Crohn's & Colitis 360, 2026, 8(3), otag070
https://doi.org/10.1093/crocol/otag070
Published: July 2, 2026
Observations and Research

Evaluating the impact of inflammatory bowel disease on mental health during pregnancy: a retrospective survey study

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Abstract

Background: **Individuals with inflammatory bowel disease (IBD) experience mental health disorders at rates 1.5-2 times higher than the general population. Many are affected during major life stages such as pregnancy, yet data on how IBD influences anxiety and depression in pregnancy remain limited.**

Methods: **This retrospective survey study included patients from the "Preconception and Pregnancy in IBD" clinic who conceived before January 1, 2022. Standardized pre-visit surveys assessed anxiety (general anxiety disorder-7 [GAD-7]), depression (patient health questionnaire-9 [PHQ-9]), and IBD activity using pMayo6 for ulcerative colitis (UC) and mHBI for Crohn's disease (CD). Demographic variables included age, marital and employment status, smoking, alcohol and cannabis use, prior anxiety/depression diagnoses, IBD subtype, surgical history, and medication use. Linear regression models evaluated associations between disease activity and mental health outcomes, adjusting for medication type and stratifying by trimester and IBD subtype.**

Results: **Ninety-four patients were included: 42 patients had UC (44.7%), and 52 patients had CD (55.3%). Median age was 32 (interquartile range [IQR] 31-35.8) for UC and 32.7 (IQR 30-35.2) for CD. Active UC in the second trimester was associated with significantly higher anxiety ($P = 0.034$) and depression ($P = 0.022$) scores compared to those with inactive UC. In the third trimester, this pattern persisted, with active UC again associated with elevated anxiety ($P = 0.030$) and depression ($P = 0.027$) scores. Active CD in the second trimester was significantly associated with higher anxiety ($P = 0.024$) and depression scores ($P = 0.021$) compared to those in remission.**

Conclusions: **Active IBD during pregnancy is significantly associated with increased anxiety and depression. Multidisciplinary care, including mental health support, is imperative for pregnant people with IBD.**

Key words: inflammatory bowel disease, Crohn's disease, ulcerative colitis, mental health

Lay Summary

A retrospective study found pregnant people with active inflammatory bowel disease (Crohn's disease or ulcerative colitis) had higher levels of anxiety and depression during specific trimesters. This highlights the importance of mental health support as part of routine pregnancy care.

Received: December 16, 2025. **Accepted:** June 8, 2026

Key messages

What is already known?

People with inflammatory bowel disease (IBD) experience higher rates of anxiety and depression, and pregnancy adds additional psychological and physiological stressors.

What is new here?

This study suggests that active IBD is significantly associated with higher anxiety and depression scores during pregnancy.

How can this study help patient care?

Recognizing that disease activity correlates with mental health symptoms during the second and third trimesters supports the need for integrated gastroenterology, obstetric, and mental health care to improve outcomes for pregnant individuals with IBD.

Introduction

Inflammatory bowel disease (IBD) is a group of chronic diseases that consists of 2 clinical phenotypes: Crohn's disease (CD) and ulcerative colitis (UC). IBD affects approximately 322 600 (0.8% of the population) individuals in Canada, according to the Crohn's and Colitis Canada report from 2023.[1] The unpredictable nature of the disease, along with the gastrointestinal symptoms, often cause significant psychological distress and mental health concerns such as anxiety and depression. Individuals with IBD experience mental health disorders at a rate 1.5-2 times higher than that of the general population.[2] A recent study found that 21% of people with IBD are clinically diagnosed with anxiety and 15% with depression, while approximately one-third of patients report heightened anxiety symptoms.[2] As a result, clinical guidelines recommend incorporating mental health screenings into routine care for individuals with IBD.[2]

With the incidence of IBD rising, many individuals are affected by the disease during significant life stages, such as pregnancy. While pregnancy itself is a period of heightened stress, with 1 study demonstrating 32.9% and 9.2% of pregnant people experiencing moderate anxiety and depression, respectively, the additional burden of managing IBD can exacerbate psychological stressors.[3] Therefore, given that people with IBD are already at an increased risk of anxiety and depression, pregnant people with IBD may face an even greater susceptibility to these conditions.[2] However, limited research exists on how IBD activity and disease severity during pregnancy affect anxiety and depression.

Evidence suggests that IBD disease activity worsens during pregnancy in 45% of UC patients and 33% of CD patients.[4] While studies such as Pederson have explored IBD clinical outcomes during pregnancy (i.e., increased risk of UC relapse during and after pregnancy, and active disease associated with a lower birth weight in patients with UC), limited studies have assessed how these IBD flares affect maternal mental health.[5,6]

This study aimed to assess the impact of active disease and disease severity on anxiety and depression, among pregnant people with IBD. The findings of this study will help inform the clinical practice and management strategies for pregnant people with IBD.

Methods

This was a retrospective survey study conducted at a specialized preconception and pregnancy IBD clinic at a tertiary care center in Ontario, Canada. The Preconception and Pregnancy IBD clinic was initiated in early 2018 and receives referrals for patients across Ontario. Patients are typically seen at preconception, the first half of each trimester of pregnancy, and as required if they have a disease flare up.

Prior to each clinic visit, patients were given a survey to complete. If a patient had 2 survey results in the same trimester, the survey collected first was used. Surveys included the following data: (1) baseline demographics such as age, marital status, occupational status, smoking habits, alcohol use, cannabis use, and previous diagnosis of anxiety and/or depression, (2) IBD characteristics such as IBD surgery and medication at conception, that is, 5-aminosalicyclic acid (5-ASA), corticosteroids, thiopurines, 6-mercaptopurine (6-MP), and biologics, (3) validated measures of mental health, that is, general anxiety disorder-7 (GAD-7) for anxiety and patient health questionnaire-9 (PHQ-9) for depression.[7,8] In a GAD-7, a score less than 5 is no anxiety, 5-9 is mild anxiety, 10-14 is moderate anxiety and over 15 signifies severe anxiety. In a PHQ-9, a score less than 5 is no depression, 5-9 is mild depression, 10-14 is moderate depression, 15-19 is moderately severe depression and over 20 is severe depression. (4) validated measures of IBD disease activity, that is, Partial Mayo Scoring Index (pMayo6) for UC and Modified Harvey-Bradshaw Index (mHBI) for CD.[9,10] In a pMayo6, a score 2 or greater is active disease, 0-1 is inactive, 2-4 is mild, 5-6 is moderate, and 7-9 is severe. In a mHBI, a score of 5 or greater is active disease, 0-4 is remission, 5-7 is mild, 8-16 is moderate, and above 16 is severe.

Study participants

Patients with diagnosis of CD or UC who attended the Preconception and Pregnancy in IBD clinic from July 1, 2020, to January 1, 2022, were included in this study. We identified patients in the preconception stage, trimester 1 (week 1 to week 12 + 6), trimester 2 (week 13 to week 26 + 6), or trimester 3 (week 27 and beyond). Only surveys during pregnancy were used in this study. For patients with more than 1 pregnancy during the study timeframe, their first pregnancy surveys were used, and subsequent pregnancy surveys were excluded. Patients who had a terminated or lost pregnancy prior to January 1, 2022, were excluded.

Outcomes

The outcomes of this study were to assess the association between (1) active IBD and anxiety/depression, and (2) IBD severity and anxiety/depression in pregnant people. To evaluate these associations, we compared anxiety and depression levels across trimesters 1, 2, and 3 in IBD people with and without active disease. Additionally, we examined the relationship between

anxiety and depression levels, and disease severity across the 3 trimesters.

Statistical analysis

All statistical analysis was performed using R version 4.0. The effect between disease activity and anxiety/depression were tested using a series of linear regressions, across different trimesters of pregnancy for patients with CD and UC, and adjusting for medication type (5-ASA, steroid, thiopurine, 6MP, and biologics). Similar linear regressions were modeled to test the effect of disease severity on anxiety and depression, also adjusting for medication type, stratified by trimester of pregnancy. Lastly, linear mixed effects models were run using the R package "lme4" to test the effect of gestational age (in weeks) on mental health scores, with patient ID as random effects for repeated measures, and stratified models for each diagnostic group.[11] All *P*-value were corrected for multiple comparisons using FDR correction.[12] A *P*-value of less 0.05 was considered statistically significant, indicating a meaningful difference in anxiety and depression.

The study was approved by the Research Ethics Board.

Results

Baseline characteristics

A total of 94 patients were included in this study, 42 patients had UC (44.7%), and 52 patients had CD (55.3%). The median age for the UC group was 32 (interquartile range [IQR] 31-35.8), and the median age for the CD group was 32.7 (IQR 30-35.2). In the UC and CD group, 7.1% and 13.5% of patients had a previous diagnosis of both anxiety and depression, respectively. Additionally, 16.7% and 30.8% of UC and CD patients had previous surgery for their IBD, respectively. In terms of medications at conception, in the UC group, 35.7% were on 5-ASA, 2.4% were on corticosteroids, 4.8% were on thiopurine, and 38.1% were on biologics. In the CD group, 11.5% were on 5-ASA 5.8% were on corticosteroids, 19.2% were on thiopurine, 5.8% were on 6-MP, and 53.8% were on biologics. These values were inclusive, that is, if a patient was on more than 1 medication, they were counted in both groups. A total of 10 patients (11.9% in the UC group and 9.6% in the CD group) were on antidepressants or antianxiety medication at the time of conception.

Employment status was explored as a socioeconomic correlate of anxiety and depression during pregnancy. Mean PHQ-9 scores were 3.2 among unemployed participants and 4.4 among employed participants, while mean GAD-7 scores were 3.47 and 3.70, respectively. There was no statistically significant difference in depression scores between employed and unemployed participants ($P = 0.492$), nor was there a significant difference in anxiety scores ($P = 0.860$). These findings suggest that, within this cohort, employment status was not independently associated with anxiety or depressive symptom burden during pregnancy. All baseline characteristics are described in Table 1.

Surveys

In total, 180 surveys were collected for this study. Thirty-one surveys were collected from patients at preconception (12 with UC and 19 with CD), 29 surveys were collected from patients in trimester 1 (12 with UC and 17 with CD), 61 surveys were collected from patients in trimester 2 (30 with UC and 31 with CD), and 59 surveys were collected from patients in trimester 3 (29 with UC and 30 with CD).

Among 94 participants, 52 (55.3%) completed surveys across multiple pregnancy stages. Specifically, 25 participants contributed data at 2 timepoints, 20 at 3 timepoints, and 7 across all 4 stages (preconception through third trimester).

GAD-7 scores

For UC, the median GAD-7 scores at trimesters 1, 2, and 3 were 2 (IQR 0.75-5.75), 2.5 (IQR 1-5), and 3 (IQR 1-5), respectively. 4 patients (33.3%) in trimester 1, 9 patients (30%) in trimester 2, and 9 patients (31.0%) in trimester 3 had a GAD-7 score of ≥ 5.

For CD, the median GAD-7 scores at trimesters 1, 2, and 3 were 3 (IQR 0-6), 2 (IQR 0-4.5), and 1.5 (IQR 0-5), respectively. 6 patients (35.3%) in trimester 1, 8 patients in trimester 2 (25.8%), and 8 patients (26.7%) in trimester 3 had a GAD-7 score of ≥ 5.

PHQ-9 scores

For UC, the scores at trimesters 1, 2, and 3 were 2 (IQR 1-5), 2 (IQR 1-4), and 3 (IQR 1-4), respectively. 4 patients in trimester 1, 4 patients in trimester 2, and 7 patients in trimester 3 had a PHQ-9 score of ≥ 5.

For CD, the PHQ-9 scores at trimester 1, 2, and 3 was 3 (IQR 2-5), 2 (IQR 1-3), and 2 (IQR 0.25-4), respectively. 5 patients (29.4%) in trimester 1, 6 patients (19.4%) in trimester 2, and 7 patients (23.3%) in trimester 3 had a PHQ-9 score of ≥ 5.

The relationship between disease status and mental health

Linear regression modeling revealed distinct relationships between disease activity and anxiety/depression, across different trimesters of pregnancy for patients with CD and UC (Figure 1). In patients with CD during the second trimester of pregnancy, a statistically significant association was observed between active disease and both depression (FDR $P = 0.021$) and anxiety (FDR $P = 0.024$). Conversely, during the first and third trimesters, no statistically significant relationships were found between active disease and either depression or anxiety.

Among patients with UC, significant relationships between active disease and depression were identified in the second (FDR $P = 0.022$) and third (FDR $P = 0.027$) trimesters. In contrast, no significant relationship was detected between active disease and depression in the first trimester. Furthermore, significant associations between active disease and anxiety were found in the second (FDR $P = 0.034$) and third (FDR $P = 0.030$) trimesters. Again, no significant relationship was observed during the first trimester.

The relationship between disease severity and mental health

A linear regression analysis was conducted to examine the relationship between disease severity and anxiety/depression, across the 3 trimesters of pregnancy (Figure 2). For CD, a

Table 1 Demographics table.

	Total patients ($n = 94$)	Ulcerative colitis patients ($n = 42$)	Crohn's disease patients ($n = 52$)
Age (mean)	33.1	33.5	32.8
Age (median)	32.8	32	32.7
Marital status (*n* %)			
Single	8 (8.5%)	5 (11.9%)	3 (5.8%)
Married	70 (74.5%)	33 (78.6%)	37 (71.2%)
Partner	14 (14.9%)	4 (9.5%)	10 (19.2%)
Unknown	2 (2.1%)	0 (0.0%)	2 (3.8%)
Occupational status (*n* %)			
Unemployed	9 (9.6%)	3 (7.1%)	6 (11.5%)
Employed	82 (87.2%)	37 (88.1%)	45 (86.5%)
Part-time	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	3 (3.2%)	2 (4.8%)	1 (1.9%)
Alcohol (*n*)			
Yes	10 (10.6%)	2 (4.8%)	8 (15.4%)
No	84 (89.4%)	40 (95.2%)	44 (84.6%)
Cannabis			
Yes	6 (6.4%)	2 (4.8%)	4 (7.7%)
No	88 (93.6%)	40 (95.2%)	48 (92.3%)
Smoking			
Yes	1 (1.1%)	0 (0.0%)	1 (1.9%)
No	92 (97.9%)	42 (100.0%)	50 (96.2%)
Unknown	1 (1.1%)	0 (0.0%)	1 (1.9%)
Previously diagnosed with mental illness			
None	73 (77.7%)	34 (81.0%)	39 (75.0%)
Anxiety	8 (8.5%)	4 (9.5%)	4 (7.7%)
Depression	3 (3.2%)	1 (2.4%)	2 (3.8%)
Anxiety and depression	10 (10.6%)	3 (7.1%)	7 (13.5%)
Previous surgery for inflammatory bowel disease (IBD)			
Yes	23 (24.5%)	7 (16.7%)	16 (30.8%)
No	71 (75.5%)	35 (83.3%)	36 (69.2%)
IBD medication at conception			
None	8 (8.5%)	4 (9.5%)	4 (7.7%)
5-aminosalicyclic acid	21 (22.3%)	15 (35.7%)	6 (11.5%)
Thiopurine	15 (16.0%)	2 (4.8%)	13 (25.0%)
Corticosteroids	4 (4.3%)	1 (2.4%)	3 (5.8%)
Biologic	44 (46.8%)	16 (38.1%)	28 (53.8%)
Type of biologic			
Infliximab	21 (22.3%)	9 (21.4%)	12 (23.1%)
Adalimumab	11 (11.7%)	3 (7.1%)	8 (15.4%)
Vedolizumab	6 (6.4%)	4 (9.5%)	2 (3.8%)
Ustekinumab	7 (7.4%)	1 (2.4%)	6 (11.5%)
Taking an antidepressant or antianxiety medication at conception	10 (10.6%)	5 (11.9%)	5 (9.6%)

significant positive relationship was found between disease severity and depression during the second trimester ($P = 0.0300$), suggesting that increased disease severity is associated with higher levels of depression. No significant relationships were observed between CD severity and depression during the first ($P = 0.421$) and third ($P = 0.421$) trimesters. Similarly, a significant positive relationship was observed between disease severity and anxiety during the second trimester of pregnancy ($P = 0.0366$). This indicates that higher disease severity correlates with increased levels of anxiety. However, no significant associations were found between CD severity and anxiety during the first ($P = 1$) and third ($P = 0.688$) trimesters.

In the case of UC, significant positive relationships between disease severity and depression were found during the second ($P = 0.0354$) and third ($P = 0.0354$) trimesters. No significant association was observed between UC severity and depression

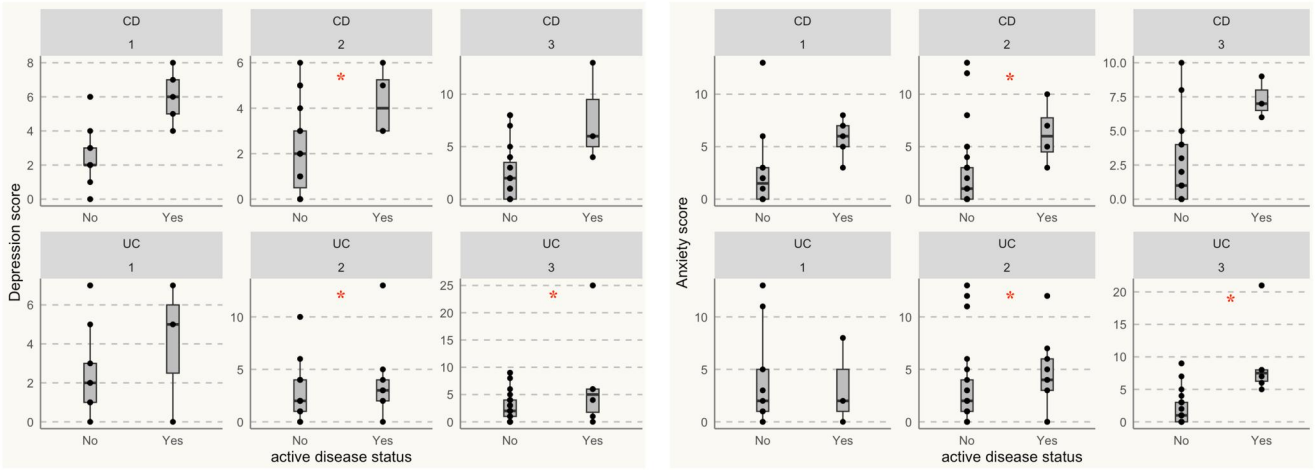

Figure 1 Depression and anxiety scores in patients with CD and UC stratified by active disease status. Boxplots show the distribution of depression (left panel) and anxiety (right panel) scores across the 3 trimesters (1, 2, and 3), comparing patients with active disease ("yes") to those without active disease ("no"). Asterisks (*) indicate statistically significant differences ($P < 0.05$) between active and non-active disease groups within each subgroup. CD, Crohn's disease; UC, ulcerative colitis.

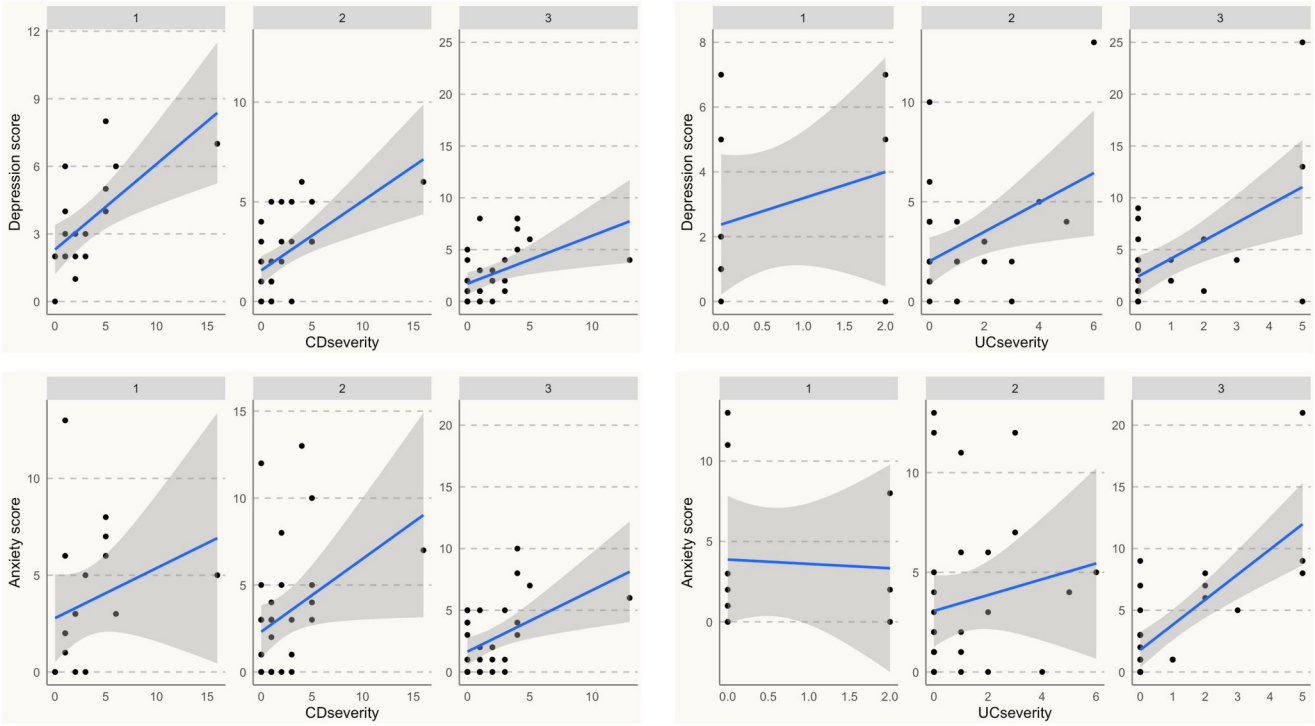

Figure 2 Linear regression plots illustrating the relationship between disease severity and mental health outcomes (depression: top row; anxiety: bottom row) across the 3 trimesters of pregnancy in patients with CD (left panels) and UC (right panels). Each panel represents a different trimester (1, 2, 3 from left to right), with blue lines indicating the linear regression fit and shaded areas representing 95% confidence intervals. CD, Crohn's disease; UC, ulcerative colitis.

during the first trimester ($P = 0.202$). For anxiety, significant positive relationships were identified during both the second ($P = 0.0418$) and third ($P = 0.0334$) trimesters. This implies that increasing UC severity is associated with elevated anxiety levels. No significant relationship was detected between UC severity and anxiety during the first trimester ($P = 0.705$).

The relationship between gestational age and mental health

An analysis was performed to determine if there was a correlation between gestational age and anxiety/depression (Figure 3). The results indicated that neither CD nor UC showed

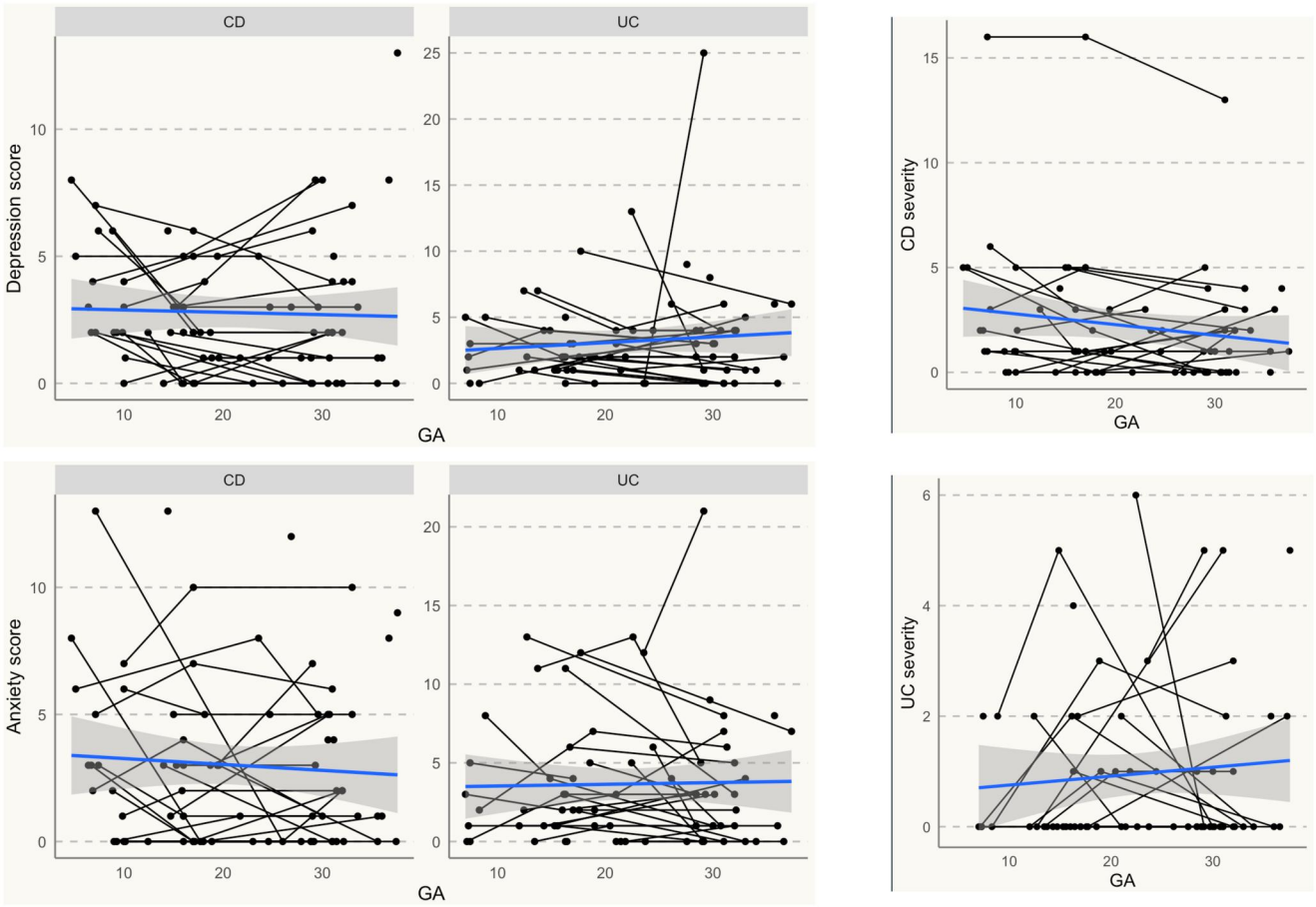

Figure 3 Individual trajectories of depression and anxiety scores across gestational age in pregnant people with CD and UC. Each line represents a single participant, illustrating within-subject changes in scores over time across pregnancy stages. CD, Crohn's disease; UC, ulcerative colitis.

statistically significant relationships between gestational age and anxiety/depression.

Discussion

This study demonstrated that active disease and disease severity, for both CD and UC, is significantly associated with increased levels of depression and anxiety in certain trimesters of pregnancy. It reinforces the heightened vulnerability of people with IBD to anxiety and depression during pregnancy.

Comparison to existing literature

These results are broadly consistent with prior studies that report higher levels of psychiatric comorbidities in patients with IBD.[13] A large systematic review conducted by Neuendorf et al., concluded that 22% of patients with IBD have depressive symptoms and 35% have anxiety symptoms, with significantly higher levels in those with active disease.[14] Our study follows this trend as active CD and UC in the second and third trimesters of pregnancy were associated with significantly higher anxiety and depression scores.

A systematic review by Dennis et al., showed that 15.2% of pregnant people experience a clinical diagnosis of any anxiety disorder.[15] Our study indicates that a larger percentage of pregnant people with IBD experience anxiety compared to the general population, with 25%-35% having a GAD-7 score of 5 or more during pregnancy.

Research regarding psychiatric comorbidities in pregnant people with IBD remains limited. One cohort study demonstrated that women with CD are at increased risk of a new-onset mood or anxiety disorders during the postpartum period, but not during pregnancy.[16] The discrepancy between this study and ours may be due to the study design. The outcome of that study was a formal diagnosis of a new-onset psychiatric illness reported in health administrative data, whereas we used validated self-reported questionnaires which are more sensitive to transient psychological distress. Additionally, our study analyzed anxiety and depression in each trimester, which allowed us to identify changes during pregnancy that could be overlooked in broader pre- vs post-natal comparisons.

Studies have also shown that women with IBD are at increased risk of experiencing depression and anxiety disorders than men.[17] Therefore, since our cohort was 100% female, the baseline risk of depression and anxiety was higher.

Potential explanations for trimester differences

There are a few possibilities for the underlying mechanism responsible for these results. One possibility is that disease severity in the

first trimester in our patient cohort was minimal and therefore, there was no relationship to elicit. However, once disease severity increased, the anxiety and depressive symptoms increased. This could be explained by the rise in progesterone during pregnancy which has been shown to have immunosuppressive effects, which could in turn exacerbate IBD symptoms.[18] Another possibility is reduced statistical power as fewer surveys in trimester 1 were completed, limiting our ability to detect significant differences. Additionally, the general psychological stress associated with pregnancy might further contribute to the mental health burden for patients with IBD. Future studies are needed to research and understand the underlying causes of the observed mental health impact in pregnant people with IBD. For instance, research comparing the mental health of patients with and without IBD across the 3 trimesters could provide insights into how general pregnancy-related stressors affect mental health in people with IBD compared to those without. These studies would be instrumental in developing targeted interventions and support strategies.

It is essential to consider the medications patients are taking, as they can influence outcomes. In our study, 4.3% of patients were taking corticosteroids at the time of conception, and corticosteroids are known to impact mental health. Corticosteroids can cause psychiatric adverse effects such as anxiety and depression, with up to 20% of patients on high dosages of glucocorticoids experiencing mental illness.[19,20] Future studies can focus on whether pregnant people with IBD and active disease are more likely to be prescribed corticosteroids, potentially contributing to poorer mental health outcomes.

Clinical implications

Our study also demonstrates the need for individualized care, including anxiety and depression monitoring, for pregnant IBD people with active disease. Currently, pregnant people with IBD are monitored by gastroenterologists to ensure disease control and medication safety. However, this study suggests that integrating mental health screenings for anxiety and depression into routine care is equally as important. It is imperative to implement a multidisciplinary team that includes not only gastroenterology and obstetrics, but also psychiatric care. Such a team can provide comprehensive support, addressing both physical and mental health challenges. The observed impact of disease severity on anxiety and depression across different trimesters further emphasizes the importance of continuous monitoring throughout pregnancy. Regular assessments throughout all 3 trimesters can help in managing both disease activity and associated anxiety and depression. The data indicates that the second trimester is particularly critical for both CD and UC, as active disease and disease severity during this period is associated with significantly higher levels of both depression and anxiety. Therefore, routine assessments and mental health screenings for anxiety and depression during the second trimester are critical.

Limitations

This study relied on self-reported testing of anxiety and depression, which may have induced response bias within the study population, especially if there are culturally significant barriers to discussing mental health. However, the GAD-7 and PHQ-9 surveys are validated assessments of anxiety and depression.[7,8] Therefore, even though these patients were not assessed by a psychiatrist for the purpose of this study, these surveys were adequate to assess patient anxiety and depression.

Although validated instruments (PHQ-9 and GAD-7) were used without modification, some items assess somatic symptoms such as fatigue, sleep disturbance, and appetite changes, which may overlap with normal pregnancy or IBD-related symptoms. This overlap may have led to overestimation of depression and anxiety scores in this population. Similarly, the pMayo6 and mHBI are not specifically validated in pregnant populations and may be influenced by physiologic and symptomatic changes of pregnancy, potentially affecting the accuracy of disease activity classification in our cohort.

A proportion of participants were receiving antidepressant or antianxiety medication at conception, which may have influenced observed symptom scores. Pharmacologic treatment could attenuate symptom severity, whereas medication use may also serve as a marker of more severe underlying psychiatric illness. The net effect of this on study findings is therefore uncertain.

Another limitation is the lack of data on parity and pregnancy intention (planned vs. unplanned). These variables may act as confounders, as first-time mothers or those with unplanned pregnancies could have increased levels of anxiety or depression compared to others.

The subjects of this study are patients at the preconception and pregnancy in IBD clinic, and therefore, we did not use a non-pregnant or non-IBD population as a control. Also, as this study was conducted in a specialized tertiary referral clinic, the study population may reflect a more complex or closely monitored subset of patients with IBD, introducing potential referral bias.

Finally, we did not collect or analyze objective markers of disease activity, that is, fecal calprotectin, as they are not currently available for all patients. We are continuing to chart review and collecting data for future studies, which can hopefully further explore these limitations.

Conclusion

In conclusion, this study demonstrates that disease activity and severity significantly affect the mental health of pregnant people with IBD. Successful management requires a multidisciplinary approach, including mental health support, and continuous monitoring of disease activity throughout pregnancy. By addressing these needs, we can appropriately support the mental well-being of pregnant people with IBD.

Funding

This study received funding from the University of Toronto GE/HEP New Pilot Investigator Award. V.H. received a University of Toronto Division of Gastroenterology and Hepatology New Investigator Award to support this study.

Conflicts of interest

Dr. Vigod reports royalties from UpToDate Inc for authorship of materials related to depression and pregnancy.

Data availability

The data used were obtained from routinely collected clinical surveys at the affiliated hospital and are not publicly available due to patient privacy. De-identified data may be made available from the corresponding author upon reasonable request and with approval from the Research Ethics Board.

Ethics statement

Ethics approval was received from Research Ethics Board.

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Crohn's & Colitis 360, 2026, 8, 1–8
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