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Relationship Between Body Mass Index and Mucosal Disease in Crohn's Diseases Patients at Bhuj, Gujarat, India: A Case-Control Study

Dr. Kashyap Buch Associate Professor, Department of Medicine, Gujarat Adani Institute of Medical Science, Bhuj, India

Dr. Sachin Thacker Assistant Professor, Department of Medicine, Gujarat Adani Institute of Medical Science, Bhuj, India

ABSTRACT

Background: In the past few decades, the prevalence of obesity all through the world has noticeably increased. This trend in obesity is reflected in patients with Crohn's disease (CD) as well. Present study was done with to test the theory that CD patients with higher BMI would be more likely than those with lower BMI to have determinedly active mucosal (endoscopic) disease.

Methods: Present study was a retrospective case-control study of patients attending at the Gujarat Adani institute of medical science, Bhuj, Kutch, Gujarat. Sample population consisted of CD patients with active disease at the commencement of observation. At the end of observation, cases had persistent active mucosal disease and controls had entered reduction. With multivariable logistic regression models, we evaluated the effect of baseline BMI as a continuous variable and a categorical variable on persistent active mucosal disease.

Results: We analyzed data from 104 patients (36 cases and 68 controls). In a model containing BMI as a continuous variable, higher BMI was significantly connected with persistent active mucosal disease in a model containing BMI as a categorical variable, obese patient were 2.7 times more expected to have importunate active mucosal disease in comparison to non-obese patients.

Conclusion: Extreme weight calculated both quantitatively as BMI and categorically as obesity in CD patients is linked with constant active mucosal disease.

KEYWORDS : BMI, Crohn's disease, Mucosal disease, Obesity

Introduction

Crohn's disease (CD) is a chronic inflammatory condition characterized by transmural inflammation and can engage several part of the gastrointestinal tract 1, 2. Regardless of well-characterized genotypic and phenotypic characteristics of affected patients, CD responds variably and erratically to treatment 3-6.

Body mass index (BMI), the most frequently used clinical measure of the degree of adipose tissue in the body and is calculated by dividing weight (in kilograms) by the height (in meters) squared and a BMI of ≥ 30 kg/m2 is categorized as representing "obesity" 6-9. In the past few decades, the prevalence of obesity all through the world has noticeably increased 10. This trend in obesity is reflected in patients with CD as well 11, 12. In spite of a rising number of obese CD patients, research on the influence of high BMI, particularly obesity on objective outcomes in CD patients leftovers thin. Study of the association between obesity and objective outcomes in CD is especially significant because of convincing molecular evidence that links adipose tissue physiology to intestinal inflammation.13, 14

Blain and colleagues found an association between obesity and rapid progression of disease (measured clinically) in CD patients 13. In a succeeding study by Hass et al, overweight or obese CD patients practiced more rapid development to first surgical intervention compared to underweight patients 14. However, this disparity in rate of progression of disease was not significantly different between obese and normal weight patients. On the basis of our observations and current findings of others, present study was aimed to test the theory that CD patients with higher BMI would be more likely than those with lower BMI to have determinedly active mucosal (endoscopic) disease 15-16.

Methods

Study design and population

Present study was a retrospective case-control study of patients attending at the Gujarat Adani institute of medical science, Bhuj, Kutch, Gujarat. Ethical clearance was taken from the institutional ethics board and informed consent was obtained from all the participents. Cases were patients 20 years or older who had weight and height documented at the beginning of observation, an established diagnosis of active CD at the beginning of observation, and persistent active mucosal ulceration upon evaluation by endoscopy at the end of observation Controls in our study were represented by CD patients seen in the same clinic as the cases. They met the first three criteria above but achieved mucosal remission at end of observation. Cumulative sampling was used for control selection.

For both cases and controls, information obtained from medical records included: demographic data, clinical data and medication history Information on family history, extra-intestinal manifestations and diabetes mellitus was also collected.

BMI was calculated as the ratio of weight to height squared documented in the medical record at initial observation. As already mentioned in the introduction, CD patients with a BMI ≥ 30 kg/m2 were categorized as obese. Those with a lower BMI were categorized as non-obese (≥ 25 and < 30 kg/m2 = overweight and ≥ 18 and < 25 kg/m2 = standard weight). BMI was assessed in two ways: 1) BMI as a continuous variable; 2) BMI as obese/non-obese. Covariates in both models were age at end of observation, ethnicity, and gender, duration of disease and observation period. In regard to location of CD, patients were divided into those with small bowel, ileocolonic or colonic disease according to the Montreal classification of CD. Patients were considered to have perianal disease if they had a history of perianal fistula or abscess. Treatment with corticosteroid medication was defined as use of an oral or parenteral corticosteroid agent for more than 1 week, of a rectal or topical agent for more than a month, or of oral budesonide for more than 3 months during the period of observation. Immune modulator treatment was defined as use of azathioprine (AZA), 6-mercaptopurine (6- MP), methotrexate (MTX) or any biological agent for at least 4 weeks during the period of observation. Smoking was defined as use of tobacco products at any time during observation period. Current, ever and never smokers were not distinguished.

Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 15 (SPSS Inc. Chicago, IL, USA) Windows software program. Descriptive statistics included computation of percentages. The statistical tests applied for the analysis were Pearson's chi-square tes, Fisher exact test, t-test, Wilcoxon rank sum test and multivariate logistic Regression analysis. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Out of the 959 patients seen at Gujarat Adani Institute of medical science for CD, we were able to identify 104 who fulfilled the stringent criteria Thirty-six of the 104 patients were cases and 68 of the 104 patients were controls. The median BMI was significantly different between cases and controls (P = 0.01). The proportion of obese patients was higher among cases compared to controls (P <0.05). A comparison of other characteristics of cases and controls appears in Table 1. A logistic regression model was applied to assess the association between BMI as a continuous variable and mucosal disease activity; the model included age, gender, ethnicity, duration of disease and observation period as covariates This model fulfilled statistical criteria for a good fit supporting the likelihood that the model appropriately explained the variation in mucosal disease activity in CD patients.

Having a higher BMI was associated in a significant manner with persistent active mucosal (endoscopic) disease (OR 1.09; 95% CI, 1.02 - 1.17; P = 0.012). In a similarly appropriately fitted logistic regression model containing BMI as a categorical variable (obese vs. non-obese patients) along with age, gender, ethnicity, duration of disease and observation period as covariates, presence of persistent active mucosal (endoscopic) disease was likewise associated with being obese vs. non-obese (OR = 2.72; 95% CI, 1.00 - 7.35; P = 0.0492). The effect of the covariates including the exposures of interest appears in Table 2.

The full multivariable models for BMI as a categorical and a continuous variable appear in Tables 3 and 4 respectively.

Table 1 Characteristic of Cases and Controls

Characteristic	Cases	Controls
BMI, median (range)	26 (19 - 43)	23 (19 - 45)
Obese	11 (32.6%)	11 (17.5%)
Age Median Range	37 (20-79)	35 (19-72)
Duration of disease, median (range)	5 (1 - 37)	7 (1 - 36)
Duration of observation, median (range)	1 (1 - 4)	2 (1 - 4)
Men/women	15/21 (42%/58%)	25/43 (37%/63%)
Age at diagnosis, median (range)	27 (10 - 75)	25 (11 - 68)
Perianal disease	12 (33%)	24 (35%)
Steroid use	16 (44%)	20 (29%)
Diabetes mellitus	4 (11%) 5	5 (7%)

Table 2 Difference in Relevant Covariates Between Cases and Controls

Covariate	Cases	Controls	P value
BMI, median (range)	26 (19 - 43)	23 (19 - 45)	0.01*
Obese	11 (32.5%)	11 (17.5%)	0.09
Age Median Range	37 (20-79)	35 (19-72)	0.25
Duration of disease, median (range)	5 (1 - 37)	7 (1 - 36)	0.45
Duration of observation, median (range)	1 (1 - 4)	2 (1 - 4)	0.26
Men/women	15/21 (42%/58%)	25/43 (37%/63%)	0.14

*** indicates statically significant difference at p=0.05**

Table 3 Multivariable Full Model for BMI as a Categorical Variable*

Effect	Point estimate	CI P value	P value
Obese vs. non-obese	2.710	1.003 - 7.349	0.03*
Age now	0.990	0.961 - 1.025	0.25
Sex	1.567	0.627 - 3.913	0.33
Race	1.748	0.725 - 4.215	0.29
Duration of observation	0.824	0.505 - 1.325	0.50
Duration of disease	0.995	0.941 - 1.052	0.90

*** indicates statically significant difference at p=0.05**

Table 4 Multivariable Full Model for BMI as a Continuous Variable

Effect	Point estimate	95% CI	P value
BMI	1.08	1.020 - 1.160	0.002*
Age now	0.991	0.954 - 1.021	0.70
Sex	1.371	0.556 - 3.381	0.40
Race	1.567	0.646 - 3.798	0.25
Duration of observation	0.787	0.477 - 1.298	0.74
Duration of disease	1.001	0.945 - 1.059	0.85

*** indicates statically significant difference at p=0.05**

Discussion

Present case-control study describes that extreme weight precise both quantitatively as BMI and categorically as obesity is associated with higher rates of active mucosal (endoscopic) disease among CD patients.

Our findings are consistent with Blain et al13 which compares the clinical course of CD patients who were obese with those CD patients who were not obese. Another group led by Hass categorized overweight and obese CD patients together into one group,. all those with a BMI greater than 25 kg/m2, and compared them to CD patients with a normal BMI (less than 25 kg/m2) 14. Within the latter group, the subset with a BMI of less than 18.5 kg/m2 was analyzed separately. Hass et al reported that patients with a BMI < 25 kg/m2 were older at diagnosis than the overweight or obese CD patients.

Corticosteroid use was not incorporated into the multivariable models regardless of the observation that its use was numerically different between cases and controls (P > 0.05) because the association was not significant based on our cutoff P < 0.1. To scrutinize its effect, supplementary sub-group analyses were performed in which steroid use was added to the adjusted models. Inclusion of corticosteroid use in the adjusted models gave the same P value for BMI (adjusted P = 0.01) and a slightly higher value for obesity. But with 36 outcomes of interest, adding additional covariates led to over-fitting; therefore we limited our adjusted models to our covariates of clinical interest. particular care was taken to comprise BMI/obesity data that were collected at the opening of observation whereas steroid use was defined as "steroid use during observation". Therefore steroid use was not likely to have causally impacted BMI/obesity. Also, based on not have of statistically significant relationships between covariates of interest in our univariate analyses, we believe that our conclusion not to match cases with controls according to those characteristics perhaps did not lead to a substantial loss of statistical competence and did not emerge to leave the findings susceptible to significant confounding.

The variety of observation for both cases and controls was 1 - 4 years with median of 1 year among cases and 2 years among controls. Duration of observation was controlled for in the multivariable analysis. We had motive to believe that those who undergo colonoscopy at the end of examination period were not essentially very different from those who did not based on the outcome of interest. The use of mucosal disease activity rather than clinical disease activity as an outcome further increased internal validity of our findings in terms of a convincing relationship between BMI and truly active Crohn's in this sample.

Retrospective Study Design, relatively small sample size and as a result, selection bias were amongst noteworthy limitations of our study. The current study strengthens the hypothesis of a detrimental effect of BMI, particularly obesity, on the course of CD. Understanding how the relationship of obesity with poorer Crohn's outcomes contributes to its causality will require a richer understanding of the biological as well as the social and environmental factors that drive the pathogenesis, management options and eventually, the course of CD. It is important to appreciate that obesity is as much a clinical construct as

it is a molecular phenomenon as every obese person does not have metabolic syndrome. Therefore, initial consideration of the clinical context of obesity and CD relationship is significant to our generation of prospect hypotheses. Future guidelines comprise superior prospective studies that permit capture of a wider range of significant data elements by addition of more covariates into adjusted models to better account for potential confounding, and to test for relationship of other measures of adipokine-mediated mesenteric inflammation with parameters of outcome in CD.

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