Effects of obesity on the course of inflammatory bowel disease

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ABSTRACT

Obesity is increasingly common among patients with inflammatory bowel disease (IBD). The interplay between proinflammatory states of obesity and the course of IBD is yet to be elucidated. We conducted a retrospective study of 55 patients with IBD over the course of 5 years (2012 to 2017). We documented various clinical outcomes (mean number of clinic visits, hospitalizations/ flares, procedures, and escalations in therapy) based on three initial weight groups: normal weight, overweight, and obese. There was an increasing trend in all clinical outcomes with increasing weight and a statistically significant difference in mean clinic visits ($P=0.048$) and mean hospitalizations/flares ($P=0.004$) when comparing normal-weight to obese individuals. Our study suggests that obesity influences burden of disease and treatment in IBD. This should encourage clinicians to treat obesity in IBD patients as an active problem because it may help improve clinical outcomes.

KEYWORDS Inflammatory bowel disease; obesity

besity has reached an epidemic status in the USA along with a concomitant increase in inflammatory bowel disease (IBD) diagnosed in overweight individuals.¹ Because adipose tissues release proinflammatory cytokines, a link between the two has been suggested.² Studies have shown that obesity impacts disease development and response to therapy in patients with various autoimmune diseases.³ The mechanism by which obesity may impact IBD is an area of active research. It may involve visceral adipose tissue, which is known to be the metabolically active fraction of body fat, and patients with IBD have been shown to have higher volumes of visceral adipose tissue.^{4,5} Because IBD causes mucosal barrier dysfunction and adipocyte activation may be related to bacterial translocation, the concept of dysbiosis is another postulated mechanism relating the two disease entities.¹ Though some studies have suggested that obesity is associated with more severe IBD, others have suggested the opposite, thus highlighting conflicting data in the literature and the need for further investigation on the outcome of obesity on the clinical course of IBD.^{6,7} The aim of this study was to evaluate the effect of obesity on the clinical course of IBD at an urban academic medical center.

METHODS

This retrospective observational study was performed at the Hill Gastroenterology Clinic, affiliated with State University of New York Upstate Medical University in Syracuse. The project was approved by the institutional review board. Charts were reviewed from 189 patients with IBD seen over a 5-year period (January 1, 2012, to December 31, 2016). Inclusion criteria consisted of age >18 years, diagnosis of ulcerative colitis (UC) or Crohn's disease (CD), and 5-year outpatient gastroenterology follow-up with documented clinic visits. Of the 189 patients, 55 were included, because the remaining did not have 5 years of consecutive gastroenterology follow-up, with at least one scheduled clinic visit per year. Body mass index (BMI) at the initial visit was recorded and divided into normal weight, overweight, and obese based on guidelines from the Centers for Disease Control and Prevention. Normal BMI was defined as 18.5 to <25 kg/m²; overweight as 25 to <30 kg/m²; and obesity as ≥30 kg/m². Parameters including number of clinic visits, hospitalizations/flares, procedures, and escalation in medical regime were reviewed over the 5-year timeline.

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Statistical analysis among the three BMI groups was performed using one-way analysis of variance with Tukey's multiple comparison for continuous variables and chi-square test for categorical variables. A *P* value of <0.05 was considered statistically significant. Analysis was performed using GraphPad Prism Version 7.

RESULTS

Of the 55 patients included in the study, 19 were in the normal weight category, 11 in the overweight category, and 25 in the obese category. Overall, the mean age was 47 years, the male-to-female ratio was 30 to 25, and 27 patients had CD and 18 had UC. There was no statistically significant difference between the three BMI groups in terms of age (*P*=0.78), gender (*P*=0.58), or type of IBD (*P*=0.14) (Table 1).

Clinical outcomes based on BMI group are shown in Table 1 and Figure 1. Overall, there was an increasing trend in mean number of clinic visits, hospitalizations/flare, and mean escalations in therapy with an increase in BMI. A statistically significant difference was found in mean clinic visits (*P*=0.048) and mean hospitalizations/flare (*P*=0.004) when comparing normal-weight to obese individuals. Although mean number of procedures was highest in obese patients (1.88), it was 1.74 and 1.27 in normal-weight and overweight individuals, respectively.

In terms of medication adjustments and/or escalation, in normal-weight patients, one patient was already on an anti-tumor necrosis factor (TNF) regimen, four patients were escalated to anti-TNF, and one patient was started on or increased dose of immunomodulatory therapy. In overweight patients, one patient was already on an anti-TNF regimen, three patients escalated to anti-TNF therapy, and three

patients were started on or increased dose of immunomodulatory therapy. In obese patients, none of the patients were receiving anti-TNF therapy; however, three patients escalated to anti-TNF therapy and five patients were started on or had an increase in the dose of immunomodulators (6-mercaptopurine or azathioprine).

DISCUSSION

IBD, including UC and CD, is thought to be a chronic inflammatory condition resulting from a combination of genetic, immunologic, and environmental factors. An estimated 2.1 billion adults worldwide are overweight (BMI > 25 kg/m²), of whom 600 million are considered obese (BMI > 30 kg/m²). From 1980 to 2013, the proportion of overweight adults increased 28% in developed countries and close to 60% in developing nations.¹ A systematic review showed that the estimated annual incidence of IBD ranges from 10 to 30 cases per 100,000 people in Western nations, with a time trend analysis suggesting that the incidence is increasing over time, especially in newly industrialized countries.⁸ Thus, the prevalence of obesity has risen in parallel with the rise in IBD, suggesting a possible shared environmental link between these two conditions. The increasing incidence of IBD has been hypothesized to be related in part to a change in dietary and lifestyle factors, including BMI.¹ Various studies have reported IBD populations to be obese (BMI > 30 kg/m²), with the incidence ranging from 15% to 40%.^{1,9,10}

As such, the correlation between obesity and IBD has developed into an active area of investigative inquiry. However, data on the clinical course and treatment of obese patients with IBD are limited, and the data on the effect of the clinical course have been conflicting. For example,

Table 1. Demographic and clinical data of patients with inflammatory bowel disease based on body mass index group

Variable	Body mass index (kg/m ²)		
	18.5–24.9 (N = 19)	25.0–29.9 (N = 11)	≥30 (N = 25)
Mean age (years)	49 ± 18	45 ± 15	48 ± 12
Male : female	7:12	5:6	7:18
Crohn's disease : ulcerative colitis	16:3	7:4	14:11
Mean clinic visits ^a	7.74 ± 5.78	8.36 ± 3.91	11.4 ± 4.79
Mean hospitalizations/flare ^b	0.53 ± 1.02	0.82 ± 0.98	2.08 ± 1.96
Mean number of procedures ^c	1.74 ± 1.85	1.27 ± 0.79	1.88 ± 1.05
Mean escalations in therapy ^d	0.68 ± 0.95	1.09 ± 1.30	1.20 ± 1.19

^aNormal-weight vs overweight, *P* = 0.94; normal-weight vs obese, *P* = 0.048; overweight vs obese, *P* = 0.22.

^bNormal-weight vs overweight, *P* = 0.87; normal-weight vs obese, *P* = 0.004; overweight vs obese, *P* = 0.066.

^cNormal-weight vs overweight, *P* = 0.64; normal-weight vs obese, *P* = 0.94; overweight vs obese, *P* = 0.43.

^dNormal-weight vs overweight, *P* = 0.61; normal-weight vs obese, *P* = 0.30; overweight vs obese, *P* = 0.96.

Figure 1. Clinical outcomes based on body mass index group. * $P < 0.05$. ** $P < 0.01$.

Pringle et al demonstrated that although there is a lower prevalence of penetrating disease complications in obese patients with CD, there was comparable risk of strictures and perianal complications compared to adults with normal BMI.¹¹ Other studies suggested that there is no statistically significant difference in the risk of IBD-related surgery, hospitalization, or emergency department use between IBD patients who were obese, overweight, or with a normal BMI.⁸ Our study showed that there was an increase in mean number of clinic visits, hospitalizations/flare, and escalations in therapy with an increase in BMI, suggesting a detrimental effect of obesity on the clinical course of IBD. We found a statistically significant difference in mean clinic visits ($P = 0.048$) and mean hospitalizations/flare ($P = 0.004$) when comparing normal-weight to obese individuals. It has already been shown that inferior IBD-related quality of life and elevations of C-reactive protein have been observed in obese IBD patients, which can theoretically extrapolate to the increased clinic visits and reported flare.¹⁰ Certain population pharmacokinetic studies of all biologic agents approved for use in IBD have identified increased body weight as a risk factor for increased drug clearance and low trough concentrations.¹² This trend is supported by the patients in the overweight and obese categories in our study who escalated anti-TNF therapy. Although the literature on the effects of obesity on immunomodulatory

therapy is scant, one IBD study demonstrated that obese individuals were less likely to achieve therapeutic 6-thioguanine nucleotide concentrations.¹³

Our study had several limitations. We had a small sample size ($N = 55$) due to lack of follow-up with the majority of the patients. A disproportionate number of patients had CD compared to UC (63% and 37%, respectively). Another limitation of the study is the use of BMI as a measure of obesity. Mesenteric fat may be the significant contributor to IBD, as opposed to subcutaneous adipose tissue, which cannot be measured by BMI. Furthermore, we did not record the levels of C-reactive protein, which correlate with the metabolic activity of mesenteric fat. Lastly, the diagnosis of CD and UC was confirmed by a physician, although not only gastroenterologists, and patients with indeterminate colitis were excluded.

In conclusion, the results of our study suggest that obesity negatively influences the clinical course of IBD and may increase the burden of disease and treatment. Our results should encourage clinicians to treat obesity in IBD patients as an active problem, because it may help improve clinical outcomes. Further studies are needed to look at the underlying physiology between obesity and IBD to gain more insight regarding their relationship and subsequent implications.

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