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Body Mass Index at Presentation of Inflammatory Bowel Disease in Children

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Conflict of Interest
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ABSTRACT

Purpose: The evidence for an association between inflammatory bowel disease (IBD) and obesity is conflicting. Therefore, we set out to review the body mass index (BMI) at presentation of IBD to understand if the rise of the obesity rate in the general population, lead to an increase of obesity in patients with IBD at the time of diagnosis.
Methods: Retrospective review of all patients with IBD seen at Children's Hospital and Medical Center from January 1st 2010 to December 31st 2014. From the initial visit and endoscopy, we obtained: age; sex; BMI; disease phenotype; disease severity.
Results: We had a total of 95 patients, 35 patients were excluded due to incomplete data or referral being made after diagnosis was made. 28 were males and 32 were females, Age range was 2–17 years. A 37 had Crohn's disease, 19 ulcerative colitis, and 4 indeterminate colitis. Disease severity in 19 cases was mild, 29 moderate and 12 severe. BMI distribution was as follows—obese (5.0%), overweight (6.7%), normal weight (65.0%), mild malnutrition (8.3%), moderate malnutrition (15.0%), severe malnutrition (1.7%).
Conclusion: Our data is consistent with other series. Showing most children had a normal BMI, regardless of disease severity or phenotypes. One confounding factor is the possibility of delay in referral to GI. This could mean some obese children may fall in the normal BMI range at the time of diagnosis due to ongoing weight loss. Future studies should include prospective cohort studies, comparing incidence of IBD in obese and non-obese patients, severity at presentation, duration of symptoms, and clinical outcomes.

Keywords: Obesity; Pediatric obesity; Inflammatory bowel diseases; Pediatric inflammatory bowel disease

INTRODUCTION

Obesity has become a common health problem affecting children in the United States. The prevalence of obesity has risen to 18.5%, affecting approximately 13.7 million children and adolescents, according to the Center for Disease Control and Prevention [1]. This change in body composition of the general population, could affect the body composition in patients with conditions where weight loss/malnutrition is common.

It has been proposed that obesity is a pro-inflammatory state, due in part to secretion of soluble mediators by the white adipose tissue, mediators involved in the promotion of this pro-inflammatory state include leptin and adiponectin among others [2]. Leptin influences both innate and acquired immunity, it's effects include activation and proliferation of monocytes, enhanced phagocytosis and leukotriene production in macrophages, increased chemotaxis and release of oxygen radicals in neutrophils, promotion of natural killer cells, dendritic cells maturation and survival, stimulation of naïve T-cells, promotes differentiation to a T-helper 1cels, inhibits T-regulatory cells [3,4]. Adiponectin unlike most adipokines is decreased in obese patients, has consistently shown to be anti-inflammatory, it inhibit expression of TNF-α induced adhesion molecules in the endothelium such as vascular adhesion molecule-1, endothelial-leukocyte adhesion molecule-2 (E-selectin), and intracellular adhesion molecule-1 [5,6]. This pro-inflammatory state appears to play a role in autoimmune diseases [2].

One such condition is inflammatory bowel disease (IBD), although it's precise cause is unknown, a dysregulated mucosal immune response leading to bowel inflammation is understood to be a critical part of the condition [7]. The estimated incidence of IBD, in Children younger than 19 years in North America is 15.2/100,000 person-years [8]. The IBD spectrum includes three distinct entities, Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis (IC). All are classically associated with weight loss; in fact, malnutrition and impaired linear growth in children are markers of disease severity [9].

The evidence for an association between IBD and obesity is conflicting. The epic trial found no association between obesity and the development of IBD in adult patients [10], another study found that obese women have an increased risk of CD; however there was no increase in risk of UC, when compared to non-obese women [11]. Regarding outcomes, although there are reports of obesity as a marker of less severe disease [12,13]; shorter time to loss of response of infliximab, decreased likelihood of response to adalimumab, increased perianal disease, earlier time to first surgery and decreased quality of life have all been reported in obese patients [14].

In our study, we set out to review the body mass index (BMI) at presentation of IBD to understand if with the historic rise of obesity in the general population [1], an increase of obesity in patients with IBD has also been noticed. Additionally, we examine the BMI in each disease severity group along with IBD phenotype.

MATERIALS AND METHODS

We proposed a retrospective cross sectional study, of all patients with IBD seen at Children's Hospital and Medical Center from January 1, 2010 to December 31, 2014. After the institutional review board approved our study, we performed a retrospective analysis of the data from the time of initial consultation and/or initial endoscopic evaluation of each patient. The following variables were used: Age in years; sex; BMI defined as the patient's weight in Kilograms divided by the square of their height in meters; Individuals were categorized according to sex specific BMI for age growth charts from the CDC [15]. Those with a BMI for age Z-score >+1.64 were categorized as obese, z-scores <+1.64 and >+1.04 or were defined as overweight, normal weight z-score <+1.04 and >−1, mild malnutrition z-score <−1 and >−2, moderate malnutrition z-score <−2 and >−3, severe malnutrition Z-score <−3. The overweight

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and obesity cut off points are equivalents to the 85th and 95th percentiles respectively which are the accepted definitions [16]; the definition of malnutrition is based on the joint guideline from the Academy of Nutrition and Dietetics, and the American Society for Parenteral Nutrition [17].

Disease phenotype was divided into CD, UC, and IC based on endoscopy, imaging and histologic examination, according to the current guidelines [18,19], Severity of the disease was established using validated clinical activity indices Pediatric Ulcerative Colitis Activity index (PUCAI) [20] or the Pediatric Crohn's Disease Activity Index (PCDAI) [21], PUCAI classifies disease activity as remission <10 points (pts). Mild activity 10–35 pts, moderate activity 35–65 pts or severe activity >65 pts, PCDAI categories are as follows remission,10 pts, mild activity 10–27.5 pts, moderate activity 27.5–37.5 pts, or severe activity >37.5 pts. Endoscopic severity was determined by reviewing the operative reports, for each patient's first endoscopy. Which in some cases includes still images. Mild cases were defined as those where there were ulcers <0.5 cm, erythema were described without strictures, moderate cased were those where ulcers between 0.5 cm and 2 cm, there was obliteration of the vascular pattern, and friability of the mucosa was noted, Severe cases were defined as those where ulcers >2 cm in diameter, oozing of frank blood from the mucosa, and strictures were described.

The sample size precluded meaningful statistical analysis. Therefore, percentages were used to describe the population.

RESULTS

A total of 95 unique patients were seen and followed for IBD at Children's Hospital and Medical Center between 01/01/2010–12/31/2014, 35 patients were excluded due to incomplete data (7) or if referral was made after the diagnosis of IBD was made (28). The remaining 60 patients were analyzed, 28 males and 32 females. Age at diagnosis ranged from 2–17 years with a median of 12 years. Regarding IBD phenotype 37 were diagnosed with CD, 19 patients with UC, and 4 patients with IC. There were 19 mild cases, 29 moderate cases and 12 severe cases (**Table 1**).

Each BMI category had the following number of patients, obese 3 (5.0%), overweight 4 (6.7%), normal weight 38 (65.0%), mild malnutrition 5 (8.3%), moderate malnutrition 9 (15.0%), severe malnutrition 1 (1.7%). Sex was evenly distributed in all groups except for overweight and severe malnutrition group which had only female patients. Normal BMI was by far the most common regardless of disease severity (**Fig. 1**).

The distribution of the different BMI categories, in each phenotype group, shows that most Patients with CD and UC had the same frequency of obesity (5.0%), none of the patients with IC were obese. Overweight patients were most commonly seen in the IC (25.0%), and UC (10.5%) group than in the CD (2.7%). When considered together, overweight and obesity where seen in 11.6% of all patients, 8.1 of patients with CD, 15.7% patients with UC, and 6% of patients with IC. At the other end of the spectrum 25% of all patients presented with some degree of malnutrition; moderate malnutrition being the most common type. Malnutrition was more common in the CD group 32.7% than in the UC 15.7% and IC group 0 (**Fig. 2**).

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Table 1. Patients characteristics

Variable	Value (n=60)
Sex	
Female	32 (53.3)
Male	28 (46.7)
Age (yr)	
<10	17 (28.3)
10–13	25 (41.7)
14–17	18 (30.0)
Median	12
Nutritional status	
Obese	3 (5.0)
Overweight	4 (6.7)
Normal	39 (65.0)
Mild malnutrition	5 (8.3)
Moderate malnutrition	9 (15.0)
Severe malnutrition	1 (1.7)
IBD phenotype	
Chron's disease	37 (61.7)
Ulcerative colitis	19 (31.7)
Indeterminate colitis	4 (6.7)
IBD severity	
Mild	19 (31.7)
Moderate	29 (48.3)
Severe	12 (20.0)

Values are presented as number (%).
IBD: inflammatory bowel disease.

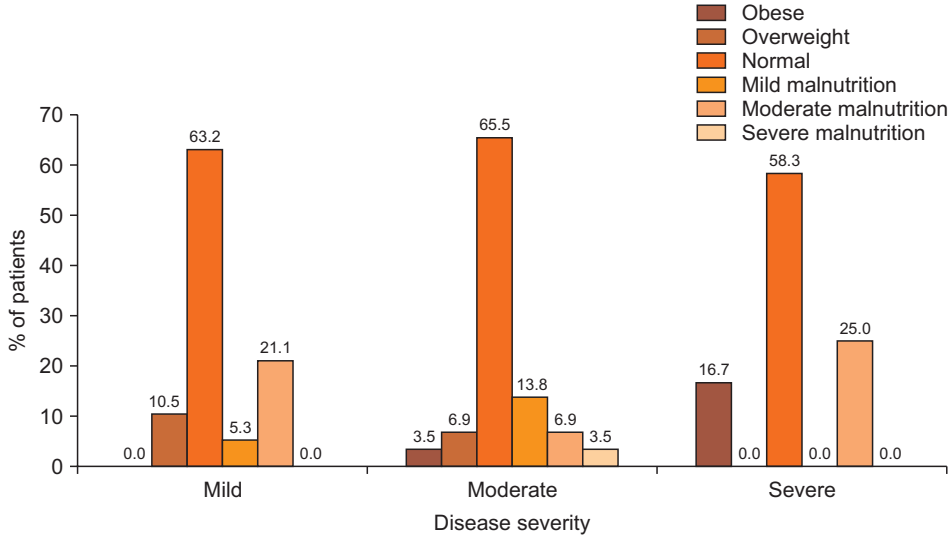

Fig. 1. Body mass index distribution by percentage of patients among disease severity groups.

DISCUSSION

Our findings were similar to other series [22-26], with most children and teens having BMI in the normal range. Kugathasan et al. [22] reviewed 2 North American cohorts of IBD patients, the rate of patients with BMI >85th percentile for age in each cohort, was 9–10% for patients with CD, and 20–34% for patients with UC. Pituch-Zdanowska and collaborators [23] report a retrospective review of 5 children's hospitals in Poland, finding that 4.3% of patients with CD and 15.7% of patients with UC are either obese or overweight. Recently Chandrakumar et al.

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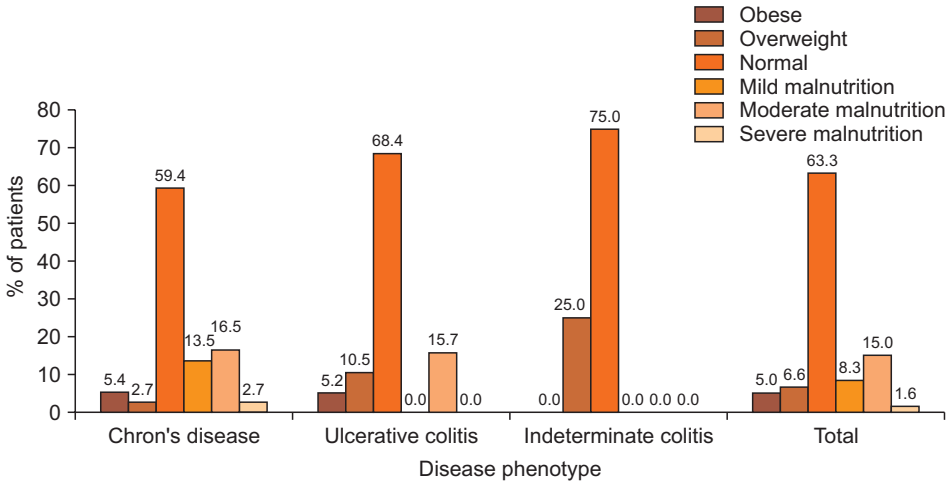

Fig. 2. Body mass index distribution by percentage of patients among disease phenotype.

Table 2. Percentage of patients who are overweight or obese by disease phenotype in recent studies

Study population	Chron's disease	Ulcerative colitis
North American IBD cohort [23]	9.0	20.0
Wisconsin IBD cohort [23]	10.0	34.0
Poland [24]	4.3	13.3
Manitoba [25]	9.0	21.0
CHMC	8.1	15.7

IBD: inflammatory bowel disease, CHMC: Children's Hospital and Medical Center.

[24] from Canada reported a Cohort of 139 pediatric patients with IBD, at presentation 71% had a normal BMI, 9.4% where overweight, 7.2% were obese, and 16.6% where either obese or overweight. Obesity was more common in patients with UC 12.7%, than in patients with CD 0.0%, 9% of both overweight and obese patients were overweight (**Table 2**) [23-25].

Two other series report BMI in children with IBD, however their methodology includes all patients with IBD, not only those who were newly diagnosed [25,26]. Similarities between the North American, Canadian, and Nebraskan groups could be due to the fact that these population are geographically closer to each other, than to the Polish group. We hypothesize this geographical proximity may result in children from this group having similar genetic backgrounds, diets, and exposure to environmental factors. It is interesting to note that in all groups, UC were more commonly obese or overweigh when compared to patients with CD. This suggest this may be an intrinsic feature of the disease rather, rather than the result of differences in the populations that were studied.

The results are also compatible with reported changes in the BMI at presentation of pediatric Celiac Disease, where patients historically have been characterized by weight loss and malnutrition. Newer data shows 19% of patients with Celiac Disease are either obese or overweight at diagnosis (12.6% overweight, 6% obese), and 74.5% of patients presented with a normal BMI [27].

In addition to the pro-inflammatory effects of obesity that were previously discussed, and the increased prevalence of obesity in the general population, another factor that should be considered is the increased awareness of IBD among pediatricians, along with improved

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diagnostic techniques. These factors could lead to earlier identification of IBD in children, hopefully leading to diagnosis before significant weight loss has occurred.

Our study has a few limitations. These include a small data set, which precluded meaningful statistical analysis; the possibility of selection bias as only children that are sufficiently symptomatic are referred to our center for evaluation, lead time bias is also possible as the time from initial symptom presentation to referral varies. Delay in referral from initial symptoms could allow children with obesity, to fall under the normal BMI by the time they see a specialist and are diagnosed. This could lead us to underestimate the role of obesity in IBD.

The lack of a standardized reporting scale for the endoscopic notes, hindered the possibility of making direct comparison between patients, this is due in part to the fact that only recently these scales have been recommended for use in the pediatric population.

In conclusion children who present with IBD, were noted to most commonly have a normal BMI. However, obese or overweight children, should not be overlooked at the time of initial presentation. Whether the pro-inflammatory effects of obesity are associated with an increase incidence, more severe presentation, or different outcomes remains to be seen. Future studies should include a prospective cohort study, comparing incidence of IBD in obese and non-obese patients, severity at presentation, and consider the duration of symptoms. Another area of further research would be to identify any association between obesity and clinical outcomes.

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