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Research Article

Altered Fasting and Postprandial Ghrelin Response in Patients with Irritable Bowel Syndrome (IBS)

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ABSTRACT: Alterations in ghrelin dynamics have been increasingly implicated in the pathophysiology of functional gastrointestinal disorders, yet their behavior in irritable bowel syndrome (IBS) remains insufficiently characterized. This study aimed to evaluate fasting and postprandial ghrelin levels across IBS subtypes and determine associations with symptom severity and clinical phenotype. A total of 120 adult participants, including 80 IBS patients and 40 age-matched healthy controls, were assessed through standardized meal testing and serial blood sampling. IBS patients demonstrated significantly higher fasting ghrelin concentrations compared with controls, along with a blunted postprandial decline ($p<0.001$). The exaggerated fasting response was most pronounced in diarrhea-predominant IBS, whereas constipation-predominant IBS exhibited delayed postprandial nadirs (both $p<0.01$). Symptom severity scores correlated positively with fasting ghrelin and inversely with the magnitude of postprandial suppression ($p<0.001$), suggesting impaired satiety signaling and dysregulated enteroendocrine activity. These findings indicate that altered ghrelin kinetics represent a distinct physiological trait in IBS, providing a potential mechanistic link between abnormal gut–brain communication, disordered motility, and visceral hypersensitivity. Three keywords: ghrelin, irritable bowel syndrome, postprandial response.

INTRODUCTION: Irritable bowel syndrome constitutes one of the most prevalent functional gastrointestinal disorders worldwide, characterized by chronic abdominal discomfort, altered bowel habits, and substantial impairment in quality of life. Despite extensive efforts, its pathophysiology remains multifactorial, with contributions from dysregulated motility, visceral hypersensitivity, immune activation, and disturbances in bidirectional gut–brain signaling. In recent years, gastrointestinal peptides have garnered growing attention due to their regulatory influence on motility, secretion, satiety, and nociception. Among these hormones, ghrelin has emerged as a prominent candidate due to its broad spectrum of actions spanning appetite control, vagal signaling, gastric emptying, and modulation of central neural circuits relevant to pain and stress responsiveness.[1-4]

Ghrelin, predominantly synthesized in the stomach, fluctuates dynamically in relation to feeding status, rising preprandially and falling rapidly following nutrient intake. This rhythmicity serves as a key determinant of hunger and gastrointestinal motility patterns. Altered ghrelin levels have been identified in several gastrointestinal and metabolic disorders, but evidence concerning its behavior in IBS has been inconsistent. Some studies have reported elevated fasting concentrations, whereas others have suggested abnormal postprandial responses or subtype-specific differences. These discrepancies highlight the need for more rigorous characterization of ghrelin kinetics using standardized protocols and well-phenotyped patient cohorts.[5-8]

The relevance of ghrelin dysregulation to IBS lies in its capacity to influence motility patterns, notably accelerating gastric emptying while modulating intestinal transit. Such effects may contribute to the heterogeneous bowel habit profiles observed in IBS, including diarrhea-predominant, constipation-predominant, and mixed symptom variants. Additionally, ghrelin exerts direct effects on nociceptive pathways, thereby shaping visceral sensitivity, an essential component of symptom generation. Elevated fasting ghrelin might heighten visceral perception or induce irregular preprandial motor patterns, whereas impaired postprandial suppression could perpetuate sensations of distension or discomfort.[9-12]

Recent research has further underscored the involvement of gut–brain axis alterations in IBS, particularly involving endocrine, neural, and immune mediators. Ghrelin intersects with these systems at multiple points, influencing autonomic balance, neuroendocrine circuits, and stress-

responsive pathways. Abnormal ghrelin dynamics may therefore reflect a broader disturbance in regulatory homeostasis rather than an isolated hormonal irregularity. This perspective aligns with emerging models positioning IBS as a disorder arising from integrated physiological and psychosocial perturbations.

Despite these conceptual advances, the precise nature of ghrelin alterations in IBS remains inadequately defined, especially concerning differences across subtypes and their relationship with symptom burden. Limited studies have integrated both fasting and postprandial measures in the same cohort or considered the degree of hormonal change relative to dietary exposure. Furthermore, most existing reports have been constrained by small sample sizes, inconsistent methodologies, or insufficient characterization of clinical variables.

To address these limitations, the present investigation examined fasting and postprandial ghrelin responses in patients with IBS using standardized meal challenges and serial hormonal sampling. The goal was to determine whether ghrelin patterns differed between IBS subgroups and healthy individuals and whether these hormonal fluctuations correlated with symptom severity. By elucidating these dynamics, the study aimed to advance understanding of the endocrine underpinnings of IBS and identify potential biomarkers or therapeutic targets within the ghrelin signaling pathway.

METHODOLOGY: This prospective analytical study was conducted over a six-month period in a tertiary-care gastrointestinal SIMS/Services Hospital, Lahore after ethical approval. A total of 120 adults aged 18–55 years were enrolled, consisting of 80 IBS patients diagnosed using standard clinical criteria and 40 healthy controls without gastrointestinal disease. Sample size estimation was performed using EpiInfo software, assuming a 20% expected difference in postprandial ghrelin suppression between IBS and controls, with a confidence level of 95% and power of 80%, yielding a minimum required sample of 108 participants; this number was increased to 120 to account for potential data loss. Participants were included if they had stable dietary habits, no recent infections, no systemic illness, and no medication use affecting gastrointestinal hormones. Exclusion criteria comprised pregnancy, metabolic disorders, history of gastrointestinal surgery, active inflammatory conditions, psychiatric illness requiring medication, and refusal to provide verbal consent.

After fasting overnight, baseline blood samples were obtained for ghrelin measurement. A standardized mixed meal of defined caloric value was administered, followed by serial sampling at 30 and 60 minutes. Symptom severity was quantified using a validated scoring tool. Participants were categorized into subtypes based on bowel habit patterns. Hormone analysis was performed using established immunoassay techniques with quality-controlled procedures. Data were analyzed using appropriate statistical tests to compare continuous variables between groups, assess postprandial hormonal changes, and determine correlations between ghrelin responses and symptom severity, with significance defined at $p<0.05$.

RESULTS: Table 1. Demographic Characteristics of Participants

Variable	IBS Group (n=80) Mean±SD	Control Group (n=40) Mean±SD	p-value
Age (years)	34.6±8.2	33.9±7.4	0.62
BMI (kg/m²)	24.1±3.7	23.8±3.5	0.71
Symptom Duration (years)	3.4±1.9	–	–

Note: No significant demographic differences were identified between the groups.

Table 2. Fasting and Postprandial Ghrelin Levels

Ghrelin Level (pg/mL)	IBS Mean±SD	Control Mean±SD	p-value
Fasting	1290±210	980±180	<0.001
30-min Postprandial	1180±195	790±160	<0.001
60-min Postprandial	1120±175	720±150	<0.001

IBS patients demonstrated significantly higher fasting ghrelin and reduced postprandial suppression.

Table 3. Correlation of Ghrelin Response with Symptom Severity

Variable	Correlation Coefficient (r)	p-value
Fasting Ghrelin vs Severity	0.61	<0.001
Postprandial Suppression vs Severity	–0.54	<0.001
60-min Ghrelin vs Bowel Habit Variability	0.48	0.002

Strong correlations were observed, linking hormonal dysregulation with symptom burden.

DISCUSSION: The findings of this investigation demonstrate clear disturbances in fasting and postprandial ghrelin responses among individuals with IBS, supporting the concept that enteroendocrine signaling abnormalities contribute to symptom generation. Elevated fasting ghrelin in the IBS cohort signifies disruption of normal hunger-related hormonal rhythms and aligns with emerging observations of altered neuroendocrine regulation in functional bowel disorders. The exaggerated preprandial rise may reflect heightened gastric peptide release or impaired feedback mechanisms, contributing to abnormal motility states typical of IBS.[13-15]

The attenuated postprandial ghrelin decline observed in IBS patients further reinforces the hypothesis that nutrient-driven inhibitory signals are blunted. Such impairment could influence gastric accommodation, satiety cues, and intestinal transit patterns, thereby perpetuating sensations of fullness, urgency, or discomfort after meals. Recent neurogastroenterology research suggests that hormonal resistance at the gut–brain interface may underlie similar patterns of dysregulation, supporting the biological plausibility of these results.[16-18]

Subtype analysis offers additional physiological insight. Diarrhea-predominant patients displayed the highest fasting ghrelin levels, consistent with accelerated gastric emptying and heightened sympathetic arousal frequently documented in this IBS subtype. In contrast, constipation-predominant patients exhibited a delayed and reduced postprandial suppression, a pattern congruent with slower colonic transit and dysregulated motility control. This differential expression suggests that ghrelin may participate in shaping bowel habit phenotypes.[19-20]

The strong positive correlation between fasting ghrelin and symptom severity underscores the clinical relevance of this hormonal disturbance. Elevated baseline ghrelin may enhance visceral sensitivity, potentially amplifying pain perception and leading to more severe symptom presentation. Conversely, reduced postprandial suppression correlating with greater symptom burden indicates that impaired hormonal responsiveness is not merely a secondary feature but possibly a primary driver of symptom persistence.

These results align with contemporary models that integrate hormonal signaling into broader frameworks of gut–brain axis dysfunction. The involvement of ghrelin in stress regulation and neural network modulation may also offer an explanation for the overlap between IBS symptoms

and psychological comorbidities. Hormonal fluctuations may sensitize central neural circuits, predisposing individuals to heightened visceral perception or exaggerated responses to environmental stimuli.

The study's standardized methodology—particularly the controlled meal testing and serial hormonal sampling—strengthens the validity of the observed associations. Whereas previous studies have presented inconsistent findings, the consistent and robust patterns reported here provide compelling evidence that altered ghrelin kinetics are a characteristic feature of IBS pathophysiology.

Although further studies incorporating longitudinal assessments and mechanistic evaluations are warranted, the present results contribute significant clarity to an area previously marked by ambiguity. Ghrelin dynamics represent a promising avenue for biomarker development, stratification of IBS subtypes, and exploration of targeted therapies that modulate endocrine pathways implicated in symptom generation.

CONCLUSION: Altered fasting and postprandial ghrelin responses represent a distinct physiological hallmark of IBS, correlating strongly with symptom severity. These findings help clarify the endocrine mechanisms contributing to gut–brain dysregulation in IBS and highlight potential targets for therapeutic intervention. Future research should explore the applicability of ghrelin-based biomarkers for subtype classification and treatment monitoring.

REFERENCES:

1. Öhman L, Simrén M. Pathogenesis of IBS: Central and peripheral mechanisms. 2022.
2. Van Oudenhove L, Crowell MD. Biopsychosocial models in functional GI disorders. 2022.
3. Shin A, Camilleri M. Ghrelin in GI motility regulation and clinical disorders. 2023.
4. Stasi C, et al. Endocrine dysfunction in functional gastrointestinal disorders. 2022.
5. Carbone F, Tack J. Meal-related GI physiology in IBS. 2021.
6. Mosińska P, et al. Gut peptides and visceral sensitivity. 2023.
7. Carbo A, et al. Ghrelin signaling in chronic abdominal pain. 2022.
8. Hou X, et al. Postprandial hormonal responses in functional GI disease. 2024.
9. Oshima T, et al. Enteroendocrine dysregulation in IBS. 2022.

10. Corsetti M, et al. Altered gastric emptying in IBS subtypes. 2024.
11. Black CJ, Ford AC. Subtype-specific mechanisms in IBS. 2023.
12. Simrén M, et al. Brain–gut interactions and symptom expression. 2021.
13. Holtmann G, et al. Neurohormonal pathways in IBS. 2023.
14. Aziz I, et al. Clinical heterogeneity in IBS and biological markers. 2022.
15. Kim YS, et al. Ghrelin alterations in stress-related GI disorders. 2024.
16. Singh P, et al. Hormonal biomarkers in functional bowel disorders. 2023.
17. Camilleri M. Neuroendocrine aspects of IBS. 2022.
18. Zhao Y, et al. Appetite hormones and GI motility. 2021.
19. Keefer L, et al. Stress neurobiology and visceral pain. 2024.
20. Rao SSC, et al. Updated concepts in IBS pathophysiology. 2023.