HHS Public Access

Author manuscript

Inflamm Bowel Dis. Author manuscript; available in PMC 2015 March 03.

Published in final edited form as:

Inflamm Bowel Dis. 2014 March ; 20(3): 534–540. doi:10.1097/01.MIB.0000441347.94451.cf.

Menstrual Cycle Changes in Women with Inflammatory Bowel Disease: A Study from the Ocean State Crohn's and Colitis Area Registry

Sumona Saha, M.D., M.S.,
Division of Gastroenterology and Hepatology, University of Wisconsin School of Medicine and Public Health

Yingqi Zhao, Ph.D.,
Department of Biostatics and Medical Informatics, University of Wisconsin School of Medicine and Public Health

Samir A. Shah, M.D.,
Division of Gastroenterology, Warren Alpert School of Medicine at Brown University

Silvia Degli Esposti, M.D.,
Division of Gastroenterology, Warren Alpert School of Medicine at Brown University

Sheldon Lidofsky, M.D.,
Division of Gastroenterology, Warren Alpert School of Medicine at Brown University

Sana Salih, M.D., M.S.,
Division of Reproductive Endocrinology, University of Wisconsin School of Medicine and Public Health

Renee Bright, M.S.,
Department of Pediatric Gastroenterology, Rhode Island Hospital

Meaghan Law,
Department of Pediatric Gastroenterology, Rhode Island Hospital

Heather Moniz,
Department of Pediatric Gastroenterology, Rhode Island Hospital

Nicole Flowers, M.D., M.P.H.,
Division of Community Health, Centers for Disease Control and Prevention

Marjorie Merrick, M.A., and
Crohn's & Colitis Foundation of America

Bruce E. Sands, M.D., M.S.
Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai

Correspondence: Please address correspondence regarding this manuscript to: Sumona Saha, M.D., M.S., Division of Gastroenterology and Hepatology, University of Wisconsin School of Medicine and Public Health, UW Medical Foundation Centennial Building, 1685 Highland Avenue, Rm 4224, Madison, WI 53705, Phone: 608-263-1995, Fax: 608-265-5677, ssaha@medicine.wisc.edu.

Abstract

Background and Aims—The effect of the inflammatory bowel diseases (IBD) on menstrual function is largely unknown. The aims of this study were to determine whether changes in menstrual function occur in the year prior to IBD diagnosis or in the initial years after diagnosis.

Methods—Women aged 18 and above in the Ocean State Crohn's and Colitis Area Registry with at least 2 years of follow-up were eligible for this study. All subjects were enrolled within 6 months of IBD diagnosis and followed prospectively. Menstrual cycle characteristics were retrospectively assessed. To assess for changes over time, general linear models for correlated data were used for continuous outcomes and generalized estimating equations were used for discrete outcomes.

Results—121 subjects were studied. Twenty-five percent of subjects experienced a change in cycle interval in the year prior to IBD diagnosis and 21% experienced a change in duration of flow. Among women with dysmenorrhea, 40% experienced a change in the intensity of their menstrual pain and 31% experienced a change in its duration. Overall cycle regularity increased over time.. Quality of life (QOL) was significantly lower in women without regular cycles across all time points.

Conclusions—Changes in menstrual function occur frequently in the year prior to IBD diagnosis; therefore screening for menstrual irregularities should be considered in women with newly diagnosed IBD. Patients can be reassured that cycles typically become more regular over time.

Introduction

The relationship between the inflammatory bowel diseases (IBD) and menstrual function has not been fully explored. Although prior studies have examined the gastrointestinal (GI) symptoms of women with IBD in relation to the menstrual cycle, in comparison, no study has adequately addressed how a diagnosis of IBD affects menstrual function (1-3). Given that menstrual disturbances can be a source of stress and morbidity, clarification of the effects of IBD on the menstrual cycle is needed.

With regards to the effects of the menstrual cycle on IBD, an initial retrospective study by Kane and colleagues found the prevalence of diarrhea to be increased in women with IBD and irritable bowel syndrome during both the premenstrual and menstrual phases of the cycle compared with healthy controls (1). A more recent study by Bernstein and colleagues confirmed that women with Crohn's disease (CD) are more likely to experience diarrhea than healthy controls during the premenstrual phase of the cycle and that women with CD or ulcerative colitis (UC) are more likely to experience diarrhea during menstruation (2). A third study by Parlak and colleagues using a prospective evaluation found that the GI symptoms of women with IBD follow a cyclic pattern across the menstrual cycle and that this pattern is mediated by disease activity and medication use (3). Furthermore, it showed that independent of disease activity women with IBD experience greater GI symptoms during menstruation compared to healthy controls. In total, these studies suggest that the hormonal fluctuations of the menstrual cycle affect the GI symptoms of women with IBD.

Regarding the impact of IBD on menstrual function, it is largely unknown whether women experience changes in their cycle or in the pain associated with menstruation due to IBD. In comparison, many other disease processes such as asthma and epilepsy are known to aggravate menstrual symptoms possibly due to changes in prostaglandin release, the immune system, and estrogen and progesterone levels (4, 5). Furthermore, autoimmune diseases such as systemic lupus erythematosus have been associated with a high frequency of menstrual disturbances due to disease activity, anti-ovarian antibodies, and side effects from treatment (6, 7).

Common menstrual abnormalities include painful menstruation (i.e. dysmenorrhea), abnormal uterine bleeding (menorrhagia and metrorrhagia), and irregularities in menstrual frequency (polymenorrhea, oligomenorrhea, and amenorrhea), (8). It has been suggested that the presence of any of these problems should elicit careful evaluation as they may be representative of significant pathology that can impact a woman's future reproductive health or current general health and well being (9). Appropriate and early management may, in turn, minimize future complications in women's reproductive ability (10). This is of particular importance in IBD as the majority of patients with UC and CD are affected during their peak reproductive years (11).

The aims of this study were: 1) to determine if women in an incident cohort of IBD experience changes in their menstrual cycle in the year preceding diagnosis and determine the nature of those changes and 2) to determine whether women with established IBD experience menstrual cycle changes in the first 2 years after diagnosis.

Methods

Participants and Procedures

Women ages 18 and above enrolled in the Ocean State Crohn's and Colitis Area Registry (OSCCAR) with a minimum of 2 years of follow-up were eligible for this study. OSCCAR is a prospective, community-based incident cohort of IBD based in the state of Rhode Island that was established in 2008. Subjects enrolled in OSCCAR have UC, CD, or indeterminate colitis (IC) based on endoscopy, radiology, and/or pathology. Eligible subjects must be enrolled within 6 months of diagnosis, with a median time to enrollment for adults of approximately 90 days from the date of diagnosis.

OSCCAR has been approved by the Institutional Review Boards at Lifespan/Rhode Island Hospital, Massachusetts General Hospital, the Icahn School of Medicine at Mount Sinai, and the University of Wisconsin School of Medicine and Public Health.

Subjects in OSCCAR undergo assessment of symptoms using a comprehensive symptom inventory, disease activity as measured by the Harvey-Bradshaw Index (HBI) (12) for subjects with CD or Simple Clinical Colitis Index (SCCAI) (13) for subjects with UC or IC, medication use, surgical history, general and disease-specific HRQOL as measured by Inflammatory Bowel Disease Questionnaire (IBDQ) (14) at the time of enrollment and then every 6 to 12 months, depending on the outcome being measured. In addition to these outcomes, adult female subjects also undergo retrospective assessment of several of the

critical dimensions to describe menstrual symptoms, including length of cycle (defined as number of days from day 1 of one period until day 1 of the subsequent cycle), duration of flow (defined as number of days of bleeding), and cycle regularity (defined as regular, fairly regular, or irregular based on the predictability of the onset of menses) at baseline and then yearly. Questions pertaining to these dimensions have been recommended to assist in the diagnosis of abnormal uterine bleeding and in the description of patients' experiences, in terms of symptom and symptom impact, with menstrual bleeding (15). Subjects are also queried about dysmenorrhea and onset of amenorrhea using an interviewer-administered questionnaire at study entry and then yearly

Changes in menstrual cycle characteristics over the past 12 months are also assessed using yes/no questions. Subjects who answer “yes” to experiencing a change in their cycle length are asked to specify whether the interval between periods has become shorter, longer, irregular (defined as some cycles longer and some cycles shorter), or had undergone another change. Subjects who answer “yes” to experiencing a change in the duration of flow are asked to specify whether the duration of bleeding has become shorter, longer, irregular (defined as some cycles with a greater number of days of bleeding and some cycles with a fewer number of days of bleeding), or had experienced another change.

Subjects with dysmenorrhea are also asked if they experienced a change in the intensity of their menstrual pain over the past 12 months and asked to qualify the change using following possible choices: more intense pain, less intense pain, no change in intensity of pain. Similarly, subjects with dysmenorrhea are asked if they experienced a change in the duration of their menstrual pain and asked to qualify the change using the following possible choices: longer duration of pain, shorter duration of pain, no change in duration of pain.

Data analysis

We characterized the demographics, IBD subtype (CD, UC, or IC), disease activity and other health measures of the study population. Descriptive statistics, including means and standard deviations for continuous variables and frequencies for categorical variables, were calculated using standard methods. To assess for changes in menstrual cycle characteristics over time, a general linear model for correlated data was used for to model duration of flow, cycle length, pain duration, and pain severity, and a general estimating equation was used to model cycle regularity, while controlling for correlation due to repeated measures within patients over time. Covariates of interest included duration (years) after enrollment, steroids usage, and disease subtype, where effects from age, body mass index (BMI), and oral contraceptive pill (OCP) use were adjusted. We assumed that time of OCP initiation was not a confounding factor for changes in menstrual cycle given that the mean differences between age at diagnosis of IBD and age at OCP use onset was large (>1 year) for subjects in our dataset.

To analyze the effects of medication exposure, we used logistic regression to calculate a propensity score for steroid, thiopurine (i.e. azathioprine and 6-mercaptopurine [6-MP]), and anti-tumor necrosis alpha (anti-TNFα) use using age, disease activity scores, total number of symptoms, and a binary indicator for other medication usage (i.e. steroid, thiopurine or anti-TNFα) as predictors. The propensity score was used as an adjustor in assessing the effects of

these classes of medications (i.e. steroids, thiopurines, or anti-TNFα) on duration of flow, length of cycle, cycle regularity, pain with menses, change in intensity of menstrual pain, and change in duration of menstrual pain.

A general linear model for correlated data was used to model IBDQ sores while controlling for correlation due to repeated measures within patients over time. Covariates of interest included continuous year and disease activity scores, where effects from age, BMI and OCP use were adjusted. All analyses were conducted using SAS 9.2.

Results

Study Population

Of 176 eligible subjects, 121 (68.8%) completed the menstrual cycle questionnaire at baseline (61 [50.4%] CD, 48 [39.7%] UC/IC, 12 [9.9%] data missing or disease subtype unknown) (Table 1). The mean age (SD) of the subjects at diagnosis was 41.5 years (15.7) and mean (SD) body mass index (BMI) was 27.1 (7.3). With regards to baseline disease activity, mean (SD) HBI score for subjects with CD was 2.1 (3.2) and mean (SD) SCCAI score for subjects with UC and IC was 1.5 (2.5). Further demographic information, disease activity scores, HRQOL scores, IBD medications, and history of OCP use of the population at baseline are summarized in Table 1. Menstrual cycle characteristics for the population at baseline are summarized in Table 2.

Changes in menstrual cycle prior to IBD diagnosis

Thirty (24.8%) subjects reported that they had experienced a change in their cycle interval in the year prior to IBD diagnosis and 25 (20.7%) reported experiencing a change in their duration of flow (Table 3). Among women with baseline dysmenorrhea (n= 48), 19 (39.6%) experienced a change in the intensity of their menstrual pain over the past 12 months with 16 reporting that pain was more intense and only 3 reporting that pain was less intense. In addition, the duration of menstrual pain changed for 15 (31.3%) subjects with baseline dysmenorrhea, with 12 subjects experiencing menstrual pain of increased duration and 3 experiencing pain of decreased duration.

To control for changes in the menstrual cycle which may be due to perimenopause, we compared subjects ages 18-40 (n=54) to subjects over 40 (n=55). This revealed no significant differences in the frequency of changes in cycle length or menstrual pain intensity or duration in the year prior to diagnosis (data not shown). The difference in the proportion of subject who experienced a change in duration of flow was, however, significantly different with the older subjects more likely to experience a change (p=0.01).

Changes in menstrual cycle after IBD diagnosis and treatment

After adjusting for age, BMI, and OCP use no changes were found for mean duration of flow, length of cycle, or pain with menses over time for the entire cohort (Table 4). Cycle regularity, however, was associated with time wherein each year of greater disease duration increased the odds of having more regular cycles by 3.53 (95% CI: 1.86, 6.05).

With regards to the association between medication exposure and menstrual cycle changes, cycle regularity was found to be associated with steroid use among subjects of both disease subtypes (p=0.048) after adjusting for age, BMI, OCP use, and propensity of steroid use (data not shown). After adjusting for other medication exposure (i.e. thiopurine and anti-TNFα) the relationship between steroid use and cycle regularity was no longer significant (Table 4). No significant associations were found between thiopurine and anti-TNFα exposure and any of the menstrual cycle outcomes assessed (Table 4).

Changes in menstrual cycle characteristics were not significantly associated with disease activity scores in subjects with UC/IC after adjusting for age, BMI and OCP use (Table 4). Using a general estimating equation to model the effects of HBI score on changes in menstrual flow we found that only duration of flow was significantly associated with disease activity in subjects with CD wherein each one unit increase in HBI score decreased the probability of having a change in menstrual flow by 0.72 (95% CI: 0.57, 0.93). No significant differences were found between CD subjects in remission (defined as HBI ≤ 3) and CD subjects with active disease (defined as HBI > 3) or between UC subjects in remission (defined as SCCAI < 3) and UC subjects with active disease (defined as SCCAI ≥ 3) after controlling for age, BMI, and hormone use.

HRQOL analysis

The average IBDQ score was found to significantly increase over time (p<0.0001) by a mean (standard error [SE]) of 9.62 (1.84). IBDQ scores were significantly associated with cycle regularity (p=0.04) across all years. IBDQ scores were estimated to be 7.2 (3.4) points lower when comparing subjects with “fairly regular” cycles to those with “regular” cycles as well as when comparing subjects with “irregular” cycles to those with “fairly regular” cycles. IBDQ scores were not found to be significantly associated with changes in menstrual pain intensity or duration.

Discussion

The menstrual characteristics of women with newly diagnosed and established IBD have largely been unstudied. Although evaluating for menstrual disorders is not generally considered to be within the purview of gastroenterologists, given that many are associated with anovulatory cycles which increase the risk for infertility (16) determining the impact of IBD on menstrual function is important for the comprehensive care of women with IBD. Using an incident cohort of IBD, we determined that many women experience some change in their menstrual cycle in the year preceding IBD diagnosis. Changes in cycle length were most common, followed by changes in duration of flow, and changes in menstrual pain. In our comparison of younger subjects to subjects over age 40, we found that apart from changes in duration of flow that the frequency of menstrual cycle alterations was not different between the 2 groups. This suggests that even among young adult women, for whom regular and persistent patterns of menstrual cycle length with little variation individually are typical (17), menstrual cycle alterations are frequent in the presence of IBD. These findings are consistent with prior work which has showed menstrual abnormalities to be common among women with IBD (18).

Although the potential causes of menstrual irregularity are vast, it has been suggested that the menstrual cycle be used as an additional vital sign in the assessment of well-being and the exclusion of pathological conditions (19). Thus, eliciting whether a woman with suspected IBD has experienced changes in her menstrual cycle may provide the clinician insight regarding the nature and severity of the underlying disease.

While the specific changes in cycle length and duration of flow were mixed with no clear majority of subjects experiencing an increase or decrease in either characteristic, we found that among women with baseline dysmenorrhea who experienced a change, the majority reported their menstrual pain to be more intense and of longer duration in the year prior to IBD diagnosis. This finding may be due to pathophysiologic mechanisms which are common to IBD and primary dysmenorrhea. Some authors have speculated that prostaglandins which when released from sloughing endometrium during menstruation induce uterine contractions and menstrual pain (20) may also play an important role in the abdominal pain and diarrhea experienced by patients with IBD due to increased contractility of GI smooth muscle (21). Alternatively, this finding may be due to the misperception of IBD symptoms as worsening menstrual pain. Given the overlap in symptoms between active IBD and dysmenorrhea (e.g. nausea and vomiting, loss of appetite, diarrhea, general aching, irritability, sleep disturbances, and depression), symptom confusion may certainly occur. A recent study by Saha et al. found that menstrual distress as measured by the Moos' Menstrual Distress Questionnaire positively correlated with CD activity scores, suggesting that menstrual symptoms may affect perception of IBD activity (22). We postulate that the reverse relationship may also be present. That is, symptoms from IBD may be perceived to be menses-related GI symptoms. For women with dysmenorrhea and IBD that has yet to be diagnosed, this misperception may have important consequences such as prolongation in the time to IBD diagnosis and incorrect therapeutic choices. For example, non-steroidal anti-inflammatory drugs which are first-line therapy for the treatment of dysmenorrhea (23) are potential exacerbating factors for IBD and usually are to be avoided (24, 25). It is important to note, however, that the majority of women with dysmenorrhea reported no change in either the intensity or frequency of their menstrual pain in the year preceding diagnosis.

With regards to changes in the menstrual cycle in women with IBD of at least 1 year duration, after controlling for age, BMI and OCP use, we found that neither flow duration nor cycle length significantly change over time. As the local balance between fibrinolysis and clotting processes in the endometrium control the volume and duration of menstrual bleeding and hypothalamic/pituitary hormones control menstrual cycle length, we postulate that IBD likely does not affect the local endometrial environment or hormone release. If endometrial thickness, an important determinant of fertility and *in vitro* fertilization (IVF) success, and hypothalamic/pituitary hormone release are truly unaltered in IBD this would correlate with the normal fertility rates reported in the literature for women with IBD who have not undergone surgery (26, 27). It would also suggest that women with IBD undergoing IVF are not at decreased odds for endometrial implantation or IVF success.

Our time analysis did show cycle regularity to change significantly over time wherein more regular cycles were found for each year of greater disease duration. For young women desiring natural pregnancy this is an important finding as it can reassure them that over time

their cycles should become more predictable. Although IBD treatment and disease control may play a role in this, we found that cycle regularity improved regardless of disease activity and after controlling for changes in BMI. We postulate, therefore, that women with incident IBD may experience unique stressors which early in their disease course adversely impact menstruation and over time are reduced. Perceived stress as well as psychological distress and altered sleep habits have all been associated with menstrual-related problems (28, 29). Further studies are needed to determine whether the prevalence of these factors differs in patients with newly diagnosed versus established IBD and whether they impact the menstrual cycle.

Before adjusting for other medication use we found cycle regularity to be associated with steroid use wherein exposure to steroids was associated with an increased risk for irregular cycles. After controlling for exposure to thiopurines and anti-TNFα agents, steroid use was not significantly associated with any menstrual cycle outcomes assessed. This suggests that the detrimental effects of steroids on the menstrual cycle are modified by use of a thiopurine or anti-TNFα agent and provides an additional reason to maximize use of steroid-sparing agents.

Finally, we found HRQOL in our population to be significantly associated with cycle regularity. Women with “fairly regular” and “irregular” cycles had lower IBDQ scores compared with those with regular cycles. This suggests that menstrual cycle predictability may be an important contributor to HRQOL in women with IBD and that the return of regular menstrual cycles should be assessed along with other outcomes when determining treatment efficacy.

Although this is the first study to describe menstrual cycle characteristics in women with newly diagnosed IBD it does have several significant limitations. First, the mean age of our cohort was 41.5; therefore, the menstrual cycle changes reported by many women may have been related to normal aging. To control for this we compared women ages 40 and younger to women over age 40 and found that other than changes in duration of flow there were no significant differences in menstrual cycle changes between the two groups. Age 40 was chosen as a cut-off based on prior data suggesting that ovarian changes typically begin in the the mid-30s and that menstrual cycle changes are common from about age 35 to menopause (30, 31). Another limitation of the study is the retrospective method by which changes in menstrual function were assessed which opens the possibility for recall bias. Furthermore, differences in the attention paid to changes in menstrual cycle among subjects and the subjective nature of our endpoints may have influenced our results. We also recognize that co-morbidities such as endometriosis and polycystic ovarian syndrome, which are common among young women and for which we did not assess, may have confounded our results. Future studies which prospectively assess for menstrual cycle changes, which control for gynecologic disorder confounders, and which include healthy age-matched controls are needed to verify our findings and determine whether women with IBD experience higher rates of menstrual cycle changes and irregularities compared to the general population.

Conclusions

Using an incident cohort of IBD we found that many women may experience changes in their menstrual cycle as part of their initial disease presentation. For women with co-morbid dysmenorrhea intensification of menstrual pain and lengthening in the duration of pain in the year prior to IBD diagnosis are common. Further studies are needed to determine whether this is due to common pathophysiologic mechanisms between IBD and dysmenorrhea or to symptom overlap and confusion. In our longitudinal analysis we found that in general, menstrual cycle regularity improves over time in women with IBD. However, steroid use is associated with more irregular cycles even after adjusting with propensity scores. Women with IBD should be counseled about these potential changes to the menstrual cycle due to their disease and/or its treatments given the importance of menstrual cycle regularity on fertility and overall well-being.

Acknowledgments

This project was supported by a grant from the CCFA through the Centers for Disease Control and Prevention (1 UO1 DP000340-03) and the National Institutes of Health (1R21DK078555-01). Sumona Saha, M.D. was supported by Award Number K12HD055894 from the National Institute of Child Health and Human Development (NICHD). The findings and conclusions in this abstract are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the NICHD.

References

1. Kane SV, Sable K, Hanauer SB. The menstrual cycle and its effect on inflammatory bowel disease and irritable bowel syndrome: a prevalence study. Am J Gastroenterol. 1998; 93:1867–1872. [PubMed: 9772046]
2. Bernstein MT, Graff LA, Targownik LE, et al. Gastrointestinal symptoms before and during menses in women with IBD. Aliment Pharmacol Ther. 2012; 36(2):135–44. [PubMed: 22621660]
3. Parlak E, Dagli U, Alkim C, et al. Patterns of gastrointestinal and psychosomatic symptoms across the menstrual cycle in women with inflammatory bowel disease. Turk J Gastroenterol. 2003; 14:250–6. [PubMed: 15048600]
4. Svanes C, Gomez Real F, Gislason T, et al. Association of asthma and hay fever with irregular menstruation. Thorax. 2005; 60:445–450. [PubMed: 15923242]
5. Herzog AG. Menstrual disorders in women with epilepsy. Neurology. 2006; 66 Suppl 3(6):S23–S28. [PubMed: 16567738]
6. Medeiros PB, Febrônio MV, Bonfá E, et al. Menstrual and hormonal alterations in juvenile systemic lupus erythematosus. Lupus. 2009 Jan; 18(1):38–43. [PubMed: 19074167]
7. Pasoto SG, Mendonça BB, Bonfá E. Menstrual disturbances in patients with systemic lupus erythematosus without alkylating therapy: clinical, hormonal and therapeutic associations. Lupus. 2002; 11(3):175–80. [PubMed: 11999882]
8. Greydanus DE, McAnarney ER. Menstruation and its disorders in adolescents. Curr Probl Pediatr. 1982; 12(10):1–61. [PubMed: 6764754]
9. Adams Hillard PJ, Deitch HR. Menstrual disorders in the college age female. Pediatr Clin North Am. 2005; 52(1):179–97. ix–x. [PubMed: 15748930]
10. Deligeoroglou E, Creatsas G. Menstrual disorders. Endocr Dev. 2012; 22:160. [PubMed: 22846527]
11. Andres PG, Friedman LS. Epidemiology and the natural course of inflammatory bowel disease. Gastroenterol Clin North Am. 1999; 28:255–81. [PubMed: 10372268]
12. Harvey RF, Bradshaw MJ. Measuring Crohn's disease activity. Lancet. 1980; 1(8178):1134–1135. [PubMed: 6103463]

13. Walmsley RS, Ayres RC, Pounder RE, Allan RN. A simple clinical colitis activity index. Gut. 1998; 43(1):29–32. [PubMed: 9771402]
14. Guyatt G. A new measure of health status for clinical trials in inflammatory bowel disease. Gastroenterology. 1989; 96:804–810. [PubMed: 2644154]
15. Matteson KA, Munro MG, Fraser IS. The Structured Menstrual History: Developing a Tool to Facilitate Diagnosis and Aid in Symptom Management. Semin Reprod Med. 2011; 29(5):423–435. [PubMed: 22065328]
16. Hamilton-Fairley D, Taylor A. Anovulation. BMJ. 2003; 327:546–549. [PubMed: 12958117]
17. Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. Int J Fertil. 1967; 12(1 pt 2):77–126. [PubMed: 5419031]
18. Weber AM, Ziegler C, Belinson JL, et al. Gynecologic history of women with inflammatory bowel disease. Obstet Gynecol. 1995 Nov; 86(5):843–7. [PubMed: 7566861]
19. ACOG Committee on Adolescent Health Care. ACOG Committee Opinion No. 349, November 2006: Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Obstet Gynecol. 2006; 108(5):1323–1328. [PubMed: 17077267]
20. Willman EA, Collins WP, Clayton SG. Studies in the involvement of prostaglandins in uterine symptomatology and pathology. Br J Obstet Gynaecol. 1976; 83(5):337–41. [PubMed: 1268141]
21. Weber AM, Belinson JL. Inflammatory bowel disease—a complicating factor in gynecologic disorders? Medscape Womens Health. 1997; 2(2):4. [PubMed: 9746678]
22. Saha S, Midtling E, Roberson E, et al. Dysmenorrhea in women with Crohn's disease: a case control study. Inflamm Bowel Dis.
23. Harel Z. Dysmenorrhea in adolescents and young adults: an update on pharmacological treatments and management strategies. Expert Opin Pharmacother. 2012 Oct; 13(15):2157–70. [PubMed: 22984937]
24. Lichtenstein GR, Hanauer SB, Sandborn WJ. Management of Crohn's disease in adults: ACG practice guidelines. Am J Gastroenterol. 2009; 104:465–483. [PubMed: 19174807]
25. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults (update): ACG, practice parameters committee. Am J Gastroenterol. 2004; 99:1371–1385. [PubMed: 15233681]
26. Baird DD, Narendranathan M, Sandler RS. Increased risk of preterm birth for women with inflammatory bowel disease. Gastroenterology. 1990; 99:987–94. [PubMed: 2394353]
27. Hudson M, Flett G, Sinclair TS, et al. Fertility and pregnancy in inflammatory bowel disease. Int J Gynaecol Obstet. 1997; 58:229–37. [PubMed: 9252260]
28. Gollenberg AL, Hedinger ML, Mumford, et al. Perceived stress and severity of perimenstrual symptoms: the BioCycle study. J Womens Health (Larchmt). 2010; 19(5):959–67. [PubMed: 20384452]
29. Strine TW, Chapman DP, Ahluwalia IB. Menstrual-related problems and psychological distress among women in the United States. J Womens Health (Larchmt). 2005; 14(4):316–23. [PubMed: 15916505]
30. Burger HG. The menopausal transition. Baillieres Clini Obstet Gyanecol. 1996; 10:347–59.
31. Sullivan Mitchell E, Fuagte Woods N, Mariella A. Three stages of the menopausal transition from the Seattle Midlife Women's Health Study: toward a more precise definition. Menopause. 2000; 7(5):334–349. [PubMed: 10993033]

Table 1

Study Population Characteristics

Characteristic	N (%)
Disease Subtype	
CD	61 (50.4)
UC/IC	48 (39.7)
Unknown or data missing	12 (9.9)
Race	
Black or African American	4 (3.7)
White	98 (89.9)
More than one race	1 (0.9)
Other	5 (4.6)
Refused	1 (0.9)
Marital status	
Married	34 (28.1)
Single/Never married	57 (47.1)
Divorced or separated	18 (14.9)
Cohabitating	8 (6.6)
Widowed	4 (3.3)
OCP use in the year before diagnosis (yes)	29 (26.6)
Medication use at enrollment	
5-aminosalicylate	79 (72.5)
Antibiotic	29 (26.6)
Steroid	58 (53.2)
Azathioprine/6-mercaptopurine	9 (8.26)
Anti-TNF	7 (6.42)
Characteristic	**Mean (SD)**
Age	41.5 (15.7)
BMI	27.1 (7.3)
Disease activity score	
HBI (CD)	4.0 (3.8)
SCCAI (UC/IC)	3.3 (2.9)
IBDO score	
CD	160.6 (34.0)
UC/IC	163.4 (33.4)
Symptom inventory score[a]	
CD	19.4 (8.3)
UC/IC	20.6 (7.6)

[a]Calculated form the total of 46 possible symptoms.

Table 2
Menstrual Cycle Characteristics at Baseline

Characteristic	
Median age at menarche, yr	13.8
Mean duration of flow (days) (SD)	5.1 (1.6)
Mean cycle interval (days) (SD)	28.1 (11.5)
Characteristic	N (%)
Severe pain with menstruation	48 (39.7)
Regularity of menstrual cycle	
Regular	73 (60.3)
Fairly regular	35 (28.9)
Irregular	10 (8.3)
Do not know	3 (2.5)

Table 3
Changes in Menstrual Cycle in the Year Before Diagnosis

Characteristic	N (%)	95% Confidence Interval
Change in cycle interval	30 (24.8)	17.1–32.5
Increased	10 (8.3)	3.4–13.2
Decreased	7 (5.8)	1.6–10.0
Irregular	11 (9.1)	4.0–14.2
Data missing	2 (6.7)	2.2–11.1
Change in duration of flow	25 (20.7)	13.5–27.9
Increased	5 (4.1)	0.6–7.6
Decreased	11 (9.1)	4.0–14.2
Irregular	7 (5.8)	1.6–10.0
Data missing	2 (8.0)	3.2–12.8
Change in intensity of menstrual pain[a]	19 (15.7)	9.2–22.2
Increased	16 (13.2)	7.2–19.2
Decreased	3 (2.5)	0–5.3
Change in duration of menstrual pain[a]	15 (12.4)	6.5–18.3
Increased	12 (9.9)	4.6–15.2
Decreased	3 (2.5)	0–5.3

[a] Among women with beseline dysmenorrhea only.

Table 4
Changes in Menstrual Cycle Over Time

Response	Variable	Estimate	*P*
Entire cohort			
Duration of flow	Year	−0.1	0.29
	Steroid use	0.13	0.48
	Anti-TNFα	−0.01	0.96
	Azathioprine/6-MP	−0.07	0.79
Length of cycle	Year	−0.37	0.21
	Steroid use	−0.21	0.73
	Anti-TNFα	−0.05	0.95
	Azathioprine/6-MP	0.06	0.94
Regularity of cycle	Year	1.26	<0.0001
	Steroid use	−0.93	0.08
	Anti-TNFα	0.44	0.52
	Azathioprine/6-MP	0.16	0.78
Pain with menses	Year	0.06	0.83
	Steroid use	0.21	0.61
	Anti-TNFα	−1.23	0.20
	Azathioprine/6-MP	−0.29	0.67
Change in intensity of menstrual pain	Year	−0.25	0.55
	Steroids	−0.12	0.81
	Anti-TNFα	−0.20	0.80
	Azathioprine/6-MP	0.09	0.93
Change in duration of menstrual pain	Year	−0.17	0.74
	Steroids	0.47	0.42
	Anti-TNFα	0.51	0.62
	Azathioprine/6-MP	1.50	0.20
Patients with CD			
Duration of flow	HBI score	−0.05	0.38
Length of cycle	HBI score	−0.56	0.10
Change in duration of flow	HBI score	−0.32	0.01
Change in length of cycle	HBI score	−0.19	0.06
Change in intensity of menstrual pain	HBI score	0.12	0.41
Change in duration of menstrual pain	HBI score	0.18	0.19
Patients with UC/IC			
Duration of flow	SCCAI score	−0.002	0.96
Length of Cycle	SCCAI score	0.01	0.92
Change in duration of flow	SCCAI score	−0.16	0.25
Change in length of cycle	SCCAI score	−0.24	0.08
Change in intensity of menstrual pain	SCCAI score	0.3	0.10
Change in duration of menstrual pain	SCCAI score	0.27	0.23

6-MP, 6-mercaptopurine.

Table 5

Changes in IBDQ Score by Menstrual Cycle Factors

Variable	Estimate	*P*
Year	8.17	<0.0001
Regularity	−7.22	0.04
Pain with menses	−0.16	0.96
Change in intensity of menstrual pain	−10.12	0.13
Change in duration of menstrual pain	−1.82	0.68