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TITLE PAGE

Title: Letter: Predictors of Dyspareunia Among Female Patients with Inflammatory Bowel Disease.

Short Title: Dyspareunia Among Females with IBD.

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Abbreviations:

FC	fecal calprotectin
HBI	Harvey-Bradshaw index
HADS	hospital anxiety and depression scale
IBD	inflammatory bowel disease

PHQ-12	patient health questionnaire-12
SF-36	short-form 36 questionnaire
SCCAI	simple clinical colitis activity index

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Sirs;

We read the recent paper published in *Clinical Gastroenterology and Hepatology* by Ona *et al.* with interest. [1] Sexual dysfunction is a well-recognized complication of chronic illness. In inflammatory bowel disease (IBD) factors such as age of diagnosis, increased bowel frequency, abdominal pain, fatigue, incontinence, perianal fistulas, abscesses, or skin tags may lead to an accumulation of physical and psychosocial factors that can impair sexual function. The authors reported that vulvovaginal discomfort was significantly associated with IBD activity, measured using validated symptom-based questionnaires, in an online survey of 1250 women in the USA. We also examined this issue in 777 adult patients with IBD seen in clinics in the Leeds Teaching Hospitals NHS Trust, UK, with similar findings, but we also measured fecal calprotectin (FC), allowing us to examine the relationship between pain during sexual intercourse (dyspareunia) and mucosal disease activity.

We recruited consecutive, unselected patients from November 2012 through to June 2015. [2] We collected demographic data, disease type, history of previous surgery, and IBD-related medications. We also obtained information concerning irritable bowel syndrome (IBS)-type symptoms, using the Rome III criteria, [3] and clinical disease activity, via the Harvey-Bradshaw index (HBI) for Crohn's disease and the simple clinical colitis activity index (SCCAI) for ulcerative colitis. [4, 5] We assessed mood and somatoform-type behavior using the hospital anxiety and depression scale (HADS) and the patient health questionnaire-12 (PHQ-12), respectively. [6, 7] The latter collects information concerning dyspareunia. Finally, we measured generic quality of life using the short-form 36 questionnaire (SF-36).

Participants provided a stool sample for FC analysis (Biohit, Finland). Due to multiple analyses we used a P value <0.001 to define statistical significance.

Among the 777 patients, 430 (55.3%) were women. The mean age of female participants was 42.7 years (range 17 to 89), and 255 (59.3%) had Crohn's disease. In total, 69 (16.0%) females reported dyspareunia. A higher proportion of patients who reported dyspareunia had clinically active disease, although this was not statistically significant (53.8% with dyspareunia vs. 44.7% of those without, P = 0.18) (Table). However, the proportion of patients with a FC of >250μg/g of stool was actually lower among those who reported dyspareunia (36.8% vs. 39.5%, P = 0.76), and mean FC levels were lower (415.4μg/g in those with dyspareunia vs. 477.4μg/g in those without, P = 0.60), although neither of these differences was statistically significant. Quality of life scores on the SF-36 for role limitations due to physical health, emotional wellbeing, social functioning, pain, and general health were significantly lower among those reporting dyspareunia (P <0.001 for all analyses). Following univariate analysis, high levels of somatoform-type behavior on the PHQ-12, (29.4% vs. 8.5%, P <0.001), and abnormal HADS anxiety or depression scores (45.6% vs. 27.2%, and 23.5% vs. 10.6%, P = 0.003 for both) were significantly associated with reporting dyspareunia. There were also trends towards younger age (38.0 years vs. 43.3 years, P = 0.002) being associated with dyspareunia, and those with IBS-type symptoms being more likely to report dyspareunia (56.5% vs. 40.9%, P = 0.017). Disease type, previous surgery, tobacco and alcohol use, marital status, educational level, and IBD-related medication were not predictors of dyspareunia. Following multivariate logistic regression, only high

levels of somatoform-type behavior predicted dyspareunia (odds ratio high vs. low 26.6; 95% confidence interval 3.26 to 216, P = 0.002). During longitudinal follow-up over a minimum period of 2 years, [8] 18 (52.9%) of 34 patients still reported dyspareunia.

Approximately one-in-six female patients with IBD reported dyspareunia in our study, and in more than 50% this was still present at least 2 years later. Dyspareunia was associated with substantial impairments in generic quality of life. Although clinical disease activity seemed to be associated with vulvovaginal pain in the study by Ona *et al.*, [1] we did not observe any significant association with either clinical disease activity indices or mucosal disease activity, according to FC levels, and dyspareunia in our study. Rather dyspareunia seemed to be associated with symptom-reporting *per se*, which may explain why a greater proportion of our patients with dyspareunia had abnormal clinical disease activity indices, and why those with high clinical disease activity scores in Ona's online survey, where mucosal inflammation was not measured, were more likely to report vulvovaginal pain.

REFERENCES

1. Ona S, James K, Ananthakrishnan AN, et al. Association between vulvovaginal discomfort and activity of inflammatory bowel diseases. Clin Gastroenterol Hepatol.doi:10.1016/j.cgh.2019.05.018.
2. Gracie DJ, Williams CJ, Sood R, et al. Negative effects on psychological health and quality of life of genuine irritable bowel syndrome-type symptoms in patients with inflammatory bowel disease. Clin Gastroenterol Hepatol. 2017;15:376-84.e5. Epub 2016/05/18.
3. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology. 2006;130:1480-91.
4. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet. 1980;1(8167):514. Epub 1980/03/08.
5. Walmsley RS, Ayres RC, Pounder RE, et al. A simple clinical colitis activity index. Gut. 1998;43:29-32.
6. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361-70.
7. Spiller RC, Humes DJ, Campbell E, et al. The Patient Health Questionnaire 12 Somatic Symptom scale as a predictor of symptom severity and consulting behaviour in patients with irritable bowel syndrome and symptomatic diverticular disease. Aliment Pharmacol Ther. 2010;32:811-20.
8. Gracie DJ, Guthrie EA, Hamlin PJ, et al. Bi-directionality of brain-gut interactions in patients with inflammatory bowel disease. Gastroenterology. 2018;154:1635-46.e3.

Table. Predictors of Dyspareunia Among 430 Female Patients with Inflammatory Bowel Disease

	Dyspareunia (n = 69)	**No dysparenuia (n = 361)**	**P value***
Mean age in years (SD)	38.0 (11.5)	43.3 (16.6)	0.002
Married or co-habiting (%)	43 (63.2)	219 (61.2)	0.75
University graduate/professional (%)	24 (34.8)	104 (29.2)	0.36
Tobacco user (%)	13 (18.8)	75 (20.9)	0.70
Alcohol user (%)	43 (62.3)	214 (59.3)	0.64
Crohn's disease (%)	42 (60.9)	213 (59.0)	0.77
Previous surgery (%)	16 (23.5)	100 (27.7)	0.48
5-aminosalicylate use (%)	35 (50.7)	157 (43.5)	0.27
Immunomodulator use (%)	18 (27.5)	125 (34.6)	0.25
Anti-tumor necrosis factor-α use (%)	15 (21.7)	62 (17.2)	0.37
Glucocorticosteroid use (%)	5 (7.2)	34 (9.4)	0.57
IBS-type symptoms (%)	39 (56.5)	147 (40.9)	0.017
Active disease on HBI/SCCAI (%)	35 (53.8)	153 (44.7)	0.18
Abnormal HADS anxiety score (%)	31 (45.6)	97 (27.2)	0.003
Abnormal HADS depression score (%)	16 (23.5)	38 (10.6)	0.003
PHQ-12 somatization categories (%)			
Mild	1 (1.5)	67 (18.9)	
Low	13 (19.1)	134 (37.9)	
Medium	34 (50.0)	123 (34.7)	
High	20 (29.4)	30 (8.5)	<0.001

Mean SF-36 score (SD)			
Physical functioning	68.7 (27.7)	76.0 (28.3)	0.056
Role limitations physical health	38.6 (42.2)	57.5 (44.1)	<0.001
Role limitations emotional problems	57.2 (44.1)	70.4 (42.1)	0.026
Energy/fatigue	33.8 (20.4)	41.7 (24.2)	0.001
Emotional well-being	56.5 (21.7)	67.1 (20.8)	<0.001
Social functioning	52.1 (27.2)	67.3 (28.5)	<0.001
Pain	45.4 (24.2)	61.0 (25.7)	<0.001
General health	30.6 (19.8)	46.6 (23.2)	<0.001
FC >250µg/g of stool	14 (36.8)	73 (39.5)	0.76
Mean FC (SD)	415.4 (644.0)	477.4 (734.2)	0.60