002;37:638–641.
2. Hegar B, Boediarso A, Firmansyah A, Vandenplas Y. Investigation of regurgitation and other symptoms of gastroesophageal reflux in Indonesian infants. *World J Gastroenterol*. 2004;10:1795–1797.
3. Colletti RB, Di Larenzo C. Overview of pediatric gastroesophageal reflux disease and proton pump inhibitor therapy. *J Pediatr Gastroenterol Nutr*. 2003;37:S7–S11.
4. Malaty HM, Takenticho M, Abudayyeh S, et al. Outcomes of recurrent abdominal pain (rap) in children and their responses to a multidimensional measure for rap (MM-RAP): A follow-up study. *JCOM.* 2008;15:28792.
5. Dore MP, Maragkoudakis E, Fraley KJ, Realdi G, Graham DY, Malaty HM. Diet, lifestyle and gender in gastro-esophageal reflux disease. *Dig Dis Sci*. 2008;53:2027–2032.
6. El-Serag HB, Graham DY, Satia JA, Rabeneck L. Obesity is an independent risk factor for GERD symptoms and erosive esophagitis. *Am J Gastroenterol*. 2005;100:1243–1250.
7. Nocon M, Labenz J, Jaspersen D, et al. Association of body mass index with heartburn, regurgitation and esophagitis: results of the Progression of Gastroesophageal Reflux Disease study. *J Gastroenterol Hepatol*. 2007;22:1728–1731.
8. Størdal K, Johannesdottir GB, Bentsen BS, Carlsen KC, Sandvik L. Asthma and overweight are associated with symptoms of gastro-oesophageal reflux. *Acta Paediatr.* 2006;95:1197–1201.
9. Shore SA, Johnston RA. Obesity and asthma. *Pharmacol Ther*. 2006;110:83–102.
10. Malaty HM, Abudayyeh S, Fraley K, Graham, DY, Gilger MA, Hollie D. Recurrent abdominal pain in school children: effect of obesity and diet. *Acta Pediatric*. 2007;96:572–576.
11. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during childhood: a pediatric practice-based survey. Pediatric Practice Research Group. *Arch Pediatr Adolesc Med*. 2000;154:150–154.
12. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during infancy: a pediatric practice-based survey. Pediatric Practice Research Group. *Arch Pediatr Adolesc Med*. 1997;151:569–572.
13. Spechler SJ. Clinical manifestations and esophageal complications of GERD. *Am J Med Sci.* 2003;326:279–284.
14. Vandenplas Y, Badriul H, Salvatore S, Hauser B. Pharmacotherapy of gastrooesophageal reflux disease in children: focus on safety. *Expert Opin Drug Saf.* 2002;1:355–364.
15. Gilger MA, Gold BD. Pediatric endoscopy: new information from the PEDS-CORI project. *Curr Gastroenterol Rep*. 2005;7:234–239.
16. World Health Organization. *The International Classification of Diseases, 9th revision*. *Clinical modification*. 3rd ed. Washington, DC: Public Health Service, US Government Printing Office; March 1989; DHHS Publication no. (PHS) 89–1260.
17. American Medical Association. *Current Procedural Terminology 2000*. Standard ed. Boston, MA: American Medical Association; 1999.
18. de Veer AJ, Bos JT, Niezen-de Boer RC, Bohmer CJ, Francke AL. Symptoms of gastroesophageal reflux disease in severely mentally retarded people: a systematic review. *BMC Gastroenterol.* 2008;8:23.

19. de Vries DR, van Herwaarden MA, Smout AJ, Samsom M. Gastroesophageal pressure gradients in gastroesophageal reflux disease: relations with hiatal hernia, body mass index, and esophageal acid exposure. *Am J Gastroenterol*. 2008;103:1349–1354.
20. Gustafsson PM, Kjellman NIM, Tibbling L. Bronchial asthma and acid reflux into the distal and proximal esophagus. *Arch Dis Child*. 1990;65:1255–1258.
21. Taylor AC, Breen KJ, Auldist A, Catto-Smith A, Clarnette T, Crameri J, Taylor R, Nagarajah S, Brady J, Stokes K. Gastroesophageal reflux and related pathology in adults who were born with esophageal atresia: a long-term follow-up study. *Clin Gastroenterol Hepatol.* 2007;5:702–706.
22. Sakaguchi M, Oka H, Hashimoto T, et al. Obesity as a risk factor for GERD in Japan. *J Gastroenterol*. 2008;43:57–62.
23. Fass R. The pathophysiological mechanisms of GERD in the obese patient. *Dig Dis Sci.* 2008;53:2300–2306.
24. Wu JC, Mui LM, Cheung CM, Chan Y, Sung JJ. Obesity is associated with increased transient lower esophageal sphincter relaxation. *Gastroenterology*. 2007;132:883–889.
25. Hirsch DP, Mathus-Vliegen EM, Dagli U, Tytgat GN, Boeckxstaens GE. Effect of prolonged gastric distention on lower esophageal sphincter function and gastroesophageal reflux. *Am J Gastroenterol*. 2003;98:1696–1704.
26. Crooks DL. Trading nutrition for education: nutritional status and the sale of snack foods in an eastern Kentucky school. *Med Anthropol Q*. 2003;17:182–99.
27. Andrews G. Comorbidity and the general neurotic syndrome. *Br J Psychiatry*.1996;168 Suppl 30:76 –84.
28. Oster J. Recurrent abdominal pain, headache and limb pains in children and adolescents. *Pediatrics*.1972;50:429–436.
29. Borge AI, Nordhagen R. Development of stomach-ache and headache during middle childhood: co-occurrence and psychosocial risk factors. *Acta Paediatr*. 1995;84:795 –802.
30. Kostikas K, Papaioannou AI, Gourgoulianis KI. BMI and gastroesophageal reflux in women. *N Engl J Med*. 2006:354:2340–2348.
31. Jacobson BC, Moy B, Colditz GA, Fuchs CS. Postmenopausal hormone use and symptoms of gastroesophageal reflux. *Arch Intern Med*. 2008;168:1798–1804.