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Observations and Research

Inflammatory Bowel Disease and Pain Interference: A Conceptual Model for the Role of Insomnia, Fatigue, and Pain Catastrophizing

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Background: People with inflammatory bowel disease (IBD) commonly experience pain influenced by complex interactions among factors, including disease activity, sleep, psychopathology, and changes in pain processing pathways. Treatments for pain in IBD are limited, highlighting the need for research that explores modifiable factors linked to pain. The aim of this study was to investigate relationships among multiple patient factors and to construct a conceptual model for pain interference in IBD.

Methods: A cross-sectional survey of adults with IBD. Study domains included demographic, comorbidity, psychological, IBD, insomnia, fatigue, and pain features. Structural equation modeling (SEM) was used to examine relationships and interactions among active IBD, insomnia, fatigue, pain experiences (severity, catastrophizing, and interference), and additional patient factors (demographics and psychological).

Results: One hundred and seventy-four participants, aged 18–85 years, reported the presence of pain. Combining the questionnaire data using SEM resulted in a final model with an excellent fit ($\chi^2(8) = 9.579$, $P = .297$, $\chi^2/N = 1.197$, CFIN = 0.997, TLI = 0.987, RMSEA = 0.034). The presence of anxiety and depression was the additional patient factors to be retained in the path analysis. SEM results indicated that greater pain interference was directly influenced by greater fatigue, worse pain catastrophizing, and worse pain severity. Pain interference was indirectly impacted by IBD activity, worse insomnia, and the presence of depression and anxiety.

Conclusions: The proposed conceptual model highlights the role of multiple potentially modifiable factors, including insomnia, pain catastrophizing, and fatigue, contributing to worse pain interference in people with IBD.

Lay Summary

Treatments for pain in inflammatory bowel disease (IBD) are limited. This study investigated the relationship of potentially modifiable factors to pain in adults with IBD. Results indicated that worse pain was related to fatigue, pain catastrophizing, insomnia, depression, and anxiety.

Key Words: insomnia, fatigue, pain, pain catastrophizing, inflammatory bowel disease

Introduction

Pain is reported to affect over 80% of individuals with inflammatory bowel disease (IBD)[1–5] and significantly influences the degree of disability experienced by patients.[6] Similar to other chronic inflammatory diseases, pain experiences in IBD are influenced by multiple factors, including disease activity, sleep disturbances, psychological factors, and changes within neural pain processing pathways, termed central sensitization.[4,7,8] Investigating the links among these factors and worse pain experiences may provide a deeper understanding of complex clinical presentations, enabling the development of targeted treatment pathways.

The complex pathophysiological mechanisms related to central sensitization can lead to pain hypersensitivity seen in persistent pain states.[9–11] Mechanisms of central sensitization are thought to not only contribute to worse pain experiences in people with active IBD,[12] but to also explain the presence of pain in patients beyond periods of active inflammation.[13,14] Specifically, investigation of pain in people with active IBD has suggested mediating effects of central sensitization leading to worse pain interference.[12] The construct of pain interference explores the extent to which pain hinders engagement with social, cognitive, and emotional activities.[15] Older pain models assume that relief from pain correlates with an improvement in function.[16] However, exploration of interference constructs highlights that although pain severity, interference, and function are related, they are ultimately distinct domains, each requiring consideration.[17,18]

In addition to the increased prevalence of pain, over 75% of individuals with active IBD also suffer from sleep disturbances,[19,20] with insomnia representing the most common sleep disorder.[21,22] Poor sleep has demonstrated a prospective association with increased likelihood of symptom flares[19,23] and is associated with an increased risk of surgery, hospitalizations,[24] and decreased quality of life.[25,26] The relationship between IBD and sleep disorders, such as insomnia,

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is likely bidirectional and may be mediated in part by inflammation.[27] Similarly, chronic insomnia is reported in over 50% of people with persistent pain.[28] Prospective studies have indicated that although pain may disrupt sleep, insomnia adversely influences pain experiences, likely due to mechanisms of central sensitization.[28,29] Consequently, the relationship between insomnia and worse pain may also be bidirectional and influenced by factors commonly seen in persistent pain and IBD populations, including fatigue and pain catastrophizing.

Nearly 80% of IBD patients with active disease[30] and 50% in remission experience fatigue[31,32] that negatively impacts their quality of life. Fatigue is also commonly seen in patients with persistent pain where underlying mechanisms of central sensitization have been proposed.[33] Likewise, pain catastrophizing has demonstrated associations with worse sleep, worse pain, and mechanisms of central sensitization.[34,35] Treatments for insomnia in patients with persistent pain demonstrated improvements in fatigue, pain experiences,[36] and pain catastrophizing.[37] As such, insomnia may represent a promising target to improve pain experiences in IBD patients.[27]

Investigation of the links among factors thought to influence pain experiences, such as active IBD, insomnia, fatigue, pain catastrophizing, and other patient factors may provide a deeper understanding of complex clinical presentations, enabling the development of targeted treatment pathways. Therefore, the aim of the current study was to use structural equation modeling (SEM) to investigate relationships between pain interference and key factors identified in the literature (ie, IBD activity, insomnia, fatigue, pain catastrophizing, and pain severity), as well as other patient factors (ie, anxiety, depression, demographics, etc). We hypothesized that people with active IBD and worse insomnia will have greater fatigue, greater pain catastrophizing, worse pain severity, and in turn, worse pain interference.

Methods

Study Design

The current study represents a subanalysis derived from data collected from a primary cross-sectional online survey of individuals with IBD.[22] This observational study was granted ethical approval by the Institutional Review Board for Dartmouth-Hitchcock Hospital, Committee for the Protection of Human Subjects (#02000126).

Study Procedure

From November to December of 2020, adult patients (18 years and older) with an established IBD diagnosis at the Dartmouth-Hitchcock IBD Center were invited to participate in the original primary study.[22] The Dartmouth-Hitchcock IBD Center has a secure online patient messaging portal system linked to their patient database, allowing for a broad recruitment strategy. Invitations were distributed through a secure online patient messaging portal system to a total of 2569 individuals, representing active and nonactive patients. Those who clicked on the study link were directed to a digital consent statement via REDCap. Following acceptance of the consent statement, participants were directed to a series of study questionnaires via Qualtrics survey website. No data were abstracted from medical records and all responses were anonymous. Participants who reported an IBD-related diagnosis other than Crohn's disease (CD) or ulcerative colitis (UC), and those who did not report the presence of pain in the past 1 month were excluded from this study. The full methodology for the original primary study is reported elsewhere.[22]

Demographics and Psychological Features

Demographics explored in the present study included age, gender, race/ethnicity, and marital status. Psychological features investigated in the present study included the presence of anxiety and depression. The presence of anxiety was assessed using the General Anxiety Disorder 7-item scale (GAD-7), which previously demonstrated a sensitivity of 0.89 and a specificity of 0.82 for detecting the presence of clinically significant anxiety using the cutoff score of ≥10.[38] The presence of depression was assessed using the Patient Health Questionnaire-9 (PHQ-9), which previously demonstrated a sensitivity of 0.88 and specificity 0.85 for detecting clinically significant depression using a cutoff score of ≥10.[39]

IBD Features

IBD in the present study was characterized by: IBD subtype (ie, CD or UC), age at IBD diagnosis, and IBD activity. Disease activity in the present study was characterized as active versus inactive IBD. To ensure measurement consistency across the IBD subtypes, the Patient-Reported Outcomes-3 items (PRO-3) was used to categorize disease activity for both UC and CD. PRO-3 requires participants to rate their stool frequency, abdominal pain (for CD only), rectal bleeding (for UC only), and general well-being on average over the past 7 days. Participants with UC were classified with active IBD based on a previously established scoring algorithm, where active disease is indicated by 2 items from the 6-point Mayo score and 1 item on general well-being from the simple clinical colitis activity index.[40] Participants with CD were classified with active IBD if they indicated: (1) at least 1 more loose stool than normal per day, mild abdominal pain or worse, and feeling "*slightly under par*" or worse; (2) at least moderate pain and either 1 or more loose stools than normal per day or feeling "*slightly under par*" or worse; (3) 5 or more loose stools than normal per day and either mild abdominal pain or worse or feeling "*slightly under par*" or worse; (4) severe abdominal pain; or (5) feeling "*generally poor*" or worse.

Insomnia Severity

Insomnia severity in the present study was investigated using the 7-item Insomnia Severity Index (ISI), where each item is rated from 0 to 4, with total scores ranging from 0 to 28.[41] Interpretation of ISI total scores include subthreshold insomnia,[8–14] moderate clinical insomnia,[15–21] and severe clinical insomnia.[22–28] The ISI previously demonstrated a sensitivity of 86.1% and specificity of 87.7% for detecting the presence of insomnia disorder using a cutoff score of ≥10.[42]

Fatigue Severity

Fatigue severity in the present study was investigated using the 20-item Multidimensional Fatigue Inventory (MFI). The MFI-20 measures self-reported responses within the subscales of general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity.[43] Subscale scores (range 4–20) were calculated as the sum of item ratings and a total fatigue score (range 20–100) was calculated as the sum of

subscale scores, where higher scores indicate a higher level of fatigue. Psychometric validation of MFI-20 has shown good validity[44] and strong internal consistency (Cronbach's α = 0.93).[45]

Pain Severity and Interference

The 9-item Brief Pain Inventory (BPI-9) was used to assess pain severity and interference in the present study.[46] Participants were asked to identify on a body chart all regions in which they experienced pain in the past month and the region that they felt the most pain. They then rated their worst, least, average, and current pain severity for the past 1 month on an 11-point numeric rating scale (NRS) from 0 (no pain) to 10 (pain as bad as you can imagine). Similarly, participants were asked to rate the degree that pain interferes with general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life on an 11-point NRS from 0 (does not interfere) to 10 (completely interferes). The BPI-9 previously displayed excellent internal consistency (Cronbach's α = 0.91) and good to excellent test–retest values (intraclass correlation coefficient [ICC] 0.84–0.90 and Kappa values >0.70) in people with IBD.[47]

Pain Catastrophizing

Catastrophizing is understood to be negative cognitive and affective responses to pain that include elements of magnification, helplessness, pessimism, and focused attention on pain.[48] The literature indicates that the tendency to "catastrophize" during painful experiences is related to worse pain perceptions and increased emotional distress.[48] The relationship between catastrophizing and worse pain-related measures, such as severity, interference, disability, and depression has shown remarkable consistency across a wide range of pain populations.[48–52] Current perspectives suggest that the tendency to catastrophize may reflect state and trait cognitions that are modifiable and responsive to treatment.[48,49,53,54]

The pain catastrophizing scale (PCS) was used to measure the extent of catastrophic thoughts about pain experiences. The PCS consists of 13 items rated on a 5-point Likert scale that measures 3 dimensions of catastrophizing: rumination, magnification, and helplessness.[55] PCS total scores range from 0 to 52, where higher scores indicate greater levels of catastrophic thoughts about pain.[56] Total PCS scores demonstrated good internal consistency (Cronbach's α value of 0.87) and acceptable test–retest reliability (ICC = 0.75).[55]

Statistical Analysis

The a priori minimum dataset for the present analysis was completion of at least 50% of each questionnaire. This cutoff value was selected to optimize participant retention and minimize sampling bias across the questionnaires. Descriptive statistics (frequencies, means, and SD) were used to characterize demographic, comorbid, IBD, and pain characteristics of study participants. All data analyses were conducted using IBM SPSS Statistics (version 28) and SPSS Amos (version 28), IBM Corp.

Exploratory analysis and visual inspection of the data indicated that all the study variables met the necessary assumptions for statistical analysis (eg, normality and linearity). Spearman rank-order and point-biserial correlation coefficients were calculated to assess bivariate relationships between primary variables (ie, active IBD, insomnia, fatigue, and pain experiences [ie, severity, catastrophizing, and interference]) and additional patient factors (ie, IBD subtype, age at IBD diagnosis, age, gender, anxiety, and depression). Significant correlations were identified as $P \leq .05$, with strength of associations identified as: very weak (<0.19), weak (0.20–0.30), moderate (0.30–0.50), strong (0.50–0.79), and very strong (≥0.80).[57] Patient factors that demonstrated significant correlation ($P \leq .05$) with a primary outcome were included in the subsequent SEM analysis.[57]

SEM is an increasingly popular tool to model multivariate relationships.[58,59] This study utilized a regressive SEM approach (SPSS Amos), specified based on an iterative process of adding and removing variables based on modification indices that resulted in pathways that were both significant and improved the model's fit. As recommended by Hu and Bentler,[60] criteria used to specify paths or variables to be added were based on inspection of standardized residuals and significant improvement in fit (ie, significant change in χ^2/N). Model performance was also evaluated across multiple indices, with a good model fit representing: χ^2 $P > .05$; χ^2/N = 1–3, CFI >0.95, TLI >0.95, RMSEA ≤0.05.

Sample Size

There is no consensus in the literature regarding sample size estimation for SEM. Common recommendations include a minimum sample size of N = 100–150 for conducting SEM.[61,62] However, consideration for adequate sampling in this study also includes post hoc investigation of misspecification power. The power to detect a misspecified model is the probability of correctly rejecting an incorrect model and is evaluated post hoc through fit indices outlined above.[63]

Results

Of the 2569 individuals who were sent information regarding the original primary study, 389 were enrolled suggesting a response rate of 15%. However, in addition to current patients, the institutional database includes individuals who are no longer active patients. Restrictions precluded the ability to filter the database for active patients, therefore the true response rate cannot be determined. As reported in the primary study,[22] 3.3% of the overall respondents in the main study were excluded due to a priori minimum dataset requirements. Specific to this subanalysis, n = 195 of the respondents indicated the presence of bodily pain within the past month, and 89% of these (n = 174) reached the minimum dataset for inclusion. Of the include participants (N = 174), 99% represented full datasets with mean imputation methods used to account for missing data for the remaining 1%. Most participants (n = 154, 88%) reported pain in more than 1 body region. Of the different body regions that were identified as painful (N = 53), the abdomen (n = 89, 51%), and low back (n = 86, 49%) were the most commonly identified regions.

Demographic, IBD, and psychological characteristics of the included participants (N = 174) are summarized in Table 1. The self-reported health history of study participants is summarized in a supplementary Table. Just over half of the study participants (57% [n = 99]) identified as married. Total GAD-7 scores ranged from 0 to 21 (mean [SD] of 6.68 [5.53]) with 25% of study participants reaching the threshold (≥10) for clinically significant anxiety. Total PHQ-9 scores ranged from 0 to 26 (mean [SD] of 7.51 [5.61]) with 34% of study

participants reaching the threshold (≥10) for clinically significant depression.

Investigation of between-group differences for survey respondents who reported the presence of pain compared to those without pain, with respect to demographic and disease characteristics, was conducted using chi-squared tests for categorical or independent *t*-tests for continuous variables. Significant ($P \leq .05$) between-group differences was identified for gender, IBD diagnosis, and IBD activity. Women represented a greater proportion (71%) of the participants with self-reported pain compared to participants without pain (60%, $P = .037$). Additionally, the proportion of CD versus UC diagnoses in respondents with pain (66% and 33%, respectively) significantly differed ($P = .002$) compared to respondents without pain (48% and 52%, respectively). Finally, the proportion of respondents with active versus nonactive IBD who reported pain (66% and 34%, respectively) significantly differed ($P < .001$) compared with respondents without pain (35% and 65%, respectively). Conversely, there were no significant age differences between respondents with pain compared to those without pain. These findings are similar to previous reports of gender and disease factors commonly present in IBD patients with pain.[12,64]

Summary of the primary variables is provided in Table 2. Mean (SD) for worst pain severity on the BPI-9 was 6.16 (1.93) and least pain severity was 1.95 (1.75). Of the study participants, 55% ($n = 96$) reached the ISI scoring threshold (≥10) for identifying the presence of insomnia disorder and 10% ($n = 18$) reached clinically meaningful scores (>30) for pain catastrophizing.

Table 1. Demographic, IBD, and psychological features of IBD study participants ($N = 174$).

Feature	*N* (%)
Age (years) (mean (SD), range)	48.40 (16.51), 18–85
Gender	
Male	49 (28)
Female	125 (71)
Other	1 (<1)
Crohn's disease	115 (67)
Ulcerative colitis	58 (33)
Age at diagnosis (mean (SD), range)	32.42 (15.93), 1–85
Anxiety (yes)	43 (25)
Depression (yes)	58 (34)

Abbreviation: IBD, inflammatory bowel disease.

Correlation Analysis

Bivariate correlations are presented in Table 3. Worse insomnia, worse fatigue, worse pain severity, and greater pain catastrophizing demonstrated significant moderate correlations with each other (rho = 0.33–0.48). Similarly, active IBD demonstrated moderate correlation with worse insomnia, worse fatigue, and worse pain experiences (severity, catastrophizing, and interference) ($r_{pb} = 0.33–0.45$). Greater pain interference demonstrated strong correlation to worse insomnia, fatigue, pain severity, and pain catastrophizing scores (rho = 0.52–0.66). The presence of anxiety and depression demonstrated very weak to strong correlations (rho = 0.19–0.59) to active IBD and worse insomnia, fatigue, and pain scores (ie, severity, catastrophizing, interference). Women demonstrated weak correlation with worse insomnia and fatigue scores ($r_{pb} = 0.22$ and 0.18, respectively). Younger age at diagnosis was correlated with CD subtype ($r_{pb} = -0.27$).

Path Analysis

Patient factors demonstrating significant correlation with a primary variable included, gender, anxiety, and depression. Thus, a path analysis was conducted to examine the relationships and interactions between active IBD, insomnia severity, fatigue severity, pain severity, pain catastrophizing, anxiety, depression, gender, and pain interference. Of the included variables, anxiety, depression, and all the primary variables were retained in the model. The final model (Figure 1) demonstrated a good fit ($\chi^2(8) = 9.579$, $P = .297$, $\chi^2/N = 1.197$, CFIN = 0.997, TLI = 0.987, RMSEA = 0.034) and accounted for a notable amount of the total variance for each of the endogenous variables (48% of fatigue severity, 37% pain catastrophizing, 28% of pain severity, and 56% of pain interference).

Active IBD and greater insomnia demonstrated significant direct relationships with greater fatigue and greater pain severity, which in turn had significant direct relationships with greater pain interference. The presence of depression demonstrated a significant direct relationship with greater fatigue, worse pain catastrophizing, and greater pain severity. The presence of anxiety demonstrated a significant direct relationship with greater fatigue and worse pain catastrophizing. Greater pain severity demonstrated a significant direct relationship with worse pain catastrophizing, which in turn had a significant direct relationship with greater pain interference.

Table 2. Primary outcome measures in IBD study participants ($N = 174$).

Outcome measure	Mean (SD)	Range
Insomnia Severity Index	10.64 (5.59)	0–26
Multidimensional Fatigue Inventory	61.88 (14.52)	24–94
Active IBD (*n*, %)	114 (66)	
Pain catastrophizing scale	13.88 (10.45)	0–46
Average pain severity (BPI-9)	3.67 (1.55)	0–9.25
Average pain interference (BPI-9)	4.09 (2.41)	0–10

Abbreviations: BPI-9, the 9-item Brief Pain Inventory; IBD, inflammatory bowel disease.

Table 3. Spearman rank-order (rho) correlations in IBD study participants (N = 174).

	1	2[a]	3[a]	4	5[a]	6[a]	7[a]	8	9	10	11	12
1. Age												
2. Gender[a]	−0.10											
3. IBD subtype[a]	−0.20*	0.03										
4. Diagnosis age	0.70*	−0.09	−0.27*									
5. Anxiety[a]	−0.22*	0.13	0.02	−0.14								
6. Depression[a]	−0.24*	0.03	−0.04	−0.13	0.20*							
7. Active IBD[a]	−0.08	0.08	0.06	−0.10	0.19*	0.56*						
8. Insomnia	−0.04	0.22*	0.11	−0.02	0.39*	0.38*	0.45*					
9. Fatigue	−0.14	0.18*	0.05	−0.11	0.43*	0.48*	0.59*	0.48*				
10. Pain severity	−0.01	0.13	0.14	−0.03	0.39*	0.19*	0.34*	0.45*	0.34*			
11. Pain catastrophizing	−0.12	0.01	0.04	−0.11	0.33*	0.43*	0.48*	0.36*	0.48*	0.47*		
12. Pain interference	−0.10	0.10	0.12	−0.11	0.45*	0.32*	0.46*	0.52*	0.60*	0.66*	0.59*	

Abbreviation: IBD, inflammatory bowel disease.
[a]Point-biserial coefficient (r_{pb}).
*Significant at $P \leq .05$.

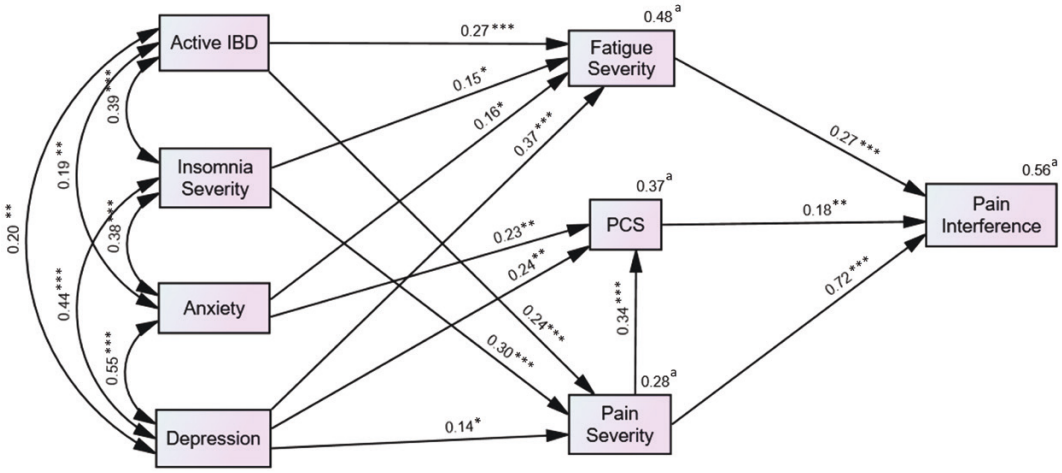

Figure 1. Final path model. Error terms have been removed, pain catastrophizing scale (PCS), [a]R^2, *$P < .05$, **$P < .01$, ***$P < .001$.

Discussion

The current study aimed to examine the relationships among active IBD, insomnia, fatigue, pain severity, pain catastrophizing, and the extent that pain interferes with daily activities. Of the additional patient factors examined, the presence of anxiety and depression was the sole factors to be retained in the path analysis. SEM results indicated that greater pain interference was directly influenced by greater fatigue, worse pain catastrophizing, and worse pain severity. Pain interference was indirectly impacted by active IBD, worse insomnia, and the presence of depression and anxiety. These results illustrate a conceptual model for multiple factors and relationships potentially driving greater pain interference in people with active IBD. As such, these factors may represent meaningful treatment targets to improve pain experiences in IBD.

Although the current study is unable to confirm the directionality of the identified relationships, the proposed conceptual model highlights a significant role for potentially modifiable factors related to worse pain interference in patients with IBD. A common view within the current literature points to a reciprocal relationship between sleep and pain.[28] However, population-based longitudinal studies suggest that sleep disorders may be stronger and more reliable predictors of pain than pain is of sleep.[28] Notably, insomnia may drive next day pain, including abdominal pain in irritable bowel syndrome.[65] Experimental studies suggest that sleep disturbances may contribute to the development of chronic pain through underlying mechanisms of central sensitization.[28,66] Future research should explore the temporal relationship between treatments for insomnia and changes to pain experiences in people with IBD.

Relationships between pain catastrophizing and pain severity, disability, poor sleep, and worse patient outcomes are well described in the literature.[34,35,67,68] The recognized fear-avoidance model[69] highlights pain catastrophizing as a cognitive precursor to greater pain interference and the transition from acute to chronic pain.[70] Reductions in pain catastrophizing have been demonstrated through targeted interventions,[71,72] as well as indirectly through treatments for insomnia.[37] Likewise, treatments for insomnia have previously demonstrated significant reductions in pain severity in

multiple populations.[28,36,73] Therefore, targeted interventions for pain catastrophizing and/or insomnia in IBD patients may lead to a decrease in pain interference and subsequent improvement in quality of life. Our research team has already begun investigations in this area.[74]

Current results also contribute to the increasing body of evidence for the adverse effects of fatigue, including a role in worse pain experiences in patients with IBD. The literature suggests fatigue is strongly associated with greater disability, disease activity, poor sleep, and worse patient outcomes,[75–77] and may be responsive to both cognitive behavioral and pharmacological interventions.[78,79]

The association of poor sleep, worse pain, fatigue, and disease activity in immune conditions[80] highlight the potential for underlying shared mechanisms related to central sensitization.[35,66] Specifically, investigations exploring mechanisms of central sensitization offer a pathophysiological rational for the bidirectionality between factors in the present model. For instance, preclinical studies indicate that sleep disturbances may trigger neuroinflammation (ie, glial activation) that contributes to the establishment and/or maintenance of central sensitization in persistent pain states.[66] This research suggests that treatments targeting insomnia, for instance, in IBD may lead to a decrease not only in fatigue and pain catastrophizing, but in pain interference as well by targeting underlying central sensitization.

There are study limitations to consider when interpreting results. A common limitation of large surveys relates to self-report bias and nonresponse bias. Although the stated response rate is likely an underestimation of the true response rates, interpretation of study results should consider the impact of the potentially lower response rates. However, it is important to note that the presence of insomnia and pain identified in this study is consistent with other IBD investigations.[81–83] This consistency with the extant literature suggests that while the current response rate is low, the resultant sample is likely not biased to a degree that undermines the validity of the study results.

Another limitation relates to assessment of IBD activity solely through self-reported measures. The standard clinical practice for estimating active IBD typically includes clinical investigations, such as colonoscopies and serum biomarkers, alongside measures used in the present study.[84] Therefore, while estimation of IBD activity in the present study may be imprecise, measures used in this study are aligned with current recommendations from clinical IBD trials.[85]

Assessment of pain experiences (ie, severity and interference) in the present study primarily explored participants' main region of pain. Therefore, results may not be reflective of all painful regions in participants with multisite pain. The goal of the present analysis was not to infer causality, but to build a conceptual model illustrating possible links between worse pain experiences and potentially modifiable patient factors to inform the next stage of research. Additionally, the cross-sectional design precluded the ability of exploring temporal causality between the study variables.

Despite these limitations, this study contributes to current evidence for the complexity of pain experiences in IBD and identifies potential pathways for targeted treatments. At present, the available treatments for pain in IBD are limited and largely unsuccessful. Current treatments typically reflect peripheral disease targets with less consideration of central mechanisms understood to participate in factors related to fatigue, poor sleep, and catastrophizing thoughts. This research intentionally explored relationships between these potentially modifiable factors to highlight opportunities for new targeted treatment approaches. Given the complexity of our model, is clear that treatment of pain in IBD cannot be "one size fits all." Future research into interventions that address the combined effect of insomnia and pain, including their impact on cognitive processes (eg, catastrophizing, anxiety) may be of particular importance in people with IBD.

The next phase of research should investigate longitudinal relationships identified in the proposed conceptual model, including the use of various experimental assessments to capture different patient constructs, such as actigraphy to measure sleep and physical activity[86] and quantitative sensory testing to examine pain processing pathways.[87] This research should also include clinical assessments and biomarkers to further explore IBD activity domains in study participants. Investigation of temporal relationships would provide a deeper understanding of these factors and opportunities to improve pain experiences in IBD patients.

Conclusion

Pain is well understood to be one of the most bothersome symptoms in patients with IBD. However, managing pain in IBD remains a significant challenge. Results from the current study illustrate a conceptual model highlighting the relationship of potentially modifiable factors to the extent that pain interferes with the daily activities in patients with IBD.

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Authors' Contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by Jessica K. Salwen-Deremer and Corey A. Siegel, analysis was performed by Carrie L. Falling. The first draft of the manuscript was written by Carrie L. Falling and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Data Availability

The data that support the findings of this study are available upon reasonable request from the corresponding author.

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