Obesity Does Not Affect Early Outcomes in Children With Newly Diagnosed Crohn Disease

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ABSTRACT

The impact of obesity on pediatric Crohn disease (CD) remains poorly characterized. We aimed to evaluate disease-related outcomes in overweight and obese children with CD, compared to normal-weight children. We conducted a retrospective cohort study of children with newly diagnosed CD enrolled in the ImproveCareNow Network. Patients were stratified into normal weight, overweight, and obese groups using standardized weight percentiles. A total of 898 children were included, with 87 children (10%) being overweight and 43 children (5%) being obese; baseline characteristics were similar between groups. There was no significant difference in number of visits in remission during 1 year between normal weight, overweight, and obese children. At 1-year follow-up, nutritional status, growth status, or medication use also did not differ between groups. Hence, obesity does not appear to adversely affect CD outcomes in children with newly diagnosed CD in the first year after diagnosis.

Key Words: body mass index, inflammatory bowel disease, obese, overweight, pediatric

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What Is Known

- The role of obesity in adults with Crohn disease is unclear, with some reports suggesting worsened disease course, whereas other reports suggest no impact.
- Little is known about the role of obesity in children with Crohn disease.

What Is New

- In this cohort of children with newly diagnosed Crohn disease, obesity appears to have no impact on Crohn disease course at 1 year.
- Further study is warranted to evaluate longer-term impact of obesity in pediatric Crohn disease.

Obesity among children is a growing challenge in the United States with approximately 15% of children being overweight and an additional 17% being obese, defined by age-specific growth charts (1,2). Although obesity is typically considered a proinflammatory state, the impact of obesity on immune-mediated diseases, such as Crohn disease (CD), is not entirely clear (3,4). Limited data in adult patients show conflicting impact of obesity on inflammatory bowel disease (IBD), with some studies suggesting increased disease flares and complications, whereas other studies show no impact or even reduced need for surgery in obese patients with IBD (5–9). Literature on obesity in pediatric IBD is even more limited, with very few reports directly addressing this issue. The aim of the present study was to use a large multicenter cohort of children with newly diagnosed CD to evaluate the impact of obese and overweight status on IBD-related outcomes.

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METHODS

Study Design

We performed a retrospective cohort study of children with newly diagnosed CD enrolled in the ImproveCareNow (ICN) Network from September 2006 to October 2014. The ICN Network includes prospectively collected data regarding demographic factors, IBD phenotype, IBD disease course, treatment course, and disease-related outcomes. Data are entered into the ICN database by clinicians or research personnel. For the present analysis, we included patients with a first visit within 90 days of CD diagnosis and at least 1 follow-up visit within 12 to 18 months after diagnosis. All children with age >2 years (24 months) and <21 years (252 months) were included. Patients were excluded if weight, height, sex, or birthdate were missing at baseline or 1-year follow-up. Underweight children, as defined by body mass index (BMI) <10th percentile at baseline or 1-year follow-up, were also excluded.

Exposure Variables (Overweight/Obese Status)

Using BMI at the initial visit, patients were categorized into obese, overweight, and normal-weight groups. For children ages 2 to 20 years, the Centers for Disease Control and Prevention age- and sex-specific nomograms were used to categorize patients by weight status. Obesity was defined as BMI ≥95th percentile and overweight was defined as BMI between 85th and 94th percentile for given age and sex. Normal weight was defined as 10th to 84th percentile. For patients ages 20 years, traditional BMI cut points

were used: normal weight BMI 18.5 to 24.9, overweight BMI 25.0 to 29.9, obese BMI $\geq$30.0 (10).

Outcome Variables

The primary outcome was the number of visits in clinical remission during 1-year follow-up based on physician global assessment (PGA). The visit closest to 1 year from diagnosis (and after a minimum of 365 days since diagnosis) was used to assess additional secondary outcomes. Secondary outcomes assessed include disease activity by short Pediatric Crohn Disease Activity Index (sPCDAI), nutritional status (satisfactory, at risk, in failure), growth status (satisfactory, at risk, in failure), serologic markers of disease (sedimentation rate, hematocrit, albumin), and medication treatment differences.

Statistical Analysis

Obese and overweight patients were evaluated as separate groups with normal-weight patients as the reference group. The *t* test or nonparametric Kruskal-Wallis rank sum test were used to look at differences in continuous variables. Pearson Chi square test or Fisher test was used to evaluate bivariate outcomes by weight group (obese vs normal; overweight vs normal). Missing data variables were omitted from the analysis (pairwise deletion). All statistical analyses were performed using R 3.0.1 (11).

The study was approved by the Nationwide Children's Hospital Institutional Review Board.

RESULTS

A total of 898 children with newly diagnosed CD were included in the analysis. Table 1 shows demographic and clinical characteristics between normal weight, overweight, and obese patients at baseline. The majority of children were normal weight (n = 768, 85.5%), whereas smaller numbers were overweight (n = 87, 9.7%) or obese (n = 43, 4.7%). Children with obesity had a younger age at CD diagnosis compared to normal-weight children (11.4 vs 12.9 years, $P = 0.016$). Compared to normal-weight children, children with obesity also had higher percentage of Medicaid insurance (35% vs 12%) and lower percentage of commercial insurance (47% vs 74%), $P < 0.001$. Other demographic characteristics, including sex and race, were similar between groups. CD phenotype and behavior at diagnosis were also similar between obese, overweight, and normal-weight children.

The primary outcome measure, number of visits in remission during 1 year, was similar for children with obesity (3.49 visits) compared to normal-weight children (3.98 visits, $P = 0.18$) and for overweight children (3.67 visits) compared to normal-weight children ($P = 0.16$). There was no difference in total number of visits between groups or number of visits in steroid-free remission. Other secondary outcome measures, including nutritional status, growth status, and sPCDAI, were assessed at the visit closest to 1 year. There was no difference in these secondary outcomes at 1 year (Table 2). Based on sPCDAI, numerically more children with obesity had moderate-severe disease compared to normal-weight children (20% vs 11%) and fewer children with obesity had inactive disease compared to normal-weight children (60% vs 72%). These trends were, however, not statistically significant ($P = 0.33$). Medication use, including use of steroids, immune suppressants, or biologics, was similar between obese, overweight, and normal-weight children at 1 year. Serum hematocrit was statistically higher for children with obesity at 1 year compared with normal-weight children (39.5 vs 37.8). Other laboratory measurements, including sedimentation rate and albumin, were, however, similar between groups (Table 2).

Some children did change weight category from baseline through the 1 year of follow-up. Among children who were normal weight at baseline, 66 children increased to overweight (9% of the normal weight cohort) and 16 children (2%) increased to obese at 1-year follow-up. Among children who were obese at baseline, 7 children (16%) decreased to overweight and 5 children (12%) decreased to normal weight. There was more movement in the group of children who were overweight at baseline. Amongst these overweight children, 22 children (25%) increased to the obese category and 28 children (32%) decreased to normal weight.

For most data fields shown in Tables 1 and 2, the proportion of missing data was small (<10% missing). Notable exceptions include Paris Classification, in which approximately 45% of children had missing data, and sPCDAI, in which 35% of children had missing data. The proportion of missing data was similar between normal-weight, overweight, and obese children.

DISCUSSION

Obesity is a growing health challenge in adults and children. The impact of obesity on CD is poorly characterized, particularly in children. Our present study looks at children with newly diagnosed CD and shows no impact of obesity or overweight status on CD outcomes at 1 year from diagnosis.

Research on the impact of obesity on CD outcomes is limited. Literature in the adult setting shows conflicting impact of obesity on IBD course. Early reports seemed to indicate higher rates of perianal disease, active disease flares, and shorter time to first surgery amongst obese or overweight adults with CD (5,6). These studies were, however, somewhat limited by their retrospective design and relatively small numbers. A more recent retrospective cohort study of almost 1500 patients showed no association between BMI and IBD outcomes, including steroid use, anti-TNF use, hospitalization, or IBD-related surgery (7). A retrospective cohort by Flores et al (9), included approximately 600 adult patients and showed *lower* rates of steroid use, anti-TNF use, hospitalization, and IBD-related surgery amongst obese adults with IBD. The authors concluded that obesity may be a marker of less severe disease.

Literature in the pediatric setting is even more limited. A 2014 study used the Kids' inpatient database to analyze more than 12,000 hospital admissions of children with IBD and demonstrated no impact of obesity on rate of perforation, hemorrhage, complex fistula, or need for surgery (12). This study was, however, limited to the hospitalized IBD population and focused only on in-hospital outcomes. In addition, only 1.3% of admissions had a code for obesity, raising concern for potential undercoding in the dataset. A 2011 study performed a cross-sectional analysis of overweight and obese children enrolled in ICN. That study showed that prior IBD-related surgery was associated with overweight or obese status, suggesting a worsened disease course for these children (13). The cross-sectional design of that study limited conclusions about causality and no weight-based differences in other clinical characteristics, including PGA, medication use, or disease phenotype, were observed.

Although our data show no signs of differing disease course at 1 year for obese compared with normal-weight children, it is possible that obesity may have a delayed effect on CD outcomes that manifests several years later. Moreover, some children with a normal weight at the time of diagnosis may develop obesity later in their disease course. Indeed, 11% of children in our cohort progressed from normal weight at baseline to overweight or obese at 1-year follow-up. It is unclear whether this subsequent obesity

TABLE 1. Study cohort demographics at baseline visit

	Total	Normal	Overweight	P^*	Obese	$P^\dagger$
Total, n	898	768	87	—	43	—
Male, n (%)	558 (62)	477 (62)	50 (57)	0.467	31 (72)	0.248
Age at diagnosis, y, M (SD)	12.8 (3.2)	12.9 (3.1)	12.8 (3.4)	0.636	11.4 (3.9)	**0.016**
Disease duration (days), Mdn(Q1-Q3)	28 (15–48)	27 (14–48)	37 (22–55)	**0.001**	31 (16–52)	0.368
BMI, median (IQR)	18.7 (17.0–21.0)	18.3 (16.7–19.9)	23.3 (21–25.6)	**<0.001**	26.8 (22.8–30.4)	**<0.001**
BMI percentile, median (IQR)	50.9 (29.1–73.7)	44.7 (26.7–63.9)	90.0 (87.6–92.4)	**<0.001**	97.7 (96.2–98.4)	**<0.001**
Race				0.064		0.053
White, n (%)	708 (79)	602 (78)	73 (84)		33 (77)	
African-American, n (%)	98 (11)	92 (12)	4 (5)		2 (5)	
Other,[‡] n (%)	46 (5)	35 (5)	6 (7)		5 (12)	
Hispanic, n (%)	24 (3)	13 (2)	6 (7)	**0.011**	5 (12)	**0.005**
Insurance				0.461		**<0.001**
Medicaid, n (%)	121 (13)	93 (12)	13 (15)		15 (35)	
Commercial, n (%)	647 (72)	568 (74)	59 (68)		20 (47)	
Paris classification						
L1: distal 1/2 ileum ± limited cecal	59 (7)	49 (6)	7 (8)	0.107	3 (7)	0.913
L2: colonic	53 (6)	42 (5)	9 (10)		2 (5)	
L3: ileocolonic	199 (22)	176 (23)	15 (17)		8 (19)	
L4a: upper disease proximal to the ligament of Treitz	128 (14)	111 (14)	11 (13)	0.578	6 (14)	0.894
L4b: upper disease distal to the ligament of Treitz	22 (2)	21 (3)	0 (0)	0.141	1 (2)	1.000
L4a and 4b	37 (4)	35 (5)	1 (1)	0.141	1 (2)	0.697
Behavior						
B1: nonstricturing, nonpenetrating	772 (86)	659 (86)	76 (87)	0.652	37 (86)	1.000
B2: stricturing	36 (4)	32 (4)	2 (2)	0.566	2 (5)	0.704
B3: penetrating	46 (5)	38 (5)	5 (6)	0.937	3 (7)	0.479
B2B3: penetrating and stricturing	9 (1)	9 (1)	0 (0)	0.610	0 (0)	1.000
Perianal	166 (18)	140 (18)	18 (21)	0.586	8 (19)	1.000
Nutritional status						
Satisfactory	733 (82)	613 (80)	82 (94)		38 (88)	
At risk	101 (11)	95 (12)	2 (2)		4 (9)	
In failure	18 (2)	18 (2)	0 (0)	0.002	0 (0)	0.669
Growth status						
Satisfactory	731 (81)	615 (80)	78 (90)	0.135	38 (88)	0.773
At risk	88 (10)	81 (11)	4 (5)		3 (7)	
In failure	35 (4)	32 (4)	2 (2)		1 (2)	
PGA[§]						
In remission	322 (36)	275 (36)	34 (39)	0.644	13 (30)	0.691
Mild	357 (40)	308 (40)	30 (34)		19 (44)	
Moderate-severe	180 (20)	152 (20)	18 (21)		10 (23)	
sPCDAI						
Inactive	317 (35)	271 (35)	36 (41)	0.115	10 (23)	0.081
Mild	151 (17)	130 (17)	13 (15)		8 (19)	
Moderate-severe	114 (13)	99 (13)	5 (6)		10 (23)	
Serologic markers						
Sedimentation rate, mean (SD)	22.8 (18.3)	22.6 (18.1)	22.7 (16.8)	0.792	26.3 (23.6)	0.720
Hematocrit, mean (SD)	36.4 (4.5)	36.4 (4.2)	37.1 (5.6)	0.021	36.1 (7.7)	0.756
Albumin, mean (SD)	3.9 (0.6)	3.9 (0.6)	4 (0.6)	0.038	4 (0.5)	0.133

Column percentages are presented by BMI percentile group. Bolded P values represent significant findings.
M = mean; Mdn = median; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; sPCDAI = short Pediatric Crohn Disease Activity Index.
[*]Comparison is between normal and overweight groups.
[†]Comparison is between normal and obese groups.
[‡]Other includes race categories <5% (American Indian/Alaska Native, Asian, Native Hawaiian/Pacific Islander, other, and multiracial).
[§]Remission status according to physician global assessment (PGA).

would have an impact on CD course, and this would be an interesting area to investigate in future studies.

A key difference between our study and prior pediatric and adult studies was our use of an inception cohort including assessment of baseline weight status within 90 days of diagnosis. In prior studies, obesity status was generally assessed several years into the patient's disease course. Because CD can lead to malnutrition and weight loss, categorizing obesity after several years of disease may in fact just be a measure of disease severity, as suggested by Flores et al. There are additional strengths of our study. In particular, the

TABLE 2. Crohn disease outcomes at 1-year follow-up

	1 Year follow-up*				
	Normal	Overweight	*P*	Obese	*P*
Visits, M (SD)	6.98 (2.91)	7.08 (2.82)	0.62	7.30 (2.44)	0.21
Visits in remission by PGA, M (SD)	3.98 (2.18)	3.67 (2.47)	0.16	3.49 (1.67)	0.18
Visits in steroid-free remission, M (SD)	3.15 (1.88)	3.10 (2.12)	0.58	2.81 (1.62)	0.28
BMI, median (IQR)	19.6 (17.6–21.7)	24.8 (21.5–27.2)	**<0.001**	27.5 (21.8–33.7)	**<0.001**
BMI percentile, median (IQR)	54.0 (33.0–73.2)	90.7 (82.0–95.0)	**<0.001**	96.8 (92.5–99.0)	**<0.001**
Nutritional status					
Satisfactory	662 (88)	83 (97)	0.066	37 (90)	1.000
At risk	71 (9)	3 (3)		4 (10)	
In failure	17 (2)	0 (0)		0 (0)	
Growth status					
Satisfactory	642 (90)	74 (95)	0.377	40 (98)	0.239
At risk	47 (7)	4 (5)		0 (0)	
In failure	21 (3)	0 (0)		1 (2)	
PGA					
In remission	556 (74)	53 (62)	0.070	32 (74)	0.646
Mild	148 (20)	25 (29)		7 (16)	
Moderate-severe	48 (6)	7 (8)		4 (9)	
sPCDAI					
Inactive	374 (72)	38 (62)	0.254	15 (60)	0.333
Mild	84 (16)	13 (21)		5 (20)	
Moderate-severe	59 (11)	10 (16)		5 (20)	
Serologic Markers					
Sedimentation rate, mean (SD)	15.9 (14.2)	19.3 (15.1)	0.079	14.9 (14.1)	0.637
Hematocrit, mean (SD)	37.8 (3.8)	38.3 (3.0)	0.218	39.5 (5.0)	**0.021**
Albumin, mean (SD)	4.2 (0.5)	4.2 (0.5)	0.389	4.3 (0.3)	0.420

*1-Year follow-up refers to visit closest to 365 days from diagnosis for each variable (within the bounds of 365 and 547 days).
BMI = body mass index; IQR = interquartile range; SD = standard deviation; sPCDAI = short Pediatric Crohn Disease Activity Index.

ICN Network is a large, multicenter cohort with robust data on clinical measures, disease activity indices, medication data, and laboratory data. Secondly, we were able to simulate an inception cohort by including only children with newly diagnosed CD.

Nonetheless, there are some key limitations. Our study only captures height/weight data within 90 days of diagnosis. Hence, the characterization of weight status could be affected by weight loss before diagnosis (resulting in potential bias toward worse outcomes for normal-weight children). Conversely, weight status could be affected by steroid use at the time of diagnosis which could bias toward worse outcomes for overweight or obese children. Also, for some data fields, most notably the sPCDAI, there was substantial proportion of missing data (~35% missing for sPCDAI). The proportion of missing data was, however, similar across normal weight, overweight, and obese children suggesting that missing data may have been random rather related to obesity status.

In conclusion, this multicenter cohort study shows no impact of obesity or overweight status on CD outcomes at 1 year after diagnosis, as measured by multiple clinical endpoints. Longer-term studies would be beneficial to see whether obesity has an impact on CD outcomes later in the disease course.

REFERENCES

1. Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA* 2014;311:806–14.
2. Ogden CL, Carroll MD, Lawman HG, et al. Trends in obesity prevalence among children and adolescents in the United States, 1988–1994 through 2013–2014. *JAMA* 2016;315:2292–9.
3. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. *Annu Rev Immunol* 2011;29:415–45.
4. Singh S, Dulai PS, Zarrinpar A, et al. Obesity in IBD: epidemiology, pathogenesis, disease course and treatment outcomes. *Nat Rev Gastroenterol Hepatol* 2017;14:110–21.
5. Blain A, Cattan S, Beaugerie L, et al. Crohn's disease clinical course and severity in obese patients. *Clin Nutr* 2002;21:51–7.
6. Hass DJ, Brensinger CM, Lewis JD, et al. The impact of increased body mass index on the clinical course of Crohn's disease. *Clin Gastroenterol Hepatol* 2006;4:482–8.
7. Seminerio JL, Koutroubakis IE, Ramos-Rivers C, et al. Impact of obesity on the management and clinical course of patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2015;21:2857–63.
8. Krane MK, Allaix ME, Zoccali M, et al. Does morbid obesity change outcomes after laparoscopic surgery for inflammatory bowel disease? Review of 626 consecutive cases. *J Am Coll Surg* 2013; 216:986–96.
9. Flores A, Burstein E, Cipher DJ, et al. Obesity in inflammatory bowel disease: a marker of less severe disease. *Dig Dis Sci* 2015;60: 2436–2445.
10. Centers for Disease Control and Prevention. Defining Adult Overweight and Obesity. *https://www.cdc.gov/obesity/adult/defining.html*. Accessed June 20, 2018.
11. R: A language and environment for statistical computing (Computer Program). Version 3.0.1. Vienna, Austria: R Core Team; 2013.
12. Zwintscher NP, Horton JD, Steele SR. Obesity has minimal impact on clinical outcomes in children with inflammatory bowel disease. *J Pediatr Surg* 2014;49:265–8.
13. Long MD, Crandall WV, Leibowitz IH, et al. Prevalence and epidemiology of overweight and obesity in children with inflammatory bowel disease. *Inflamm Bowel Dis* 2011;17:2162–8.