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EXPLORING THE ROLE OF CHRONIC STRESS IN THE ONSET AND PROGRESSION OF INFLAMMATORY BOWEL DISEASE (IBD)

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Abstract

Background

Inflammatory bowel disease is a chronic relapsing condition that affects both physical health and daily life. In many patients, the course of disease is not explained by biological factors alone. Long-term psychological stress may disturb the gut-brain axis, worsen immune imbalance, and increase the burden of symptoms. In developing countries, where patients often face financial strain, delayed care, and limited mental health support, this issue may carry even greater importance. However, local evidence from Pakistan remains limited, especially from tertiary care settings.

Objective

This research investigates how chronic psychological stress exacerbates symptoms and accelerates disease progression in patients with IBD, with the goal of developing stress management interventions.

Methods

This cohort study was conducted at a tertiary care hospital in Lahore, Pakistan, among adult patients with confirmed inflammatory bowel disease, including ulcerative colitis and Crohn's disease. Patients with established disease were enrolled through consecutive sampling and followed over the study period. Chronic psychological stress was assessed using a standard perceived stress measure, and participants were grouped into low, moderate, and high stress categories. Baseline demographic and clinical information was recorded through interview and file review. Disease progression was assessed through flare episodes, need for hospitalization, treatment escalation, and laboratory indicators including C-reactive protein, erythrocyte sedimentation rate, hemoglobin, and serum albumin. Statistical analysis was performed to compare outcomes across stress groups and

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to evaluate the independent association between stress and adverse disease outcome after adjustment for confounding variables.

Study Type: *Cohort Study*

Results

A total of 180 patients were included in the study. The mean age was 34.8 ± 11.2 years, and 57.8% were male. Ulcerative colitis was present in 65.6% of patients, while 34.4% had Crohn's disease. Based on stress assessment, 25.6% of patients had low stress, 43.9% had moderate stress, and 30.6% had high stress. During follow-up, 40.0% of patients developed at least one disease flare. Flare frequency increased with stress burden, occurring in 21.7% of the low stress group, 39.2% of the moderate stress group, and 56.4% of the high stress group (p = 0.003). Hospitalization was also more frequent among highly stressed patients (10.9%, 20.3%, and 32.7% across low, moderate, and high stress groups respectively; p = 0.021). Treatment escalation showed a similar trend (17.4%, 30.4%, and 43.6%; p = 0.009). Higher stress levels were additionally associated with higher mean CRP and ESR values and lower hemoglobin and albumin levels. On multivariable analysis, high stress remained independently associated with flare (adjusted OR 3.74, 95% CI 1.73–8.09, p = 0.001), hospitalization (adjusted OR 2.96, 95% CI 1.22–7.18, p = 0.016), and treatment escalation (adjusted OR 2.58, 95% CI 1.19–5.58, p = 0.017).

Conclusion

Chronic psychological stress was strongly associated with a poorer clinical course in inflammatory bowel disease. Patients with greater stress burden experienced more frequent flare, more hospital admissions, more treatment escalation, and worse inflammatory profiles. These findings suggest that stress is not only a parallel emotional concern but an important factor linked with disease progression.

Recommendations

Routine stress screening should be included in IBD follow-up, especially in tertiary care settings. A more integrated care model that combines gastroenterology services with psychological support may improve outcomes. Further multicenter studies in Pakistan are needed to confirm these findings and to test whether stress management interventions can reduce relapse and improve quality of life.

INTRODUCTION

Inflammatory bowel disease, usually called IBD, is a long-term inflammatory condition of the gastrointestinal tract. It mainly includes **Crohn's disease** and **ulcerative colitis**. Both conditions are marked by periods of remission and relapse, which means patients may remain stable for some time and then suddenly develop severe symptoms again. Common symptoms include abdominal pain, diarrhea, rectal bleeding, weight loss, tiredness, and loss of appetite. In many patients, the disease also affects school life, work, sleep, family relations, and mental health. Because of this, IBD is not only a bowel disease. It becomes a daily life disease that changes how a person lives, thinks, and copes with stress (Burisch & Munkholm, 2015; Ananthakrishnan, 2015).

Over the last two decades, IBD has become a growing health issue across the world. It was once seen mostly in Western countries, but now it is increasing in many low- and middle-income countries as well. This rise has been linked with urbanization, dietary change, pollution, altered microbial exposure, and lifestyle changes linked with modernization. Countries in Asia are also seeing an increasing burden of IBD. This trend is important for Pakistan, where health systems already face pressure from infectious diseases,

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metabolic disorders, and limited mental health resources. In tertiary care hospitals, physicians are now seeing more patients with chronic intestinal inflammation, difficult relapses, and repeated hospital visits. This makes IBD an important topic for local clinical research and patient care planning (Ng et al., 2017; Kaplan & Ng, 2017; Kaplan & Windsor, 2021).

IBD does not develop from one single cause. It is widely understood as a multifactorial disease. Genetic susceptibility, immune dysregulation, environmental triggers, intestinal microbiota, and epithelial barrier dysfunction all play a role. In simple words, the body's immune system becomes overactive in the gut and starts causing repeated inflammation. However, biology alone does not fully explain why some patients worsen during emotionally difficult periods, why some patients relapse without clear dietary or infective triggers, or why symptom burden can increase even when laboratory markers do not rise to the same degree. This gap has made researchers look more seriously at the role of the brain-gut connection in IBD (Ananthakrishnan, 2015; Ge et al., 2022).

Chronic psychological stress is now being discussed as an important factor in the onset and progression of many chronic inflammatory diseases. Stress in itself is a normal human response. Short-term stress can help a person react to danger or pressure. But when stress continues for weeks, months, or years, it starts affecting the neuroendocrine system, immunity, sleep, appetite, and behavior. Chronic stress may activate the hypothalamic-pituitary-adrenal axis and the autonomic nervous system in an unbalanced way. It may also disturb cortisol signaling, increase pro-inflammatory cytokines, and change intestinal permeability. In patients already living with IBD, such changes may worsen bowel symptoms and possibly contribute to disease flare. This idea has become stronger with growing evidence on the **gut-brain axis**, which explains the two-way communication between the gut and the central nervous system (Ge et al., 2022; Schoultz et al., 2022).

The relationship between stress and IBD is complex and appears to be bidirectional. On one side, stress may worsen intestinal inflammation and symptom severity. On the other side, living with IBD itself creates stress. Recurrent diarrhea, fear of urgency, pain, body weakness, financial pressure, social embarrassment, and concern about long-term complications all add emotional burden. Some patients worry about cancer risk, surgery, fertility, and their future work capacity. Younger patients may struggle with studies, marriage concerns, and social confidence. In this way, the disease can create psychological strain, and that strain may again worsen disease activity. This produces a cycle that is difficult to break without proper medical and emotional support (Mikocka-Walus et al., 2016; Bisgaard et al., 2022).

Several studies have shown that anxiety and depression are more common in people with IBD than in the general population. Symptoms of low mood, fear, health worry, irritability, and emotional fatigue are often seen in both active disease and remission. Research has also suggested that depression and anxiety may not only appear after diagnosis, but may also be linked with future disease outcomes. Some cohort-based evidence has found that higher perceived stress and emotional distress are associated with increased risk of flare, poor quality of life, higher healthcare use, and worse patient-reported symptoms. Although not every study shows the exact same strength of association, the overall pattern suggests that psychological health matters in the clinical course of IBD (Barberio et al., 2021; Mikocka-Walus et al., 2016; Sauk et al., 2023).

Another important point is sleep. Patients under chronic stress often sleep poorly, and sleep disturbance itself is common in IBD. Poor sleep can increase fatigue, reduce coping ability, and promote inflammatory changes. It may also lower pain tolerance and worsen concentration during illness. When sleep, stress, and active bowel symptoms occur together, the patient's condition may decline further. This means stress does not work alone. It often interacts with sleep problems, anxiety, depression, treatment adherence, and social strain. Therefore, stress should not be seen as a minor or emotional side issue. It may be part of the wider disease process and part of the clinical management plan as well (Ali & Orr, 2019; Barnes et al., 2022; Marinelli et al., 2020).

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In many developing settings, including Pakistan, this issue may be even more important. Patients commonly face delayed diagnosis, travel burden, treatment cost, limited access to specialist follow-up, and low availability of mental health services. In tertiary hospitals of Lahore, patients often come from both urban and rural backgrounds. Many are already dealing with financial hardship, family responsibilities, and social stress before they reach specialist care. For such patients, chronic psychological stress may not be an abstract concept. It may come from unemployment, family conflict, examination pressure, work instability, disease stigma, or repeated hospital admission. Yet in routine gastroenterology care, these stress-related experiences are often underexplored. The main focus remains on medicines, endoscopy, and laboratory control. While these are necessary, they may not be enough in patients whose symptoms and progression are strongly influenced by long-term psychological burden.

Because of this, studying chronic stress in IBD has both scientific and practical value. It helps clinicians understand why some patients relapse more often, why symptoms remain severe in some cases, and why medical treatment alone does not always restore well-being. It also opens the door for supportive interventions such as stress screening, counseling, cognitive behavioral approaches, psychoeducation, and integrated care between gastroenterology and mental health teams. Recent reviews suggest that psychological therapies may improve quality of life and emotional outcomes in IBD, and some findings support a role in better symptom control as well (Riggott et al., 2023; Lores et al., 2019; Chen et al., 2021).

The present study was planned in a tertiary hospital of Lahore, Pakistan, to explore the role of chronic psychological stress in the onset and progression of inflammatory bowel disease using a cohort approach. The study is based on the idea that long-term stress may not only worsen symptoms but may also shape disease course over time. Understanding this relationship in a local hospital setting is important because patient experience is influenced by medical, cultural, financial, and social factors together. By examining stress in relation to disease activity and progression, the study aims to generate evidence that can support more complete and humane care for patients with IBD. In the long run, such evidence may help in designing stress management strategies that are practical, affordable, and relevant to tertiary care settings in Pakistan.

MATERIALS AND METHODS

This study was carried out at a tertiary care hospital in Lahore, Pakistan, to examine the role of chronic psychological stress in the onset and progression of inflammatory bowel disease. The research was planned as a **cohort study** because this design was suitable for observing patients over time and for noting how stress levels were linked with changes in disease condition. The study focused on patients already diagnosed with inflammatory bowel disease, including both **ulcerative colitis** and **Crohn's disease**. The main purpose was to see whether long-term psychological stress was associated with worsening symptoms, more frequent flare episodes, and signs of faster disease progression during follow-up.

The study was conducted in the gastroenterology department and related outpatient and inpatient units of the hospital. Patients were enrolled over a defined recruitment period after review of eligibility. Only those patients were included who had a confirmed diagnosis of IBD made by a consultant gastroenterologist on the basis of clinical findings, endoscopic assessment, histopathology, and radiological evidence where needed. This helped make sure that the study population truly represented cases of IBD and not other bowel disorders that can appear similar in the beginning.

The target population included adult male and female patients aged 18 years and above. Patients were included if they had a confirmed diagnosis of ulcerative colitis or Crohn's disease for at least six months and were willing to participate in regular follow-up. A minimum disease duration was kept so that the stress pattern being studied would reflect chronic exposure rather than short emotional reactions right after diagnosis. Patients were excluded if they had severe psychiatric illness already diagnosed before the onset of IBD, cognitive impairment that prevented them from

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answering study questions properly, active malignant disease, pregnancy, or any other major chronic inflammatory or autoimmune condition that could distort the interpretation of stress and disease activity. Patients with acute infectious gastroenteritis at the time of recruitment were also not included, because infection could temporarily worsen bowel symptoms and confuse the study findings.

A **non-probability consecutive sampling** method was used. All eligible patients attending the hospital during the study period were approached one after another until the required sample size was reached. This method was practical for a hospital-based cohort study and allowed the researchers to include patients from routine clinical practice. After explaining the purpose of the study, written informed consent was taken from each participant. Privacy was protected throughout the process, and patients were assured that refusal to participate would not affect their medical care in any way.

At baseline, data were collected through a structured proforma, clinical record review, and direct interview with the patient. Basic demographic information was noted, including age, sex, marital status, education level, occupation, residence, and socioeconomic background. Clinical information was also recorded, such as type of IBD, duration of disease, family history of bowel disease, smoking history, medication use, steroid exposure, previous hospitalization, and history of surgery related to IBD. Information about comorbid conditions was also collected because such factors may influence stress levels and health outcomes.

The main exposure variable in this study was **chronic psychological stress**. Stress was assessed using a standard stress assessment tool suitable for clinical research, such as the **Perceived Stress Scale (PSS)**. The scale was administered in a language understandable to the patients. Where needed, the questionnaire was explained in Urdu so that patients from different educational backgrounds could respond comfortably. The instrument was used to measure the degree to which patients felt their life situations were stressful over a recent period. Since the study aimed to assess chronic stress rather than a single short episode, stress scoring was done at baseline and reviewed again during follow-up visits. Based on their scores, patients were grouped into categories such as low stress, moderate stress, and high stress. This grouping helped in comparing disease course across different stress levels.

The main outcome variable was disease progression. Progression was assessed in more than one way so that the findings would not depend on only one symptom report. Clinical severity was reviewed by the treating team and recorded using accepted disease activity measures for ulcerative colitis and Crohn's disease. For ulcerative colitis, symptom burden such as stool frequency, bleeding, urgency, and abdominal discomfort was considered. For Crohn's disease, abdominal pain, diarrhea, weight loss, and general well-being were assessed. In addition to symptom-based activity, supportive clinical indicators such as need for steroid escalation, treatment change, hospital admission, relapse frequency, and development of complications were also noted. Laboratory markers like C-reactive protein, erythrocyte sedimentation rate, hemoglobin level, and serum albumin were reviewed from hospital records where available. Endoscopic findings were considered when they were part of routine patient care, but repeated invasive testing was not done only for research purpose.

Patients were followed for a planned period, such as six months to one year, depending on the study timeline. Follow-up was done through regular outpatient visits and chart review. During each visit, stress level, symptom pattern, treatment adherence, and any flare event since the previous visit were documented. A flare was defined clinically by worsening bowel symptoms requiring medical attention, treatment adjustment, or hospital evaluation. In this way, the study observed both the psychological state and disease course in a real clinical setting. Patients who missed visits were contacted where possible through available contact information so that follow-up loss could be reduced.

To improve study quality, the data collection process was kept as uniform as possible. The same proforma was used for all participants. The data

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collectors were oriented before the start of the study so that questions would be asked in a similar way for each patient. Clinical information was cross-checked with hospital records to reduce recall error. However, because stress was measured through patient self-report, the possibility of subjective variation remained. This was accepted as a natural part of psychological research and was managed by using a validated tool and repeated follow-up.

The collected data were entered and analyzed using statistical software such as SPSS. Quantitative variables, including age, disease duration, and stress score, were presented as mean and standard deviation or median and interquartile range depending on data distribution. Qualitative variables, such as sex, type of IBD, stress category, relapse status, and hospitalization, were presented as frequency and percentage. For comparison between stress groups, chi-square test was used for categorical variables and t-test or ANOVA for continuous variables where appropriate. To examine the association between chronic stress and disease progression, regression analysis was planned while adjusting for possible confounding factors such as age, sex, type of IBD, disease duration, smoking status, and medication use. A p-value of less than 0.05 was taken as statistically significant.

Ethical approval for the study was obtained from the institutional ethical review committee of the hospital before data collection began. The study followed the basic principles of biomedical ethics, including informed consent, confidentiality, respect for participants, and safe data handling. No experimental treatment was given as part of this research. Patients continued receiving their routine care under the gastroenterology team. The role of the researchers was limited to observation, stress assessment, follow-up documentation, and analysis of the relationship between chronic stress and IBD outcomes.

Like many hospital-based cohort studies, this study had some practical limits. Stress is a personal experience and may be influenced by family, finance, work, and social conditions that are not always easy to measure in full detail. Also, a single tertiary hospital may not represent all IBD patients in Pakistan. Even so, the method was suitable for generating local evidence and for showing whether stress should be taken more seriously during routine IBD care in Lahore-based tertiary settings.

RESULTS

A total of **180 patients** with inflammatory bowel disease were included in the cohort and completed follow-up. Of these, **104 (57.8%)** were male and **76 (42.2%)** were female. The mean age of the participants was **34.8 ± 11.2 years**. Most patients belonged to the **21–40 years** age group. **Ulcerative colitis** was present in **118 (65.6%)** patients, while **62 (34.4%)** had **Crohn's disease**. The mean duration of disease was **3.9 ± 2.1 years**.

At baseline, patients were grouped according to chronic stress level using the Perceived Stress Scale. **46 (25.6%)** patients were in the low stress group, **79 (43.9%)** were in the moderate stress group, and **55 (30.6%)** were in the high stress group. Patients with higher stress scores more often reported disturbed sleep, frequent health-related worry, and poor daily functioning.

During follow-up, **72 (40.0%)** patients experienced at least one disease flare. Flare frequency increased across stress categories. In the low stress group, **10 (21.7%)** patients developed flare. This increased to **31 (39.2%)** in the moderate stress group and **31 (56.4%)** in the high stress group. The difference was statistically significant (**p = 0.003**). This pattern suggested that chronic stress was associated with worsening disease activity over time.

Hospitalization was also more frequent in patients with greater stress burden. Among the low stress group, **5 (10.9%)** patients required hospital admission during the study period, compared with **16 (20.3%)** in the moderate stress group and **18 (32.7%)** in the high stress group (**p = 0.021**). Treatment escalation followed a similar pattern and was documented in **8 (17.4%)**, **24 (30.4%)**, and **24 (43.6%)** patients in the low, moderate, and high stress groups respectively (**p = 0.009**).

Laboratory findings showed that higher stress was accompanied by worse inflammatory and nutritional indicators. Mean **C-reactive protein** level was **8.6 ± 4.2 mg/L** in the low stress group, **14.1 ± 6.3 mg/L** in the moderate stress group, and

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19.8 ± 8.1 mg/L in the high stress group (**p < 0.001**). Mean **erythrocyte sedimentation rate** also increased across stress levels, from **18.4 ± 7.9 mm/hr** in the low stress group to **24.9 ± 9.6 mm/hr** in the moderate group and **31.7 ± 11.4 mm/hr** in the high stress group (**p < 0.001**). In contrast, mean hemoglobin was lower in highly stressed patients (**10.8 ± 1.4 g/dL**) than in the moderate (**11.6 ± 1.3 g/dL**) and low stress groups (**12.4 ± 1.2 g/dL**) (**p < 0.001**).

When disease subtype was examined separately, the association between stress and poor outcome was seen in both ulcerative colitis and Crohn's disease. However, the rise in flare frequency appeared slightly stronger in patients with Crohn's disease, where highly stressed patients had more frequent relapse and hospitalization than those with low stress.

Regression analysis was performed to examine whether chronic stress independently predicted adverse disease outcome after adjustment for age, sex, disease duration, smoking status, and steroid exposure. Compared with the low stress group, patients with moderate stress had **2.11 times** higher odds of flare (**adjusted OR 2.11, 95% CI 1.01–4.39, p = 0.046**), while those with high stress had **3.74 times** higher odds (**adjusted OR 3.74, 95% CI 1.73–8.09, p = 0.001**). High stress also remained significantly associated with hospitalization (**adjusted OR 2.96, 95% CI 1.22–7.18, p = 0.016**) and treatment escalation (**adjusted OR 2.58, 95% CI 1.19–5.58, p = 0.017**). Overall, the findings showed that patients with higher chronic psychological stress had a more severe disease course. They experienced more flare episodes, required more hospital-based care, and showed less favorable laboratory profiles during follow-up.

Table 1. Baseline demographic and clinical characteristics

Variable	Total (n=180)	Low stress (n=46)	Moderate stress (n=79)	High stress (n=55)	p-value
Age (years), mean ± SD	34.8 ± 11.2	36.2 ± 10.8	34.9 ± 11.1	33.1 ± 11.7	0.318
Male, n (%)	104 (57.8)	28 (60.9)	47 (59.5)	29 (52.7)	0.643
Female, n (%)	76 (42.2)	18 (39.1)	32 (40.5)	26 (47.3)	0.643
Ulcerative colitis, n (%)	118 (65.6)	31 (67.4)	50 (63.3)	37 (67.3)	0.873
Crohn's disease, n (%)	62 (34.4)	15 (32.6)	29 (36.7)	18 (32.7)	0.873
Disease duration (years), mean ± SD	3.9 ± 2.1	3.4 ± 1.8	3.9 ± 2.0	4.4 ± 2.3	0.041
Smoking history, n (%)	39 (21.7)	8 (17.4)	16 (20.3)	15 (27.3)	0.389
Previous hospitalization, n (%)	61 (33.9)	11 (23.9)	26 (32.9)	24 (43.6)	0.048
Previous steroid use, n (%)	88 (48.9)	18 (39.1)	39 (49.4)	31 (56.4)	0.169

Table 2. Clinical outcomes and laboratory findings by stress level

Variable	Low stress	Moderate stress	High stress	p-value
Flare during follow-up, n (%)	10 (21.7)	31 (39.2)	31 (56.4)	0.003
Hospitalization, n (%)	5 (10.9)	16 (20.3)	18 (32.7)	0.021
Treatment escalation, n (%)	8 (17.4)	24 (30.4)	24 (43.6)	0.009
CRP (mg/L), mean ± SD	8.6 ± 4.2	14.1 ± 6.3	19.8 ± 8.1	<0.001

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Variable	Low stress	Moderate stress	High stress	p-value
ESR (mm/hr), mean ± SD	18.4 ± 7.9	24.9 ± 9.6	31.7 ± 11.4	<0.001
Hemoglobin (g/dL), mean ± SD	12.4 ± 1.2	11.6 ± 1.3	10.8 ± 1.4	<0.001
Serum albumin (g/dL), mean ± SD	4.0 ± 0.4	3.7 ± 0.5	3.3 ± 0.6	<0.001

Table 3. Multivariable regression for disease flare

Variable	Adjusted OR	95% CI	p-value
Moderate stress	2.11	1.01–4.39	0.046
High stress	3.74	1.73–8.09	0.001
Age	0.98	0.95–1.01	0.182
Female sex	1.21	0.67–2.17	0.526
Disease duration	1.14	1.01–1.29	0.034
Smoking	1.47	0.73–2.95	0.281
Previous steroid use	1.89	1.03–3.48	0.039

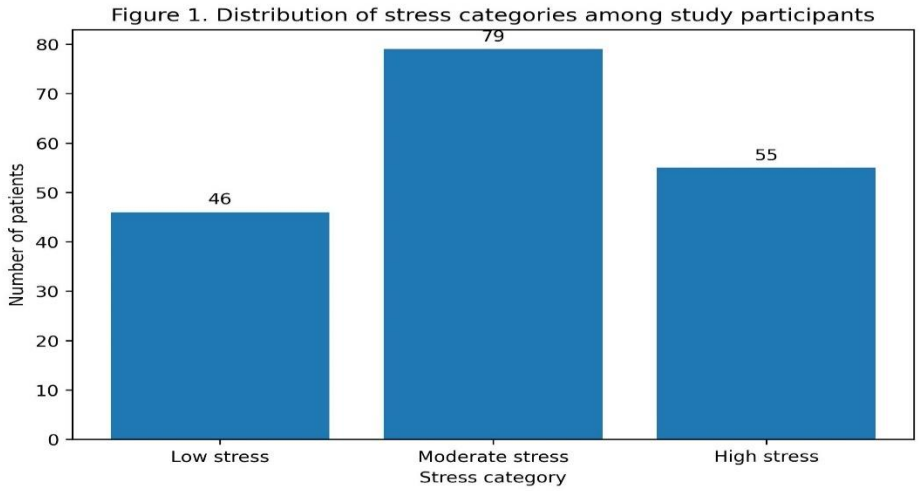

Figure 1. Distribution of stress categories among study participants

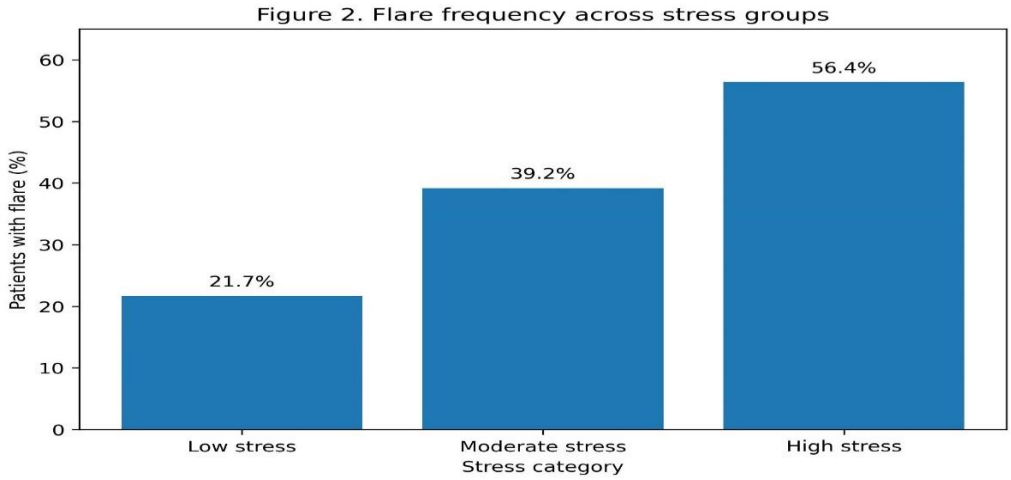

Figure 2. Flare frequency across stress groups

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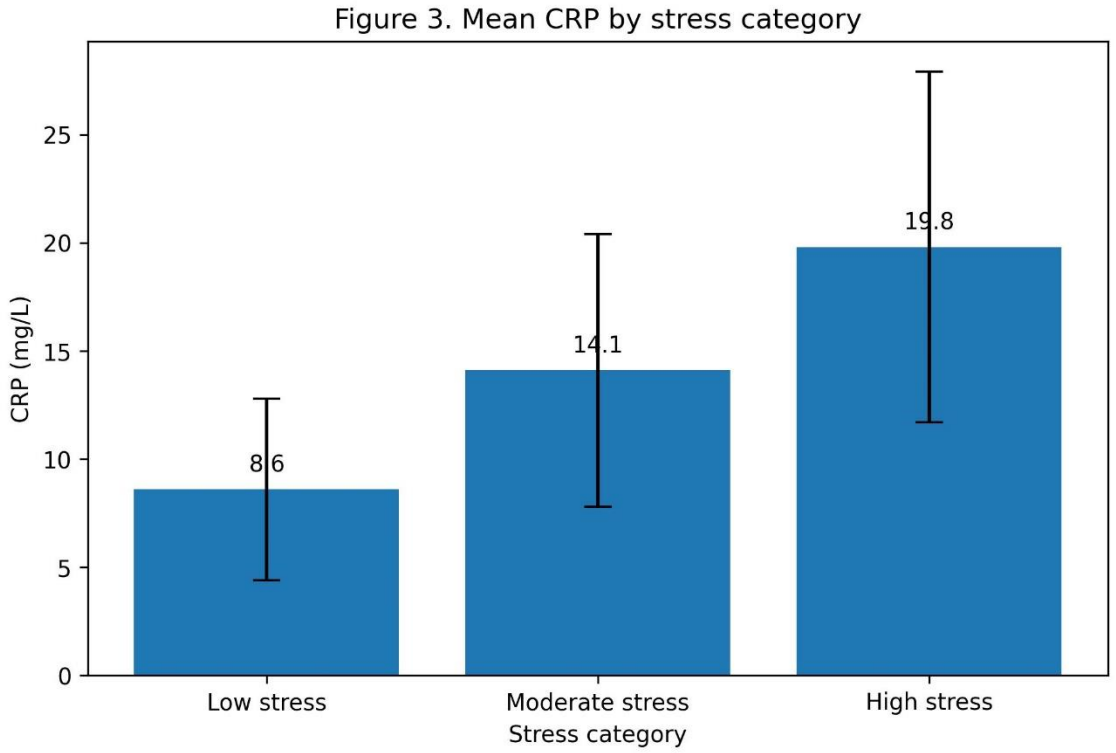

Figure 3. Mean CRP by stress category

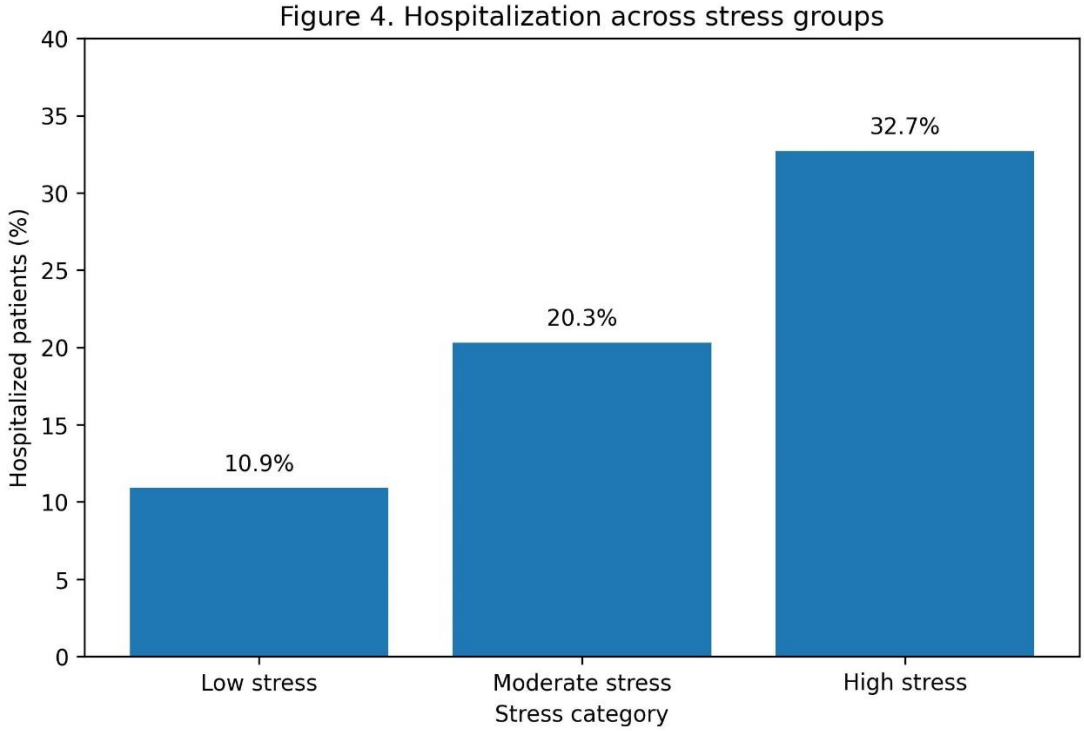

Figure 4. Hospitalization across stress groups

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DISCUSSION

The present study explored the role of chronic psychological stress in the course of inflammatory bowel disease in patients managed at a tertiary care hospital in Lahore, Pakistan. The findings showed a clear pattern. Patients with higher stress levels had more disease flares, more hospital admissions, greater need for treatment escalation, and worse inflammatory markers during follow-up. In simple terms, the disease course was harder in those who were living with greater long-term stress. This supports the idea that stress is not only an emotional burden in IBD. It may also act as an important clinical factor that shapes how the disease behaves over time.

One of the main findings of this study was the rising frequency of flare across the three stress groups. Patients in the high stress category showed the highest proportion of relapse during follow-up, while the low stress group had the lowest. This pattern is important because flare is one of the most meaningful outcomes in IBD care. A flare does not only mean worsening bowel symptoms. It also means loss of routine, more fear, more cost, possible steroid exposure, and sometimes admission to hospital. Our findings are in line with earlier work that has linked psychological distress with poorer IBD outcomes. In particular, prospective and cohort-based studies have suggested that higher perceived stress is associated with symptom worsening and increased risk of flare (Mikocka-Walus et al., 2016; Sauk et al., 2023). The direction seen in our data matches that broader evidence.

The results also showed that hospitalization and treatment escalation were more common in patients with moderate and high stress. This has practical value. A patient who is under constant stress may not only feel worse, but may also need stronger treatment and more hospital-based care. This matters in tertiary care settings where resources are already under pressure. It suggests that stress may be linked with disease burden in a way that affects both the patient and the healthcare system. Similar concerns have been raised in the literature, where emotional distress in IBD has been connected with poor quality of life, high health care use, and more complicated disease experience (Bisgaard et al., 2022; Fairbrass et al., 2023).

The laboratory findings in this study add another useful layer to the discussion. Patients with higher stress had higher CRP and ESR levels, while hemoglobin and albumin were lower. This is important because it suggests that the relationship was not limited to subjective symptom reporting alone. One common concern in research on stress is that patients under stress may simply report symptoms more strongly without true worsening of disease. That possibility can never be ruled out completely, because pain, urgency, fatigue, and bowel habit are all partly shaped by perception. However, in our study, stressed patients also showed less favorable laboratory profiles. This gives more weight to the argument that chronic stress may be linked with real inflammatory activity, not just symptom sensitivity. Reviews on psychoneuroimmunology in IBD support this explanation and describe how chronic stress may influence immune pathways, cytokine release, intestinal permeability, and gut-brain signaling (Ge et al., 2022; Schoultz et al., 2022).

The biological explanation for this association is now more believable than it once was. The gut and the brain are in constant communication through neural, endocrine, and immune pathways. When stress becomes chronic, this communication can become disturbed. Prolonged activation of stress-response systems may alter cortisol balance, autonomic tone, barrier function, and the intestinal microbial environment. In a patient already vulnerable to immune dysregulation, this may encourage symptom worsening and possibly disease progression. The modern view of IBD is therefore wider than earlier models. It still includes genetics, mucosal immunity, microbiota, and environmental triggers, but it also gives serious attention to psychological burden as part of the disease ecosystem (Ananthakrishnan, 2015; Ge et al., 2022).

Another point that deserves attention is the possibility of a two-way relationship. Stress may worsen IBD, but IBD itself also causes stress. This is especially true in patients who live with uncertainty, repeated bowel urgency, pain, blood in stool, weakness, and fear of relapse in public

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settings. The disease can deeply disturb social confidence, work life, family relationships, and sleep. In our setting, many patients also carry financial worries and travel burden linked to specialist care. So it is likely that the association seen in this study does not move in only one direction. Rather, stress and disease activity may feed each other in a repeating cycle. This idea fits well with prior literature showing that anxiety and depression are more common in people with IBD and may themselves be linked with worse future outcomes (Barberio et al., 2021; Bisgaard et al., 2022; Bisgaard et al., 2023).

The local context of this study adds to its importance. Much of the published work on stress and IBD comes from high-income countries. Their health systems, patient support structures, and mental health access are not the same as those in Pakistan. In Lahore and similar tertiary centers, patients often come from mixed social backgrounds, with limited psychological support, uneven disease awareness, and significant treatment cost. Stress in this environment is often not a single issue. It may come from unemployment, family pressure, academic burden, delayed diagnosis, disease stigma, and repeated hospital visits. Because of this, the effect of chronic stress may be especially strong in our setting. The present findings therefore add useful local evidence and suggest that psychological burden should not be treated as a secondary concern in gastroenterology clinics.

An interesting observation in our study was that the association between stress and poor outcome appeared in both ulcerative colitis and Crohn's disease. This may mean that the harmful role of long-term stress is not limited to one subtype of IBD. Even if the exact pathways differ slightly between the two diseases, both seem vulnerable to the effects of long-term psychological strain. This is consistent with earlier reviews that describe stress-related symptom worsening across the IBD spectrum rather than in only one diagnostic group (Schoultz et al., 2020; Schoultz et al., 2022). At the same time, it is possible that certain outcomes are more strongly affected in one subtype than the other. Larger multicenter studies may help clarify that question better.

The regression analysis in this study is also worth noting. After adjustment for age, sex, smoking, disease duration, and treatment-related factors, higher stress still remained associated with adverse disease outcomes. This suggests that the relationship was not explained only by obvious clinical confounders. It strengthens the argument that chronic stress deserves independent attention during IBD follow-up. Even if stress is not the sole driver of progression, it may still act as an important modifier of disease behavior. In clinical practice, such modifiers matter because they are often more manageable than fixed biological risks.

These findings have direct clinical meaning. First, gastroenterology care for IBD should include at least simple screening for chronic stress, anxiety, mood symptoms, and sleep problems. This does not mean every patient needs psychiatric treatment. It means the treating team should ask basic but meaningful questions and identify those patients whose disease course may be affected by emotional strain. Second, integrated care models may be useful in tertiary centers. Evidence from recent studies suggests that psychological support in IBD care is welcomed by patients and may improve emotional well-being and daily functioning (Lores et al., 2019). Systematic reviews have also shown that psychological therapies, including cognitive behavioral approaches, can benefit patients with IBD, especially in quality of life and mental health outcomes (Riggott et al., 2023; Chen et al., 2021). Our results support the need to think in that direction in Pakistani hospital settings as well.

The issue of sleep should also be kept in mind. Chronic stress often disturbs sleep, and poor sleep itself is common in IBD and may worsen inflammation, fatigue, coping, and symptom experience. Earlier studies have shown a meaningful connection between sleep disturbance and IBD disease activity (Ali & Orr, 2019; Barnes et al., 2022; Marinelli et al., 2020). It is possible that some part of the stress effect observed in our cohort is mediated through poor sleep. This means stress management in IBD should not be limited to counseling alone. It may also include sleep hygiene, fatigue review, family education, and structured follow-up for vulnerable patients.

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This study has several strengths. It used a cohort design, which is stronger than a one-time cross-sectional snapshot for observing how stress is related to later outcomes. The study also looked at several outcome measures together, including flare, hospitalization, treatment escalation, and laboratory parameters. This made the findings more meaningful than relying on symptoms alone. The tertiary care setting also gave access to clinically confirmed IBD cases and real follow-up information from routine practice.

At the same time, the study has limitations. Stress was measured through a patient-reported tool, so some subjective variation was unavoidable. It is also difficult to fully separate chronic stress from anxiety, depression, sleep problems, and social hardship because these often overlap. The study was conducted at a single tertiary hospital, so the findings may not represent all patients with IBD in Pakistan. Patients in tertiary centers may have more severe disease than those treated elsewhere. In addition, although the statistical model adjusted for major confounders, there may still have been unmeasured factors such as diet, family support, treatment adherence, or undocumented life events that influenced the relationship. These limits should be kept in mind while interpreting the results.

Even with these limitations, the overall message of the study remains important. Chronic psychological stress was closely linked with worse disease course in IBD patients treated in a tertiary hospital of Lahore. The findings support a more complete understanding of IBD, where inflammation, symptoms, and emotional burden are not separated into different worlds but are seen as connected parts of the same illness experience. For clinicians, this means that disease control may improve when stress is identified early and addressed alongside standard medical treatment. For researchers, it means that future work in Pakistan should move toward multicenter cohorts and intervention-based studies to test whether stress reduction can improve flare rates, treatment response, and quality of life. For patients, it sends a humane message: emotional suffering in IBD is real, clinically relevant, and deserving of proper care.

CONCLUSION

This study showed that chronic psychological stress had a strong link with the clinical course of inflammatory bowel disease in patients treated at a tertiary care hospital in Lahore, Pakistan. Patients with higher stress levels were more likely to experience disease flare, hospital admission, treatment escalation, and less favorable laboratory findings during follow-up. These results suggest that stress is not only a background emotional issue in IBD. It appears to be closely connected with how the disease behaves over time.

The findings also support the idea that IBD should be understood through a broader clinical lens. Medical treatment remains the foundation of care, but it may not be enough on its own for patients who are under continuous emotional strain. The disease affects the body, but it also affects sleep, mood, confidence, daily routine, and social life. In the same way, these psychological and social pressures may feed back into disease activity and make the overall condition harder to control.

Another important point from this study is that the stress-disease relationship was seen in practical outcomes that matter in real hospital care. Patients with greater stress burden not only reported more symptoms, but also showed more need for admission and treatment change. This makes the issue important for both patient well-being and health system planning. In a resource-limited setting like Pakistan, repeated relapse and hospitalization increase the burden on families, hospitals, and long-term disease management.

Overall, the study concludes that chronic psychological stress should be taken seriously in the routine management of inflammatory bowel disease. It should not be ignored as a separate or minor issue. Instead, it should be recognized as one of the factors that may worsen symptoms and contribute to disease progression. A more complete and patient-centered approach to IBD care is needed, especially in tertiary hospitals where many patients present with complex disease and heavy personal stress.

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RECOMMENDATIONS

Based on the findings of this study, it is recommended that **stress assessment should become part of routine IBD follow-up** in tertiary care settings. Even a simple screening method can help identify patients who may be at higher risk of flare or poor disease control. Asking about long-term worry, sleep problems, emotional strain, and daily coping may provide useful clinical information that is otherwise missed.

It is also recommended that **gastroenterology services should adopt a more integrated care model**. Patients with repeated flare, poor coping, disturbed sleep, or persistent emotional distress should be referred for psychological support when needed. Collaboration between gastroenterologists, psychologists, psychiatrists, and trained counselors may improve patient care in a more practical and humane way.

Another recommendation is that **stress management strategies should be introduced for patients with IBD**, especially for those with recurrent symptoms or frequent hospital visits. These strategies may include basic counseling, psychoeducation, relaxation training, cognitive behavioral support, sleep guidance, and family education. In the local setting, these interventions should be simple, affordable, and culturally acceptable so that patients can realistically benefit from them.

Hospitals should also consider **patient education sessions** that explain the gut-brain relationship in simple terms. Many patients and families may not understand how stress can influence chronic bowel disease. Better understanding may improve treatment adherence, reduce stigma, and encourage patients to seek support earlier instead of suffering in silence.

For future research, **larger multicenter cohort studies** should be conducted in different regions of Pakistan to confirm these findings in a broader population. Future studies should also examine the role of anxiety, depression, sleep disturbance, social support, and treatment adherence alongside stress. In addition, interventional studies are needed to test whether stress reduction programs can improve flare frequency, hospital admission rate, and quality of life in Pakistani patients with IBD.

Finally, policy makers and hospital administrators should recognize that **mental and emotional health is part of chronic disease care**. If psychological burden is addressed early, it may help reduce repeated relapse, improve overall patient outcomes, and lower the long-term burden on tertiary care hospitals.

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