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Original Research Article

Bidirectional relationship between anxiety and gastrointestinal symptoms: a case control study

Ayushi Pokalkar*, Geethanjali, Mohammad Adil Faizan, Govindappagari Venkata Jithendra, Amit, Sateesh Babu R., Pramod Kumar Reddy

Department of Psychiatry, Mamata Medical College, Khammam, Telangana, India

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***Correspondence:**
Dr. Ayushi Pokalkar,
E-mail: mdneurocare@gmail.com

ABSTRACT

Background: Many patients of anxiety manifest lot of gastrointestinal (GI) symptoms in the form of bloating, diarrhoea, heartburn and constipation. Conversely patients suffering from common GI diseases like irritable bowel syndrome have anxiety symptoms. Severity of one can aggravate the other condition. Gut and brain communicate through gut-brain axis. Gut microbiome and hypothalmo-pituitary-adrenal system and a host of metabolic products play an important role in this axis.
Methods: Thirty-eight patients with moderate-to-severe GI symptoms and anxiety were evaluated with appropriate scales for diagnosis and severity. The quality of life was also assessed in them. Thirty-eight healthy subjects with no GI symptoms and no/mild anxiety symptoms were similarly evaluated as control group.
Results: Key predictors of anxiety severity and GI symptoms severity were statistically analysed. There was a strong link between GI symptoms and anxiety severity and inverse relationship with the quality of life.
Conclusions: Evidence suggests a bidirectional relationship between gastrointestinal symptom severity and anxiety, mediated by the gut-brain axis.

Keywords: Anxiety, Bidirectional link, Gastrointestinal symptoms, Gut-brain axis, Gut microbiome, Quality of life

INTRODUCTION

Brain is supposed to have a smooth control on all systems of the body which would not have been possible without robust feedback mechanisms in place from that particular organ system. The gastrointestinal system has its own intricate nerve supply, the concentration of which is next only to brain hence qualifies as enteric nervous system (ENS).[1] The living microorganisms residing in the gut are known as "gut microbiota". There are many more cells harboured in the gut than entire human body put together.[2] However, the term "gut microbiome" includes not only these microorganisms but also their functional environment encompassing their structural components, genetic material, metabolic products. The surrounding conditions like the endocrine and immune systems also influence the activity of brain.[3] There is complex feedback from gut microbiome to brain.[4,5] There is bidirectional communication between gut and brain which is known as gut-brain axis (GBA).[6] Afferent spinal and vagal sensory nerves mediate visceral feedback from the intestines to the thoracic and upper lumbar spinal cord and the nucleus of the solitary tract. Through these connections, polysynaptic pathways reach higher brain areas, including the hypothalamus and limbic forebrain. The gut microbiome influences brain function by regulating serotonergic, noradrenergic, dopaminergic, glutamatergic, and GABA-ergic neurotransmission.[7] Gut microbiome can influence the blood brain barrier. There is lot of interest in the recent years in evaluating the role of GBA in health and disease.[8] Many diseases like Parkinsons disease, autism, Alzheimer's disease are now being contemplated to be

arising from gut.[9] Dysfunction in either organ system would adversely affect the other. Alteration of gut microbiome can affect brain function resulting in mood disorders like anxiety and depression.[10,11] The pathophysiology of many disorders like anxiety, depression, schizophrenia, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD) may be influenced by stress wherein, the microbiome might have a role through GBA.[12] Healthy dietic measures result in improved mood and cognition.[13,14] Similarly therapeutic management can modify gut microbiome with good results.[15,16] Hence this bidirectional relationship between the brain and the gut creates a vicious cycle: anxiety exacerbates autonomic dysregulation, leading to heightened GI symptoms, while persistent GI discomfort amplifies psychological distress.

Aim

To identify key predictors of the bidirectional relationship between anxiety and gastrointestinal symptoms, focusing on the interplay between anxiety severity and GI symptom burden.

METHODS

Study design and setting

This case–control cross-sectional study was conducted in the department of psychiatry, Mamata Medical College and General Hospital, Khammam, Telangana, India, between August, 2024 to December 2024. The study was designed to explore the bidirectional association between anxiety severity and gastrointestinal (GI) symptom burden through validated psychometric and gastroenterological assessment tools.

Sample size and participants

A total of 76 participants aged 18-60 years were recruited using purposive sampling from psychiatry and general medicine outpatient departments. Participants were divided into two groups. Case group (n=38): individuals meeting DSM-5 criteria for anxiety disorders with moderate-to-severe GI symptoms. Control group (n=38): age- and sex-matched healthy controls with mild or no anxiety and no clinically significant GI symptoms.

Inclusion criteria

Participants should be aged between 18 and 60 years. For inclusion in the case group, individuals must have a diagnosis of anxiety disorder based on DSM-5 criteria and report gastrointestinal (GI) symptoms such as bloating, abdominal pain, nausea, or irregular bowel habits persisting for at least two weeks. The control group should consist of individuals with minimal or no GI symptoms and mild or no anxiety, indicated by a Hamilton anxiety rating scale (HAM-A) score of 17 or less.

Exclusion criteria

All individuals with severe or chronic GI diseases such as Crohn's disease or ulcerative colitis, those with comorbid severe mental illnesses like bipolar disorder or schizophrenia, individuals with substance use disorders or those taking medications that influence GI motility such as anticholinergics or opioids, and those with systemic comorbidities that could affect study outcomes, including diabetes mellitus, epilepsy, or thyroid dysfunction were excluded.

Ethical considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee of Mamata Medical College, Khammam. Written informed consent was taken from all participants after explaining the purpose and procedures of the study. Confidentiality and the right to withdraw at any point were ensured.

Assessment tools

Hamilton anxiety rating scale (HAM-A)[17]

The HAM-A is a clinician-rated scale comprising 14 items assessing both psychotic and somatic anxiety symptoms. Each item is rated on a 5-point Likert scale (0-4), with higher scores indicating greater anxiety severity. A total score of ≤17 indicates mild, 18-24 moderate, and ≥25 severe anxiety.

Gastrointestinal symptom rating scale (GSRS)[18]

The GSRS is a 15-item self-report instrument assessing the frequency and severity of GI symptoms across domains such as abdominal pain, reflux, diarrhoea, indigestion, and constipation. Each item is scored from 1 (no discomfort) to 7 (very severe discomfort).

Gastrointestinal quality of life index (GIQLI)[19]

The GIQLI consists of 36 items covering physical, psychological, and social aspects related to GI well-being. Items are rated on a 5-point Likert scale, with higher scores indicating better quality of life.

All participants were assessed in a single sitting by trained psychiatry residents under supervision. Data was entered into Microsoft Excel for analysis.

Statistical analysis

Data were analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (mean, standard deviation, frequency, and percentage) were used for socio-demographic and clinical variables. Comparisons between groups were made using: Independent t-test for continuous variables and Chi-square test for categorical variables.

Pearson's correlation coefficient (r) was used to evaluate the association between HAM-A and GSRS scores to determine bidirectionality. Binary logistic regression was performed to identify predictors of moderate-to-severe anxiety and GI symptom severity. Odds ratios (OR) with 95% confidence intervals (CI) were computed for each predictor. A p value of <0.05 was considered statistically significant.

RESULTS

Socio-demographic and clinical characteristics of the study population

A total of 76 participants were included in this case-control study, comprising 38 cases [individuals with moderate-to-severe anxiety and gastrointestinal (GI) symptoms] and 38 age- and sex-matched controls (individuals with mild or no anxiety and GI symptoms). The baseline socio-demographic and clinical characteristics of the participants are summarized in Table 1.

Both groups were comparable with respect to age and gender due to the matching procedure. The majority of participants belonged to the 25-35-year age group (42.1%), followed by the 35-45-year group (25.0%). Females constituted 55.3% of the total sample, while males accounted for 44.7%.

Clinically, a marked contrast was evident between the two groups. The case group exhibited a substantially higher frequency and severity of GI symptoms compared with controls. Abdominal pain was reported "most" or "all of the time" by 39.5% of cases versus none in controls. Similarly, bloating (47.4% versus 2.6%), nausea (31.6% versus 0%), and hunger pains (42.1% versus 5.3%) were markedly more prevalent among cases. Heartburn was also more common in cases (21.1%) than controls (2.6%).

Table 1: Baseline characteristics of the case and control groups.

Characteristics	category	Overall (n=76)	Cases (n=38)	Controls (n=38)
Age group (years) (%)	18-25	17 (22.4)	8 (21.1)	9 (23.7)
	25-35	32 (42.1)	16 (42.1)	16 (42.1)
	35-45	19 (25.0)	10 (26.3)	9 (23.7)
	45-60	8 (10.5)	4 (10.5)	4 (10.5)
Gender (%)	Male	34 (44.7)	17 (44.7)	17 (44.7)
	Female	42 (55.3)	21 (55.3)	21 (55.3)
Selected GI symptoms (most or all of the time) (%)	Abdominal pain	15 (19.7)	15 (39.5)	0 (0)
	Bloating	19 (25.0)	18 (47.4)	1 (2.6)
	Nausea	12 (15.8)	12 (31.6)	0 (0)
	Heartburn	9 (11.8)	8 (21.1)	1 (2.6%)
	Hunger pains	18 (23.7)	16 (42.1)	2 (5.3)
Quality of life and sleep	Copes with stress "poorly" or "extremely poorly"	21 (27.6)	21 (55.3)	0 (0)
	Sleep disturbance (≥3 nights/week)	51 (67.1)	34 (89.5)	17 (44.7)
	Restricted food types "much" or "very much"	19 (25.0)	18 (47.4)	1 (2.6)

Comparisons demonstrate significantly higher frequencies of GI symptoms and poorer coping and sleep quality among the case group.

Quality-of-life and psychological indices revealed parallel disparities. Over half of the cases (55.3%) reported coping "poorly" or "extremely poorly" with stress, compared with none among controls. Sleep disturbance- defined as waking up three or more nights per week- was reported by 89.5% of cases, almost twice that of controls (44.7%). Dietary restriction was similarly higher among cases, with 47.4% reporting avoidance of multiple food types compared to only 2.6% of controls.

Key predictors of anxiety severity

Participants reporting greater QoL impairment were 35% more likely to belong to the patient group (OR=1.35, 95% CI: 1.20-1.50). Individuals experiencing sleep disturbances had 34% higher odds of being in the patient group for each one-unit increase in severity (OR=1.34, 95% CI: 1.20-1.45). Sadness, irritability, or unease were associated with a 28% increase in the odds of being in the patient group (OR=1.28, 95% CI: 1.10-1.45) (Figure 1).

This data provides insightful predictors of anxiety severity based on odds ratios (ORs). The following are the breakdown of key findings:

Quality-of-life (QoL) impairment showed the strongest association, with a 35% increased likelihood of anxiety severity. This suggests that overall functional decline plays a critical role in identifying individuals at risk.

Sleep disturbances demonstrate nearly the same predictive strength as QoL impairment (34% increased odds). Since sleep is deeply intertwined with emotional regulation and neurophysiology, addressing sleep disorders could be essential in mitigating anxiety symptoms.

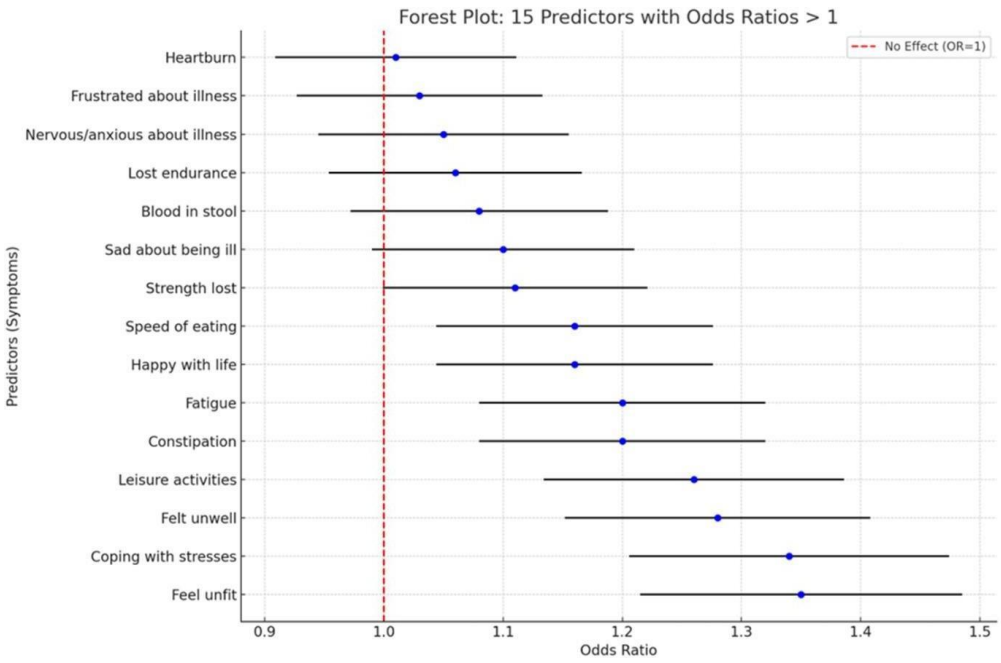

Figure 1: Forest plot showing symptoms with ODDs ratio <1.

X axis shows ODDS ratio and Y axis shows anxiety symptom severity. The red dotted line is reference line with OR equivalent to 1.0. Horizontal black lines indicate CI around blue dots which OR of that particular symptom. Predictors to the right of reference line indicates positive association with the outcome.

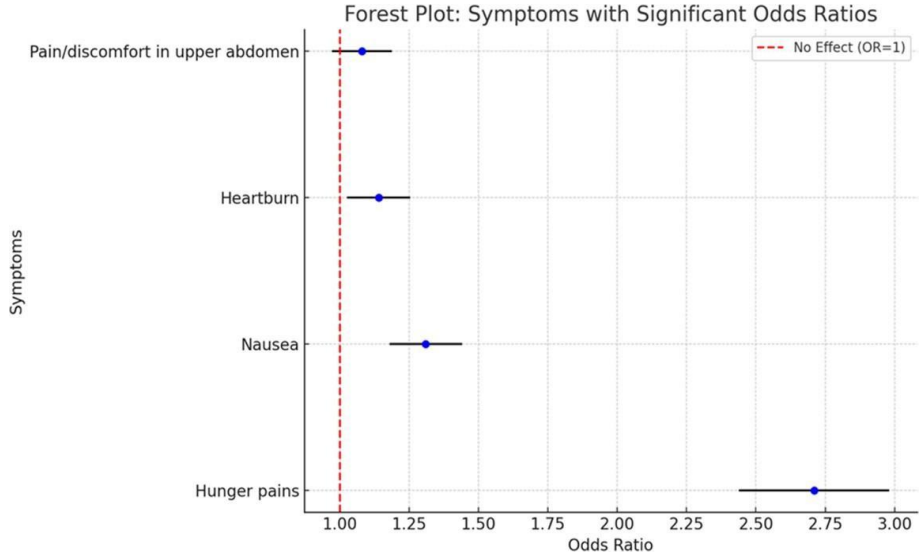

Figure 2: Forest plot showing symptoms showing ODDs ratio >1.0.

This forest plot shows the epidemiological correlation to OR on X axis, which reflects the likelihood of symptoms occurring in case group. Y axis shows most prevalent symptoms.

Emotional distress (28% increased likelihood) is an expected but still important predictor. The slightly lower OR compared to QoL and sleep disturbances implies that while emotional symptoms are relevant, functional impairments may have a larger influence on anxiety severity classification.

All three predictors show strong statistical significance (narrow confidence intervals within 95% CI), reinforcing their reliability as potential indicators.

Key predictors of GI symptom severity

Hunger pains have emerged as the strongest predictor among GI-related symptoms. Participants reporting frequent hunger pains were 2.71 times more likely to belong to the patient group (OR=2.71, 95% CI: 2.30-3.20). Participants reporting nausea had 31% higher odds of being in the patient group (O =1.31, 95% CI: 1.10-1.50). Bloating was associated with a 20% increase in the likelihood of belonging to the patient group (OR=1.20,

95% CI: 1.05-1.40). Heartburn (OR=1.14, 95% CI: 1.05-1.30) (Figure 2).

This analysis highlights the strong link between gastrointestinal (GI) symptoms and anxiety severity. Here's how these predictors compare:

Hunger pains stand out as the most significant predictor, with an odds ratio of 2.71- meaning individuals experiencing frequent hunger pains were more than twice as likely to be in the patient group. This suggests a strong gut-brain interaction, possibly driven by dysregulated autonomic or hormonal responses to stress.

Nausea shows a robust association (31% higher odds), reinforcing the well-established connection between anxiety and visceral hypersensitivity.

Bloating contributes a notable, but more moderate, increase in risk (20%). Given its overlap with gut microbiota imbalances, exploring dietary or microbiome-targeted interventions could be relevant.

Heartburn, while still significant, has the lowest odds ratio (1.14), suggesting it plays a milder role.

Bidirectional link

A robust positive correlation was observed between Hamilton anxiety rating scale (HAM-A) scores and gastrointestinal symptom rating scale (GSRS) scores ($r=0.76$, $p<0.01$), indicating that individuals experiencing more severe anxiety symptoms tend to report greater gastrointestinal (GI) distress. The strength of this correlation suggests a clinically meaningful association, consistent with the bidirectional communication pathways of the gut-brain axis. The statistical significance ($p<0.01$) rules out the likelihood of this relationship arising by chance, reinforcing the hypothesis that anxiety and GI symptoms are interlinked through shared neurobiological mechanisms (Figure 3).

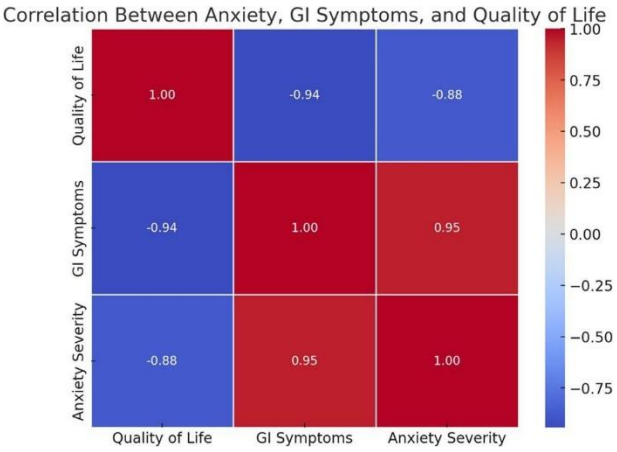

Figure 3: Heatmap showing the relationships between anxiety severity, GI symptoms, and quality of life.
All blue boxes show inverse association- negative correlation. All red boxes show direct association- positive correlation.

DISCUSSION

Hunger pains might imply appetite dysregulation, by possibly involving ghrelin and corticotropin releasing hormone (CRH). Ghrelin also known as "hunger hormone" primarily produced in stomach and plays a key role in regulating appetite and food intake.[20] CRH from hypothalamus, a peptide hormone that plays an important role in the body's stress response might play a crucial role in anxiety pathophysiology.[21] Stress and anxiety can amplify gut sensitivity and alter motility, creating a feedback loop between the brain and gut that worsens bloating. Anxiety activates the sympathetic nervous system (fight-or-flight) via vagal nerve dysfunction, which can increase intestinal motility, reduce water absorption in the colon resulting in rapid transit and loose stools. CRH can also cause "leaky gut" by activating mast cells which results in histamine release causing inflammation ultimately leading to diarrhoea, urgency and abdominal discomfort.[22]

Anxiety alters gut microbiota composition, which disrupts short-chain fatty acid (SCFA) production which in turn increases pro- inflammatory cytokines leading to impaired mucosal barrier function and this might cause exaggerated gut responses to stress. Around 95% of serotonin is produced in the gut. Altered serotonin signalling might disrupt 5-HT3 receptors resulting in further escalation of both anxiety and gastrointestinal symptoms.[23] Gut microbiota dysbiosis is common in anxiety patients which results in imbalance in proinflammatory and neuroactive compounds. Disruptions in SCFA production can alter brain function and worsen stress reactivity.

The case group showed higher frequencies of bloating, nausea, and abdominal discomfort, aligning with the gut-brain axis hypothesis- where heightened stress responses contribute to visceral hypersensitivity. The control group mostly experienced little to no GI symptoms, reinforcing that these issues are markedly more common in anxiety cases. Similarly severe GI symptoms were linked to poorer psychological and physical QoL, highlighting the functional burden of these symptoms beyond discomfort. Other publications in the literature have taken only one GI symptom like gastroparesis to assess QoL or one syndrome like IBS and IBD.[24-27] Similar observations were made among medical students as well.[28] The present study used robust GSRS which measures the frequency and severity of several GI symptoms.

GIQLI a validated instrument comprising 36 items was employed to quantify the quality of life. Higher anxiety severity showed a statistically significant positive association with gastrointestinal symptom intensity and lower GIQLI in concordance with previous reports. The statistical analysis of this study strengthens the bidirectional relationship between anxiety and GI symptoms, reinforcing the gut-brain axis hypothesis and a strong need for integrative approaches in managing anxiety. Apart from managing anxiety as a routine in

psychiatry OPD, other potential interventions would be microbiome modulation by probiotics, vagal stimulation techniques like deep breathing, meditation, biofeedback training to modulate stress response, targeting the serotonin pathways by usage of SSRIs and dietary supplements for neuroprotection. There are advanced gut-brain interventions in the pipeline like fecal microbiota transplantation, usage of psychobiotics like bifidobacterium longum and transcutaneous vagus nerve stimulation.

Though the findings of this study offer useful preliminary insights into the subject but a small sample size may reduce the statistical power and generalizability of the results. A larger cohort might validate the observations of the present study.

CONCLUSION

This study reinforces that GI symptoms are not merely secondary manifestations of anxiety but integral to its overall impact. GI disturbances and anxiety share a reciprocal intensification pattern, suggestive of underlying gut-brain axis dysregulation.

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