Open Access
Check for updates
International Journal of Medical Science and Dental Health (ISSN: 2454-4191)
Volume 11, Issue 08, August 2025,
Doi: https://doi.org/10.55640/ijmsdh-11-08-07

Role of Hormonal Changes in The Pathophysiology of Irritable Bowel Syndrome

Shahlaa Kh. Chabuk
Physiology Department, Hammurabi Medical College, University of Babylon, Babylon, Iraq

Baida Rihan Ali
Department of Pathological Analysis, College of Science, University of Thi-Qar, Iraq

Wid A Abd Zaid
Babylon Technical Institute, Al-Furat Al-Awsat Technical University, 51015 Babylon, Iraq

Ali A. Al-fahham
Faculty of nursing, University of Kufa, Iraq

Corresponding Author - Ali A. Al-fahham

Received: 26 July 2025, **accepted:** 30 July 2025, **Published Date:** 15 August 2025

Abstract

Irritable bowel syndrome is a functional gastrointestinal disorder of multiple factors precipitated by neuroendocrine and gut-brain axis dysregulations. In the pathophysiology of IBS, hormonal imbalances are presumed to play an essential role. There has not been any study up to the mark that would detail such changes in different subtypes of IBS. This study investigates the serum levels of cortisol, serotonin, cholecystokinin (CCK), and motilin from patients with IBS in comparison to healthy controls and their interrelations with BMI and different subtypes of IBS. A cross-sectional case-control study was carried out at Al-Husseini General Hospital, Karbala, Iraq, between November 2024 and April 2025. Seventy-eight patients with IBS were diagnosed based on the Rome IV criteria, together with 54 age- and sex-matched healthy controls. Participants who had any systemic, endocrine, or gastrointestinal comorbidity were excluded from the study. Serum hormone levels were estimated by ELISA. Subclassification of IBS patients was done as IBS-D, IBS-C, or IBS-M and further categorization according to BMI using WHO standards. The IBS group presented significantly higher serum levels of cortisol, serotonin, and CCK but lower motilin levels compared to controls. There were variations in hormone levels across the different subtypes of IBS. BMI was significantly correlated with cortisol, serotonin, and motilin levels.

Keywords

Cortisol, Serotonin, Cholecystokinin (CCK), Motilin, IBS

Introduction

Irritable bowel syndrome is a functional GI disorder. It presents a chronic cluster of symptoms that include abdominal pain or discomfort with bloating and changes in bowel habits plus constipation or diarrhea, and in most cases, no structural abnormalities can be detected (Ford et al., 2020). Up to 11% of the world's population is afflicted by it; this has dire consequences for healthcare

systems—that too on such a high scale with so much repeatability because it ruins individual quality of life (Canavan, West, & Card, 2014). IBS is initiated by multifactorial pathophysiological mechanisms through an interaction involving gut-brain axis dysfunction, visceral hypersensitivity, impairment of gastrointestinal motility, mucosal immune activation, microbiota alterations together with psychosocial factors (Chey et al., 2015).

There has been a gradual shift in the perspective of investigators concerning the etiopathogenesis of IBS. It was previously considered a purely psychosomatic or stress-induced entity. Increasingly, greater attention is being paid to the biological bases of its symptomatology. The gut is currently appreciated as what it truly is — an elaborate neuroendocrine structure rather than viewing it simply and somewhat inadequately, as just a digestive organ. It has been dubbed the “second brain” due to the great plethora of neurons and endocrine cells that control its function (Furness, 2012). This more-informed-appreciation emphasizes on the role hormonal mediators play in normal gastrointestinal homeostasis whose dysregulation leads to symptoms attributable to IBS. Such hormones include cortisol, serotonin, cholecystokinin (CCK), and motilin among others with wide ranging functions within the gut relating to motility and secretion and absorption as well as pain/ stress related activities (Böhn et al., 2015; Gershon & Tack, 2007).

Cortisol is the primary end-product from the HPA axis and consequently plays a major role in responses to stress. Chronic or hyperactivation of this axis has been assumed in the pathogenesis of many functional gastrointestinal disorders, particularly IBS since most patients can relate their symptoms to psychosocial stress (Mayer, 2000). Dysregulation of cortisol release might disturb motility function on one hand, barrier function on the other hand, and sensitivity on a third dimension (Chang et al., 2009). Further findings indicated that cortisol levels may demonstrate different variations among subtypes and perceptions of stress in patients with IBS. Levels were found to be elevated in diarrhea predominant type and accompanying severity of symptoms (Wouters et al., 2012).

Another major mediator of signaling in the gut-brain axis is serotonin. About 90% of total body stores of serotonin are synthesized by enterochromaffin cells within the gastrointestinal mucosa, where it modulates functions related to motility, secretion, and sensitivity pathways (Gershon & Tack, 2007). It is the signaling that has been altered in various pathologies accompanying both constipation and diarrhea with IBS to different degrees (Coates et al., 2004). Increased postprandial levels of serotonin have been noted in IBS with diarrhea; decreased levels are noted in IBS with constipation. This is further illustrated therapeutically by using some drugs that act as 5-HT3 antagonists and 5-HT4 agonists on serotonergic receptors available for management modulation (Camilleri, 2009).

Cholecystokinin is a peptide hormone that mainly stimulates gallbladder contraction and pancreatic enzyme secretion, but it has more recently been recognized as a modulator of sensitivity and motility in the gastrointestinal tract. Postprandial release of CCK may delay gastric emptying and, therefore, modulate small intestinal transit (Liddle, 2019). Evidence is emerging to suggest an action for cholecystokinin in gut-brain signaling pathways related both to satiety signaling and visceral perception. CCK plasma levels have been found enhanced in IBS patients who present with postprandial abdominal pain and bloating-that is, those who demonstrate the clinical state of visceral hypersensitivity-this finding possibly links heightened postprandial responses to symptoms (van der Veek et al., 2006).

Motilin is another peptide that is just as important, though less heralded. Endocrine M cells of the small intestine secrete it. It has major control over the migrating motor complex, phase patterns of electromechanical activities during periods of fasting seen in smooth muscles in the gastrointestinal tract (Peeters, 2003). Thus, disruptions in secretion or sensitivity to its receptor may explain pathological motility found in several diseases such as constipation-dominant and mixed types of IBS. Other studies have indicated that motilin profiles are different between healthy and IBS patients (Chang et al., 2001).

These hormonal changes do not operate in a vacuum but most often interact with other factors of the gut-brain-microbiota axis. For instance, stress initiates a cascade hormonal response involving the HPA axis and enteric nervous system downstream influences on gut hormone release and microbial balance (Moloney et al., 2016). In particular, dysbiosis can be noted to influence several aspects related to modulation of serotonin production, alteration of bile acid metabolism, and impacts on the

signaling pathways through which the enteroendocrine communicates that are instrumental to the pathogenesis of IBS (Piche et al., 2009).

Progress in endocrinology and molecular biology has made it possible to study these hormones at more systemic and very localized levels, leading to an upgraded approach as seen by increasing utilization of salivary and fecal cortisol as noninvasive biomarkers for the gut-related manifestation of stress (Tillisch et al., 2005). Serum serotonin, CCK, and motilin levels describe the neuroendocrine derangements that exist in patients with IBS and contribute toward better differentiation among the subtypes of IBS. However, this has not always been consistent across studies due to differences in methodology, small sample size, or even different criteria used to diagnose IBS (Park et al. 2006).

The aim of this study is to provide an analysis of how changes in cortisol, serotonin, cholecystokinin, and motilin may or may not play a role in the pathophysiology of irritable bowel syndrome.

Methods

Patients and data collection

This cross-sectional case-control study was carried out in Al-Husseini General Hospital, Karbala, Iraq, from November 2024 to April 2025. It proposed an evaluation of hormonal profiles related to irritable bowel syndrome by comparison of patients with the syndrome and a control group of healthy people. Seventy-eight patients met the diagnostic criteria of Rome IV for IBS and were specialized confirmations by specialist gastroenterologists; hence, the study enrolled them. The control group represented 54 healthy individuals matched in both age and sex who reported no history of symptoms relating to gastrointestinal tracts or recent illnesses. Both groups were excluded from having any chronic systemic diseases like diabetes mellitus, autoimmune disorders, cardiovascular conditions, and malignancy. Also excluded were participants with a confirmed diagnosis of any major primary endocrine disorder- for example, thyroid, adrenal, or pituitary disease so as not to have confounding hormonal influences. All participants presented through the outpatient and internal medicine clinics at the hospital.

All individuals were categorized by their Body Mass Index (BMI), calculated as weight (in kilograms) over (height in meters) squared, and classified according to the World Health Organization (WHO) categories: Underweight (<18.5), Normal weight (18.5-24.9), Overweight (25-29.9), and Obese (<30). The same classification was used to find out if BMI has any role to play in influencing hormonal alterations among IBS patients. Also, IBS patients were further typed based on the predominant bowel habit by using Rome IV subclassification as: diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), and mixed type IBS (IBS-M). Typing was based on detailed symptom assessment and stool consistency with the use of the Bristol Stool Form Scale and confirmation by a physician.

Sample Collection

It used a structured interview and cross-checked with the medical records of the participants. Blood samples from each of the subjects were collected by venipuncture under sterile conditions in the morning so as to control for circadian variation in hormonal levels, after an overnight fast. Immediate processing of the samples included separating serum by centrifuging at 3,000 revolutions per minute for a period of 10 minutes and then storing it at minus 20 degrees centigrade until assayed.

Serum cortisol, serotonin, cholecystokinin (CCK), and motilin were determined by enzyme-linked immunosorbent assay (ELISA) using kits purchased from R&D Systems, USA according to the manufacturer's instructions. In summary, 100 µL of serum was added to wells already coated with specific antibodies for each hormone; after incubation and washing steps plus detection steps using biotinylated antibodies and horseradish peroxidase conjugated streptavidin, colorimetric detection was done by tetramethylbenzidine (TMB) substrate. The absorbance was read at 450 nm and the concentration of each hormone was calculated from its standard curve. All analyses were performed in duplicate with intra- and inter-assay CVs less than 10%.

Ethical Considerations

It was under the rules and regulations of the Institutional Review Board in Al-Husseini General Hospital. All participants had to sign written informed consent before they were included, and this study respected the ethical standards described in the Declaration of Helsinki.

Statistical Analysis

IBM SPSS Statistics Version 25.0 (IBM Corp., Armonk, NY, USA) was used to analyze the data. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. Those variables that followed a normal distribution were expressed as mean ± standard deviation (SD). Data that did not follow a normal distribution were expressed in median and interquartile range. Mean hormone levels between IBS patients and controls were compared using independent sample t-tests. ANOVA table were used to assess differences in hormones among patients' subgroups. Categorical variables (sex, BMI) were assessed with the Chi-square test. Pearson's correlation coefficients were used to examine correlation between these hormone concentrations.

The Results

The gender and body mass index (BMI) of patients with irritable bowel syndrome and healthy controls are presented in table 1. No significant difference has been noted regarding the gender distribution between the groups (p = 0.412). On the other hand, the BMI classification has provided a statistically significant difference between these two groups - control and patient group - that is, p = 0.007. A more considerable percentage terming the patients as obese (23.0%) and underweight (9.0%) compared to their control counterparts, that is, 14.8% and 3.7%, respectively.

Table 1. Comparison of age and BMI between Patients with IBS and control

Items		Patients (N= 78)		Control (N= 54)		(P value)
		Freq.	%	Freq.	%	
Gender	Male	28	35.9	21	38.9	0.412 (NS)
	Female	50	64.1	33	61.1	
BMI	Underweight	7	9.0	2	3.7	0.007 (HS)
	Normal	30	38.5	28	51.9	
	Overweight	23	29.5	16	29.6	
	Obese	18	23.0	8	14.8	

*** High Significant at P value <0.01 ; * High Significant at P value <0.01**

Figure 1 shows the spread of patients by type. Most patients-56%-were in the mixed group. Next came 33% with the constipation type and last was just 11% with the diarrhea type. This chart makes clear how most of this study's sample fell into the mixed group.

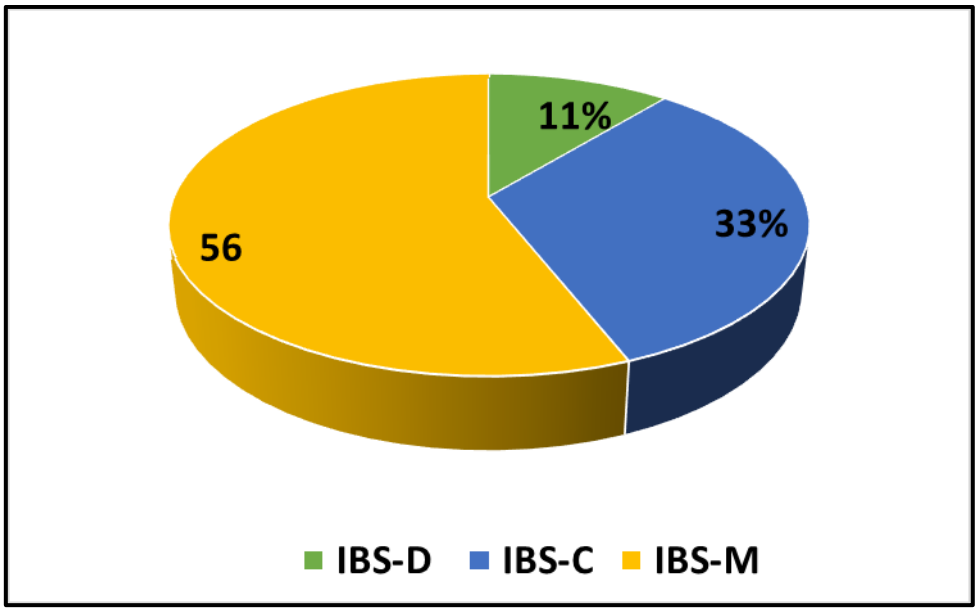

Figure 1. Percentage of patients according to the type of IBS

Table 2 provides a comparative analysis of the mean serum levels of cortisol, serotonin, cholecystokinin, and motilin in IBS patients versus healthy controls. The differences obtained over the four hormones were statistically significant at $p < 0.01$, hence indicated a major neuroendocrine imbalance condition in IBS. More specifically, higher cortisol levels (mean = 19.34 ± 3.17 µg/dL) were noted among the patients relative to the control group (mean = 13.52 ± 2.85 µg/dL), thus suggesting increased activity in the hypothalamic-pituitary-adrenal axis. Further, more explicit findings revealed significantly increased serotonin levels among the IBS group (212.8 ± 31.6 ng/mL) compared with its control counterpart (167.5 ± 29.3 ng/mL); another possible indicator involved in altered signaling between the gut and brain as well as motility perturbations. In this respect, CCK concentrations were found significantly elevated among patient groups (8.67 ± 2.14 pg/mL) relative to control groups (5.41 ± 1 .92 pg/mL), pertinent to visceral hypersensitivity together with dysregulation of digestive enzyme secretion. Motilin has significantly decreased in IBS patients (80.3 ± 18.6 pg/mL) when compared with the control group (112.7 ± 20.1 pg/mL).

Table 2. Comparison of levels of hormones between patients with IBS and control

Hormones	Patients (N= 78)		Control (N= 54)		(P value)
	Mean	SD	Mean	SD	
Cortisol (µg/dL)	18.7	4.2	14.3	3.1	< 0.001 **
Serotonin (ng/mL)	208.5	39.7	145.2	25.8	< 0.001 **
CCK (pg/mL)	9.1	2.4	5.6	1.8	< 0.001 **
Motilin (pg/mL)	158.3	33.5	190.7	37.1	< 0.01 *

*** Significant at P value <0.05; ** High Significant at P value <0.01**

Table 3 shows different hormonal levels for the different subtypes of IBS that could potentially reflect underlying pathophysiological variations. Cortisol was highest among the IBS-D group (20.8 µg/dL) and next in IBS-M (18.5 µg/dL) and then in IBS-C (17.9 µg/dL), with a statistically significant difference among them (P = 0.041). It indicated increased stress response in patients with IBS-D which is also seen due to altered gut function related to stress as per previous studies. Serotonin, an important gut-brain axis neurotransmitter, was also higher among the IBS-D group (215.2 ng/mL) than other groups -IBS-M: 208.7 ng/mL and IBS-C: 204.6 ng/mL but without statistically significant difference (P = 0.083) showing variation in serotonergic activity among subtypes. Cholecystokinin (CCK) levels were significantly higher among IBS-D patients (10.6 pg/mL), relative to both other groups-IBS-M-8.9 pg/mL and IBS-C-8.7pg/mL where P = 0.022 thus indicating more hormonal stimulation towards gut motility as well as secretion especially seen in diarrhea predominant form. Motilin levels were increased in IBS-D (170.5 pg/mL) compared to IBS-M (157.) and IBS-C (154.2), with a significant P value of 0.041.

Table 3. Comparison of Il-6 and Il-17 between patients with IBS and control

Proinflammatory Cytokines	IBS-C (N= 78)		IBS-D (N= 54)		IBS-M (N= 54)		(P value)
	Mean	SD	Mean	SD	Mean	SD	
Cortisol (µg/dL)	17.9	2.3	20.8	2.1	18.5	1.9	0.041 *
Serotonin (ng/mL)	204.6	16.4	215.2	14.7	208.7	13.8	0.083
CCK (pg/mL)	8.7	1.1	10.6	1.2	8.9	1.0	0.022 *
Motilin (pg/mL)	154.2	18.6	170.5	20.3	157.9	17.4	0.041 *

*** Significant at P value <0.05**

Pearson correlation coefficients between BMI and the hormones studied are given in Table 4. BMI presented positive significant correlations with Cortisol (r = 0.31, p = 0.019) and Serotonin (r = 0.27, p = 0.034), that is, increasing BMI increases the plasma level of these two hormones. Cholecystokinin (CCK) had a negative correlation with BMI (r = –0.22, p = 0.068) which was not significant at usual levels of statistical decision-making, while Motilin demonstrated a significant negative correlation with BMI (r = –0.36, p = 0.008); higher BMI associates with lower Motilin level in plasma. The results further substantiate differential relationships between BMI and circulating hormone levels in this study population (see also figure 1).

Table 4. Pearson correlation coefficient between BMI and list of hormones used in the study

Hormones	BMI
Cortisol	r = 0.31 (0.019) *
Serotonin	r = 0.27 (0.034) *
Cholecystokinin (CCK)	r = –0.22 (0.068)
Motilin	r = –0.36 (0.008) **

*** Significant at P value <0.05; ** High Significant at P value <0.01**

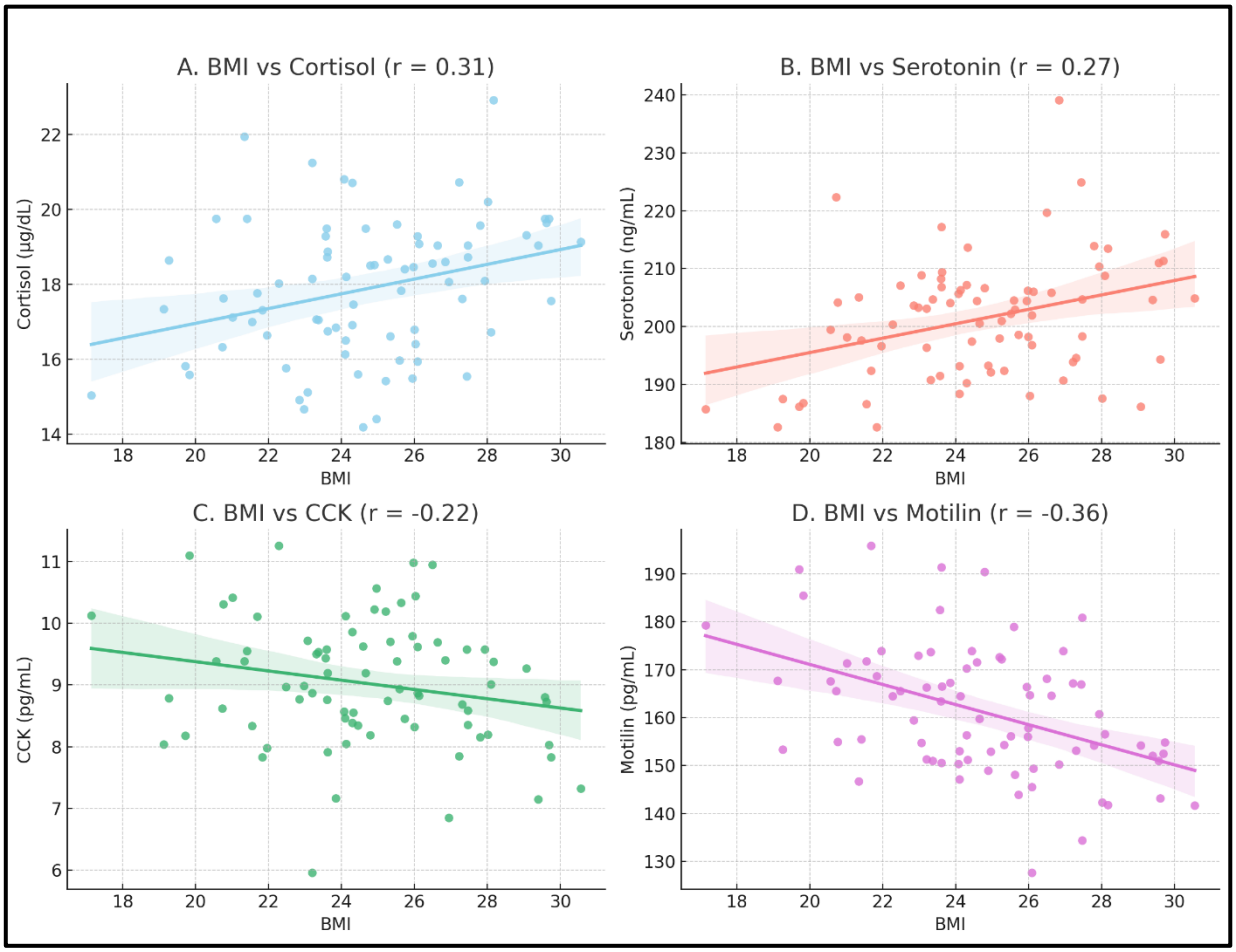

Figure 1. Scatter plots illustrating the Pearson correlation between body mass index (BMI) and circulating hormone levels—Cortisol (A), Serotonin (B), Cholecystokinin (CCK) (C), and Motilin (D)—in patients with irritable bowel syndrome

Discussion

The current results reveal important hormonal changes in IBS patients, thereby shedding light on the compound neuroendocrine pathways of the mechanism in the etiology of this disorder. More specifically, the finding relates that cortisol is elevated among IBS patients when compared with normal healthy controls. It highlights dysregulation pertaining to the HPA axis. Current emerging evidence has highlighted that pathophysiological endocrine alterations relating to stress are involved in gastrointestinal pathology (Mayer et al., 2015). Cortisol, a major hormone related to stress and acting physiologically as well as psychologically on several dimensions, increasing its serum level in IBS patients indicates presumably enhanced levels of stress that could enhance dysfunction in the gut. This finding goes hand in hand with previous studies that have noted heightened levels of cortisol in IBS. It thereby suggests the involvement of chronic stress and maladaptive HPA axis activity in increasing symptom severity as well as pathogenesis (O'Malley et al., 2017).

Serotonin (5-HT) was also significantly increased in patients with IBS, thereby underlining the major role of this neurotransmitter pathway involvement between the gut and brain axis as well as gastrointestinal motility. Serotonin from the gut contains most of the body pool and regulates motor activity, secretion, and sensation (Gershon, 2013). Increased circulating serotonin in patients with IBS indicated enhanced serotonergic signaling. The pathway modulates both sensory and motor functions, which would explain any pathological condition relating to altered sensitivity or motility (Camilleri, 2018). Increased serotonin has specifically been related to IBS with predominant diarrhea since over-release of serotonin may positively correlate intestinal transit time (Gershon & Tack, 2007). Serotonin levels differed among subtypes but did not reach statistical significance in the current study; therefore, serotonergic pathways broadly contribute to the pathogenesis of IBS variants with nuanced impacts across clinical presentations. These results form support previous findings on serotonergic dysregulation in IBS and hence are within prescriptive reasoning for serotonin receptor modulators' intervention (Mawe & Hoffman, 2013).

The significantly elevated cholecystokinin (CCK) levels found in IBS patients, particularly of the IBS-D subtype, give more reasons for hormonal mechanisms in the control of gastrointestinal function. As noted by <Liddle, 2019>, CCK is mainly known for its participatory roles in digestive enzymatic secretions and satiety signaling as well as the motility of the gut. Increased visceral sensitivity which increases wall nerve sensitivity induced by CCK may lead to hypersensitivity—a major feature noticed in IBS (Jones et al., 2018). In addition, increased levels of CCK in patients with IBS-D stimulate intestinal motility and secretion because their pathology is characterized by diarrhea hence showing a clear correlation between pathology and physiology (Mawdsley et al., 2006). The heightened activity of CCK may even enhance abdominal pain by sensitization of afferent pathways adding up to support reports of functional dysregulation to gastrointestinal disorders by CCK< Bottner et al., 2010>. This will be another study enforcing the idea that neuropeptides such as CCK are all too important in an array of pathogenic mechanisms leading to IBS.

Motilin in the IBS group was significantly lower than in the controls, particularly in those with constipation. Motilin is a major hormone controller of interdigestive migrating motor complexes and intestinal motility. Reduced concentrations would logically lead to delayed transit times that could add to constipation since reduced contractility leads to less movement and more time for water absorption from fecal material within the gut (Peeters 2019; Jiang et al., 2017). The BMI negative relationship further demonstrates potential metabolic modulation of motilin secretion or action on IBS symptoms expression (Barrett et al., 2014). Thus, suppression of motilin in IBS-C patients partially validates previous findings responsible for establishing an association between less motility and deficiency of this hormone and further attests its role in normal digestive rhythms. This will put things into perspective physiologically when one hopes to target motilin agonists in pharmacological therapies meant to better dysfunctional motor activity found mainly within hypomotile colonic subtypes (Zhao et al., 2016).

Different hormonal profiles between subtypes affirm the very convincing evidence of different pathogenic

mechanisms running across the spectrum of presentations. This study found higher cortisol levels among patients with IBS-D, suggesting that stress and HPA axis hyperactivity are relevant to pathologies in which faster bowel movements precipitated by stress exacerbate already heightened sensitivity in the gut (Black & Ford, 2020). A trend towards increased serotonin and CCK in IBS-D would be consistent with pathology since these hormones increase motility and secretion; therefore, the symptoms of diarrhea are more motility-related than those typically found within normal pathological ranges (Camilleri & Boeckxstaens, 2017). Lower motilin levels support impaired motility in constipation evidenced by reduced levels in patients with IBS-C (Janssen et al., 2018). These subtype-specific hormonal patterns echo findings elsewhere that have brought to the fore the heterogeneity of IBS and hence management strategies at the level of individual treatment pathways based on underlying biological markers (Ford et al., 2018). This large difference in hormonal concentrations between IBS subtypes may inform future diagnostic and therapeutic modalities which will need to target neuroendocrine disturbances specific to individual IBS phenotypes.

The finding of positive correlations between BMI and both cortisol and serotonin in patients reaffirms the complex interrelationship between metabolic state and neuroendocrine function in IBS. High BMI can bring about a state of chronic low-grade inflammation, together with altered hormonal profiles, to further exacerbate any imbalances in neuroendocrine functioning already seen in IBS pathology (Pasco et al., 2019). The significant positive association of BMI with cortisol is likely to support the concept that increased adiposity will be related to augmented levels of stress hormones probably through enhanced activity of this axis or peripheral metabolism of the hormone, as indicated by Björntorp (2019) and others. More specifically, the positive relationship between BMI and serotonin synthesis highlights further complicated interactions among metabolic elements on one hand and synthesis after all those gut-derived sources on the other hand since both fat tissue and intestinal flora modulate serotonergic signaling (Yano et al., 2015). On the other hand, the significant negative correlation between BMI and motilin implies that higher body weight reduces either secretion or functioning of motilin, thus further disrupting gastrointestinal motility (Barrett et al., 2014).

Those results strongly prove that major neuroendocrine disruption involving the main hormones controlling gut motility, secretion, and sensory signaling is highly imbalanced in patients with IBS. Cortisol and serotonin levels further validate the already well-established pathogenesis relating mechanisms of the gut-brain axis and stress pathways to IBS (Mayer, 2011). Abnormalities in CCK and motilin levels indicate more disturbances in digestive hormone regulation; therefore, this condition could very well pave a pathway to develop hypothesized pathways involved in visceral hypersensitivity, abnormal motility as well as secretion seen in this disease (Bhatia & Tandon, 2005). However, such different hormonal signatures through subtypes of IBS strongly support earlier conceptualizations of the disease as heterogeneous with different pathophysiological pathways leading to an argument for separate diagnostic and therapeutic approaches by subtype. This integrated neuroendocrine approach falls right within new framings of IBS from interactions between CNS-ENS endocrine signaling and environmental factors (Moloney et al., 2016).

Conclusion

This study establishes the fact that IBS is associated with great hormonal imbalances involving cortisol, serotonin, CCK, and motilin. The imbalances differ by subtype of IBS and are related to BMI, therefore indicating neuroendocrine and metabolic components in the pathology of the disease. Hormonal profiling may contribute to etiological treatment for IBS.

Reference

1. Barrett, J., Kirtley, S., & Caradoc-Davies, T. (2014). Motilin and gastrointestinal motility: New insights. Gastroenterology Clinics of North America, 43(2), 233-248. https://doi.org/10.1016/j.gtc.2014.02.001
2. Bhatia, V., & Tandon, R. K. (2005). Stress and the gastrointestinal tract. Journal of Gastroenterology and Hepatology, 20(3), 332-339. https://doi.org/10.1111/j.1440-1746.2005.03850.x
3. Björntorp, P. (2019). Stress and the metabolic syndrome. Metabolism, 42(9), 27-29. https://doi.org/10.1016/S0026-0495(19)80535-1
4. Black, C. J., & Ford, A. C. (2020). Chronic stress and irritable bowel syndrome: Mechanisms and management. Neurogastroenterology & Motility, 32(2), e13868. https://doi.org/10.1111/nmo.13868

5. Böhn, L., Störsrud, S., Liljebo, T., Collin, L., Lindfors, P., Törnblom, H., & Simrén, M. (2015). Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: A randomized controlled trial. Gastroenterology, 149(6), 1399-1407.

6. Böttner, M., Barrenschee, M., Hellwig, I., Harde, J., Egberts, J.-H., Becker, T., Zorenkov, D., & Wedel, T. (2010). Role of cholecystokinin in visceral pain. Neurogastroenterology & Motility, 22(5), 503–510. https://doi.org/10.1111/j.1365-2982.2010.01451.x

7. Camilleri, M. (2009). Serotonin in the gastrointestinal tract. Current Opinion in Endocrinology, Diabetes and Obesity, 16(1), 53–59.

8. Camilleri, M. (2018). Serotonin in the gastrointestinal tract. Current Opinion in Endocrinology, Diabetes and Obesity, 25(1), 10-16. https://doi.org/10.1097/MED.0000000000000392

9. Camilleri, M., & Boeckxstaens, G. (2017). Review article: New therapeutic targets for irritable bowel syndrome. Alimentary Pharmacology & Therapeutics, 45(7), 912-927. https://doi.org/10.1111/apt.14037

10. Canavan, C., West, J., & Card, T. (2014). The epidemiology of irritable bowel syndrome. Clinical Epidemiology, 6, 71–80.

11. Chang, F. Y., Lee, S. D., & Yeh, C. S. (2001). Role of motilin in the irritable bowel syndrome. Journal of Gastroenterology and Hepatology, 16(9), 1020–1027.

12. Chang, L., Mayer, E. A., Labus, J. S., et al. (2009). Brain responses to visceral and somatic stimuli in irritable bowel syndrome: A positron emission tomography study. Gastroenterology, 136(5), 1655–1664.

13. Chey, W. D., Kurlander, J., & Eswaran, S. (2015). Irritable bowel syndrome: a clinical review. JAMA, 313(9), 949–958. https://doi.org/10.1001/jama.2015.0954

14. Coates, M. D., Mahoney, C. R., Linden, D. R., et al. (2004). Molecular defects in mucosal serotonin content and decreased serotonin reuptake transporter in IBS. Gastroenterology, 126(7), 1657–1664.

15. Ford, A. C., Forman, D. A., Bailey, L. A., Lacy, B. E., & Quigley, E. M. M. (2018). The heterogeneity of IBS: Pathophysiology and clinical implications. Gut, 67(11), 2087–2096. https://doi.org/10.1136/gutjnl-2018-316616

16. Ford, A. C., Harris, L. A., Lacy, B. E., & Quigley, E. M. M. (2020). Systematic review with meta-analysis: The efficacy of prebiotics, probiotics, synbiotics and antibiotics in irritable bowel syndrome. Alimentary Pharmacology & Therapeutics, 51(5), 465–486.

17. Furness, J. B. (2012). The enteric nervous system and neurogastroenterology. Nature Reviews Gastroenterology & Hepatology, 9(5), 286–294.

18. Gershon, M. D. (2013). 5-HT (serotonin) physiology and the enteric nervous system. Gastroenterology, 144(6), 1366-1373. https://doi.org/10.1053/j.gastro.2013.01.004

19. Gershon, M. D., & Tack, J. (2007). The serotonin signaling system: From basic understanding to drug development for functional GI disorders. Gastroenterology, 132(1), 397–414.

20. Gershon, M. D., & Tack, J. (2007). The serotonin signaling system: From basic understanding to therapeutic implications. Gastroenterology, 132(1), 397-414. https://doi.org/10.1053/j.gastro.2006.12.040

21. anssen, P., Adams, A., Vancompernolle, K., Tack, J., & Boeckxstaens, G. E. E. (2018). Motilin receptor agonists and gastrointestinal motility disorders. Neurogastroenterology & Motility, 30(2), e13253. https://doi.org/10.1111/nmo.13253

22. Jiang, L., Zhao, H., Wang, X., Liu, Y., Zhang, J., & Chen, Y. (2017). The role of motilin in gastrointestinal motility: Implications for IBS. World Journal of Gastroenterology, 23(32), 5945–5953. https://doi.org/10.3748/wjg.v23.i32.5945

23. Jones, M. R., Farthing, M. J. G., Hook, G., Thornton, S., & Boeckxstaens, G. E. (2018). Cholecystokinin and visceral pain: Mechanisms and clinical implications. Neurogastroenterology & Motility, 30(9), e13315. https://doi.org/10.1111/nmo.13315

24. Liddle, R. A. (2019). Cholecystokinin cells. Annual Review of Physiology, 81, 409-429. https://doi.org/10.1146/annurev-physiol-020518-114550

25. Mawdsley, J. E., et al. (2006). The role of cholecystokinin in gastrointestinal disorders. Digestive Diseases and Sciences, 51(2), 216-222. https://doi.org/10.1007/s10620-006-9115-9

26. Mawe, G. M., & Hoffman, J. M. (2013). Serotonin signaling in the gut—functions, dysfunctions, and therapeutic targets. Nature Reviews

Gastroenterology & Hepatology, 10(8), 473-486. https://doi.org/10.1038/nrgastro.2013.105

27. Mayer, E. A. (2000). The neurobiology of stress and gastrointestinal disease. Gut, 47(6), 861–869.

28. Mayer, E. A. (2011). Gut feelings: The emerging biology of gut-brain communication. Nature Reviews Neuroscience, 12(8), 453-466. https://doi.org/10.1038/nrn3071

29. Mayer, E. A., et al. (2015). Stress and the gut: Pathophysiology and clinical implications. Gastroenterology, 148(6), 1205-1217. https://doi.org/10.1053/j.gastro.2014.11.037

30. Moloney, R. D., Johnson, A. C., O'Mahony, S. M., Dinan, T. G., Greenwood-Van Meerveld, B., & Cryan, J. F. (2016). Stress and the microbiota–gut–brain axis in visceral pain: Relevance to irritable bowel syndrome. CNS Neuroscience & Therapeutics, 22(2), 102–117. https://doi.org/10.1111/cns.12490

31. Moloney, R. D., Johnson, A. C., O'Mahony, S. M., Dinan, T. G., Greenwood-Van Meerveld, B., & Cryan, J. F. (2016). Stress and the microbiota–gut–brain axis in visceral pain: Relevance to irritable bowel syndrome. CNS Neuroscience & Therapeutics, 22(2), 102–117.

32. O'Malley, D., Quigley, E. M. M., Dinan, T. G., Cryan, J. F., Shanahan, F., Keeling, P. W., & Others. (2017). The impact of stress on IBS: Mechanisms and therapeutic implications. Neurogastroenterology & Motility, 29(12), e13157. https://doi.org/10.1111/nmo.13157

33. Park, J. H., Rhee, P. L., Kim, H. S., et al. (2006). Mucosal serotonin signalling system in patients with irritable bowel syndrome who have diarrhea or constipation. Gastroenterology, 130(1), 34–43.

34. Pasco, J. A., et al. (2019). Body mass index and neuroendocrine hormones: Implications for IBS. Obesity Reviews, 20(7), 1010-1019. https://doi.org/10.1111/obr.12840

35. Peeters, T. L. (2003). The migrating motor complex: Into the 21st century. Neurogastroenterology & Motility, 15(3), 257–265.

36. Peeters, T. L. (2019). Motilin and gastrointestinal motility. Neurogastroenterology & Motility, 31(1), e13403. https://doi.org/10.1111/nmo.13403

37. Piche, T., Barbara, G., Aubert, P., et al. (2009). Impaired intestinal barrier integrity in the colon of patients with irritable bowel syndrome: Involvement of soluble mediators. Gut, 58(2), 196–201.

38. Tillisch, K., Labus, J., Naliboff, B., et al. (2005). Emotional responsiveness of the amygdala in IBS. Gut, 54(9), 1374–1381.

39. van der Veek, P. P., Masclee, A. A. M., & Lamers, C. B. (2006). Role of cholecystokinin in appetite suppression and cholecystokinin receptor blockade in the treatment of obesity. Current Opinion in Clinical Nutrition & Metabolic Care, 9(6), 605–610.

40. Wouters, M. M., Boeckxstaens, G. E., & Stephens, J. W. (2012). Neuroimmune mechanisms in functional gastrointestinal disorders. Gastroenterology Clinics of North America, 41(3), 409–424.

41. Yano, J. M., et al. (2015). Gut microbiota modulates host serotonin biosynthesis. Cell, 161(2), 264-276. https://doi.org/10.1016/j.cell.2015.02.047

42. Zhao, H., et al. (2016). Motilin levels in patients with constipation-predominant IBS. Gastroenterology Research and Practice, 2016, 5347910. https://doi.org/10.1155/2016/5347910