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Original Research Article

Gut-Brain Axis in Obesity: The Role of Gastrointestinal Hormones and Microbiota in Metabolic Regulation

Nitesh Mishra

Assistant Professor, Department of Physiology, Ajay Sangaal Institute of Medical Sciences & Research and Ayushmaan Hospital, District - Shamli (U.P.), India

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Corresponding author: Dr. Nitesh Mishra
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Abstract

Background: Obesity is a major global health problem associated with metabolic, cardiovascular, and endocrine disorders. Recent evidence has highlighted the role of the gut–brain axis, gastrointestinal hormones, and gut microbiota in regulating appetite, satiety, glucose metabolism, and body weight.

Aim: The present study was conducted to evaluate the role of the gut–brain axis in obesity, with particular emphasis on gastrointestinal hormones and gut microbiota in metabolic regulation.

Methods: This hospital-based observational cross-sectional study included 90 participants, comprising 45 obese individuals and 45 age- and sex-matched non-obese controls. Demographic, anthropometric, clinical, biochemical, hormonal, and gut microbiota parameters were assessed. Serum leptin, ghrelin, glucagon-like peptide-1, peptide YY, insulin, and inflammatory markers were measured. Stool microbiota analysis was performed using 16S rRNA sequencing. Statistical analysis was carried out using independent t-test, Mann–Whitney U test, Chi-square test, and Spearman's correlation.

Results: Obese participants had significantly higher body mass index, waist circumference, blood pressure, fasting blood glucose, HbA1c, insulin, HOMA-IR, total cholesterol, triglycerides, LDL cholesterol, leptin, and hs-CRP levels compared to non-obese controls ($p < 0.001$). In contrast, HDL cholesterol, ghrelin, glucagon-like peptide-1, peptide YY, Bacteroidetes abundance, Actinobacteria abundance, and microbial diversity index were significantly lower among obese participants ($p < 0.001$). Firmicutes abundance, Firmicutes/Bacteroidetes ratio, and Proteobacteria abundance were significantly higher in the obese group. BMI showed positive correlations with leptin, HOMA-IR, and Firmicutes/Bacteroidetes ratio, whereas negative correlations were observed with ghrelin, glucagon-like peptide-1, peptide YY, and microbial diversity index.

Conclusion: The present study demonstrated that obesity was associated with significant dysregulation of gastrointestinal hormones and gut microbiota, suggesting an important role of the gut–brain axis in obesity-related metabolic dysfunction.

Keywords: Obesity, Gut–Brain Axis, Gastrointestinal Hormones, Gut Microbiota, Metabolic Regulation.

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Introduction

Obesity has emerged as one of the most significant global public health challenges and its prevalence has increased markedly over recent decades. According to the World Health Organization, nearly 1.9 billion adults were overweight in 2016, among whom more than 650 million were obese. In addition, approximately 39 million children below five years of age were estimated to be overweight or obese by 2020. Since 1975, the prevalence of obesity worldwide has nearly tripled, with around 39% of adults being overweight and 13% being obese.[1,2] The increasing burden of obesity has been attributed to rapid urbanization, sedentary lifestyle, unhealthy dietary habits, reduced physical activity, genetic susceptibility, and various environmental factors.[3]Obesity is a chronic metabolic disorder characterized by excessive accumulation of adipose tissue that adversely affects health over time.[3] It is associated with a wide range of complications including type 2 diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, metabolic dysfunction-associated steatotic liver disease, obstructive sleep apnea, osteoarthritis, infertility, certain malignancies, and reduced quality of life.[3-5] Obesity is also associated with psychological disorders such as anxiety, depression, and low self-esteem. The risk of these complications is particularly high in individuals with excess visceral adipose tissue.[6]White adipose tissue not only

increases in quantity in obesity but also becomes dysfunctional. Visceral adipose tissue is metabolically more active and contributes to chronic low-grade systemic inflammation through increased release of pro-inflammatory cytokines, adipokines, and inflammatory mediators into the circulation.[6-8] These inflammatory mediators adversely affect organs such as the liver, skeletal muscle, pancreas, and cardiovascular system, resulting in insulin resistance, impaired glucose metabolism, altered energy utilization, and an increased risk of obesity-related metabolic disorders.[5-8]

Traditionally, obesity was considered merely a consequence of excessive caloric intake and reduced physical activity. However, recent advances in metabolic research have shown that obesity is a highly complex and multifactorial disorder involving interactions among genetic, hormonal, neural, immune, and environmental factors.[5,9] Among these, the gut–brain axis has gained increasing attention because of its essential role in regulating appetite, satiety, food intake, glucose metabolism, energy expenditure, and body weight.[10,11]The gut–brain axis refers to the bidirectional communication network between the gastrointestinal tract and the central nervous system. This communication occurs through neural, endocrine, immune, and metabolic pathways.[4,10-12] The major components of the gut–brain axis include the central nervous system, autonomic nervous system, enteric nervous system, vagus nerve, hypothalamus, enteroendocrine cells, gastrointestinal hormones, and gut microbiota. Through this network, the brain receives signals regarding nutrient intake, intestinal distension, microbial composition, and hormonal status, while the gut responds to neural and endocrine signals that influence digestion, secretion, motility, and feeding behavior.[4,10,12]The hypothalamus is the principal brain region involved in appetite and energy homeostasis. It integrates peripheral signals related to hunger and satiety and modulates food intake through specific neuronal pathways. Orexigenic neurons stimulate appetite, whereas anorexigenic neurons suppress hunger and promote satiety.[9] These pathways are influenced by several gastrointestinal hormones secreted in response to nutrient intake. Among the gastrointestinal hormones, ghrelin is primarily produced by the stomach and is commonly known as the hunger hormone because it stimulates appetite and food intake. Ghrelin levels generally rise before meals and decline after eating. In contrast, satiety hormones such as peptide YY, glucagon-like peptide-1, cholecystokinin, oxyntomodulin, and pancreatic polypeptide are released after food intake and reduce hunger.[13,14]Glucagon-like peptide-1 is secreted by enteroendocrine L-cells located in the distal intestine and plays a major role in stimulating insulin secretion, suppressing glucagon release, delaying gastric emptying, and inducing satiety. Peptide YY is released in proportion to caloric intake and acts on hypothalamic centers to reduce appetite. Cholecystokinin, secreted by the small intestine in response to dietary fat and protein, promotes early satiety and decreases meal size. Alterations in the secretion, sensitivity, or signaling of these hormones may contribute to overeating, impaired satiety, and obesity.[10,13,14]

Leptin and insulin are additional hormones involved in appetite and energy balance. Leptin, secreted by adipose tissue, normally suppresses appetite and enhances energy expenditure. However, obesity is often associated with leptin resistance, which reduces the effectiveness of this satiety signal. Similarly, insulin resistance contributes not only to impaired glucose metabolism but also to dysregulation of central appetite pathways.[9,10]In recent years, gut microbiota has emerged as another major component of the gut–brain axis. Gut microbiota refers to the diverse community of microorganisms, mainly bacteria, viruses, fungi, and archaea, residing in the gastrointestinal tract.[4,15] These microorganisms play an essential role in maintaining host homeostasis through regulation of digestion, nutrient absorption, vitamin synthesis, immune function, intestinal barrier integrity, and energy metabolism.[15-17]A healthy gut microbial environment, commonly referred to as eubiosis, is necessary for normal physiological functioning. However, obesity is often associated with gut microbial imbalance or dysbiosis. Dysbiosis in obese individuals is characterized by reduced microbial diversity, increased abundance of pro-inflammatory bacterial species, impaired gut barrier function, increased intestinal permeability, and altered production of microbial metabolites.[11,15,18] Obese individuals frequently exhibit an increased Firmicutes-to-Bacteroidetes ratio, which has been associated with enhanced energy harvest from food and increased fat storage.[11,19]Gut microbiota influences body weight and metabolism through multiple mechanisms including modulation of appetite-regulating hormones, production of short-chain fatty acids, regulation of bile acid metabolism, and induction of chronic low-grade inflammation. [10,11,20] Short-chain fatty acids such as acetate, propionate, and butyrate are produced by bacterial fermentation of dietary fiber in the colon. These metabolites regulate glucose homeostasis, lipid metabolism, inflammation, and appetite.[16,17,20] In addition, short-chain fatty acids stimulate the secretion of glucagon-like peptide-1 and peptide YY, thereby linking gut microbial activity with satiety regulation.[10,20,21]Gut microbiota can also influence the brain through neural and immune

pathways. Microbial metabolites, inflammatory cytokines, and neurotransmitter-like compounds produced by intestinal bacteria may affect mood, stress responses, appetite, and eating behavior.[4,17,22,23] Dysbiosis-related inflammation may contribute to insulin resistance, leptin resistance, and hypothalamic dysfunction, thereby promoting obesity and metabolic disturbances.[11,22,23]

The enteric nervous system, often described as the "second brain," is another important component of the gut–brain axis. It coordinates intestinal motility, secretion, and local reflexes, while transmitting microbial, hormonal, and nutritional signals to the central nervous system through vagal afferent pathways.[12,24] In addition, the hypothalamic–pituitary–adrenal axis may be influenced by obesity-related inflammation and gut dysbiosis, leading to altered stress responses and further metabolic imbalance.[4,22]

Recent therapeutic strategies for obesity have increasingly targeted the gut–brain axis. Glucagon-like peptide-1 receptor agonists and dual incretin-based therapies have demonstrated significant benefits in terms of weight reduction, glycemic control, and cardiovascular risk reduction. Drugs such as semaglutide and tirzepatide have shown remarkable effectiveness in reducing appetite and body weight by modulating gut–brain signaling pathways. Similarly, probiotics, prebiotics, synbiotics, fecal microbiota transplantation, and bariatric surgery are being explored as potential interventions to improve obesity-related metabolic dysfunction.[11,13,25]

Despite growing knowledge regarding the gut–brain axis, several aspects of its role in obesity remain incompletely understood.

The interactions among gastrointestinal hormones, gut microbiota, neural signaling, inflammation, and metabolic pathways are highly complex and may vary among individuals. Further research is needed to better understand these mechanisms and identify novel biomarkers and therapeutic targets for obesity management.

Therefore, the present study was conducted to evaluate the role of the gut–brain axis in obesity, with particular emphasis on gastrointestinal hormones and gut microbiota in metabolic regulation. The study aimed to improve understanding of the mechanisms underlying appetite regulation, energy balance, obesity-related metabolic dysfunction, and potential therapeutic interventions for obesity management.

Material and Methods

Study Design and Setting: The present study was conducted as a hospital-based observational cross-sectional study in the Department of Physiology at a tertiary care teaching hospital.

Study Population: The study included adult participants aged 18 years and above who attended the outpatient department or were admitted to the inpatient department during the study period. Participants were divided into obese and non-obese groups based on body mass index criteria. Obesity was defined as body mass index ≥30 kg/m².

Sample Size: A total sample size of 90 participants was included in the study. Among them, 45 obese individuals and 45 age- and sex-matched non-obese controls were enrolled for comparison.

Inclusion Criteria

1. Adults aged ≥18 years.
2. Individuals willing to participate and provide written informed consent.
3. Participants with obesity defined as body mass index ≥30 kg/m².
4. Apparently healthy non-obese individuals with body mass index between 18.5 and 24.9 kg/m² included as controls.

Exclusion Criteria

1. Pregnant or lactating women.
2. Individuals with chronic gastrointestinal diseases such as inflammatory bowel disease, chronic pancreatitis, malabsorption syndrome, or gastrointestinal malignancy.
3. Patients with known endocrine disorders affecting weight, including hypothyroidism, Cushing syndrome, and polycystic ovarian syndrome.
4. Individuals with chronic liver disease, chronic kidney disease, active infection, malignancy, or autoimmune disease.
5. Participants receiving antibiotics, probiotics, corticosteroids, immunosuppressive drugs, or weight-loss medications within the previous three months.
6. Individuals with previous bariatric surgery.

Data Collection: Detailed demographic and clinical data were collected from all participants using a structured proforma. Information regarding age, sex, dietary habits, physical activity, smoking history, alcohol consumption, family history of obesity, and comorbidities was recorded. Anthropometric measurements including height, weight, body mass index, waist circumference, hip circumference, and waist-hip ratio were measured using standard techniques. Blood pressure was measured in the sitting position after adequate rest.

Laboratory Investigations: Fasting venous blood samples were collected from all participants after an overnight fast of 8–10 hours. The following biochemical parameters were assessed:

1. Fasting blood glucose
2. Glycated hemoglobin (HbA1c)
3. Serum insulin
4. Lipid profile including total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol
5. Liver function tests
6. Serum leptin levels
7. Serum ghrelin levels
8. Serum glucagon-like peptide-1 levels
9. Serum peptide YY levels
10. Serum insulin levels
11. High-sensitivity C-reactive protein

Insulin resistance was calculated using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR).

Gut Microbiota Assessment: Fresh stool samples were collected from all participants in sterile containers and transported immediately to the microbiology laboratory. Stool microbiota analysis was performed using 16S rRNA gene sequencing techniques. The relative abundance of major bacterial phyla including Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria was assessed. The Firmicutes-to-Bacteroidetes ratio was calculated for each participant. Microbial diversity indices were also evaluated.

Outcome Measures: The primary outcome measures included the association of obesity with gastrointestinal hormones and gut microbiota composition. Secondary outcome measures included the relationship of gut microbiota and hormonal parameters with insulin resistance, lipid abnormalities, inflammatory markers, and anthropometric indices.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 25.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on data distribution.

Categorical variables were presented as frequencies and percentages. The independent t-test or Mann–Whitney U test was used to compare continuous variables between obese and non-obese groups.

Chi-square test or Fisher's exact test was used for categorical variables. Correlation analysis was performed using Pearson's or Spearman's correlation coefficient as appropriate. Multivariable linear regression analysis was performed to identify independent predictors of obesity-related metabolic dysfunction. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 90 participants were included in the study, comprising 45 obese individuals and 45 non-obese controls.

Table 1: Demographic, Anthropometric, and Clinical Characteristics of Study Participants

Variable	Obese Group (n=45)	Non-Obese Group (n=45)	Test Used	p-value
Age (years), mean ± SD	43.8 ± 9.6	41.2 ± 8.9	Independent t-test	0.18
Age (years), median (IQR)	44 (37–51)	40 (35–48)	Mann–Whitney U test	0.21
Male, n (%)	24 (53.3%)	22 (48.9%)	Chi-square test	0.67
Female, n (%)	21 (46.7%)	23 (51.1%)	Chi-square test	0.67
Weight (kg), mean ± SD	89.6 ± 11.8	63.5 ± 8.7	Independent t-test	<0.001
BMI (kg/m²), mean ± SD	33.8 ± 3.2	22.4 ± 1.9	Independent t-test	<0.001
BMI (kg/m²), median (IQR)	33.5 (31.6–35.8)	22.1 (21.0–23.8)	Mann–Whitney U test	<0.001
Waist circumference (cm), mean ± SD	108.4 ± 10.6	84.3 ± 8.4	Independent t-test	<0.001
Waist-hip ratio, mean ± SD	0.98 ± 0.07	0.84 ± 0.05	Independent t-test	<0.001
Systolic blood pressure (mmHg), mean ± SD	136.8 ± 14.2	122.6 ± 10.8	Independent t-test	<0.001
Diastolic blood pressure (mmHg), mean ± SD	86.4 ± 8.6	78.5 ± 7.2	Independent t-test	<0.001

The mean age of participants in the obese group was 43.8 ± 9.6 years, whereas the mean age in the non-obese group was 41.2 ± 8.9 years. There was no statistically significant difference in age and sex distribution between the two groups ($p > 0.05$). However, weight, BMI, waist circumference, waist-hip ratio, systolic blood pressure, and diastolic blood pressure were significantly higher in the obese group compared to the non-obese group ($p < 0.001$).

Table 2: Biochemical, Hormonal, and Inflammatory Parameters of Study Participants

Variable	Obese Group (n=45)	Non-Obese Group (n=45)	Test Used	p-value
Fasting blood glucose (mg/dl), mean ± SD	112.6 ± 18.4	91.8 ± 11.5	Independent t-test	<0.001
HbA1c (%), mean ± SD	6.4 ± 0.9	5.4 ± 0.5	Independent t-test	<0.001
Serum insulin (µIU/ml), mean ± SD	18.7 ± 5.8	9.6 ± 3.2	Independent t-test	<0.001
HOMA-IR, mean ± SD	5.2 ± 1.8	2.1 ± 0.8	Independent t-test	<0.001
Total cholesterol (mg/dl), mean ± SD	212.5 ± 34.8	176.4 ± 28.6	Independent t-test	<0.001
Triglycerides (mg/dl), mean ± SD	186.2 ± 48.5	121.6 ± 36.8	Independent t-test	<0.001
HDL cholesterol (mg/dl), mean ± SD	38.6 ± 7.2	48.8 ± 8.4	Independent t-test	<0.001
LDL cholesterol (mg/dl), mean ± SD	136.4 ± 28.7	102.5 ± 24.6	Independent t-test	<0.001
Leptin (ng/ml), mean ± SD	32.8 ± 10.6	12.4 ± 4.8	Independent t-test	<0.001
Ghrelin (pg/ml), mean ± SD	486.5 ± 92.4	612.8 ± 105.6	Independent t-test	<0.001
GLP-1 (pmol/L), mean ± SD	18.6 ± 4.5	24.8 ± 5.2	Independent t-test	<0.001
Peptide YY (pg/ml), mean ± SD	78.4 ± 16.8	102.6 ± 18.5	Independent t-test	<0.001
hs-CRP (mg/L), median (IQR)	5.8 (4.1–8.2)	2.1 (1.4–3.5)	Mann–Whitney U test	<0.001

Participants in the obese group had significantly higher fasting blood glucose, HbA1c, serum insulin, HOMA-IR, total cholesterol, triglycerides, LDL cholesterol, leptin, and hs-CRP levels compared to the non-obese group. In contrast, ghrelin, GLP-1, peptide YY, and HDL cholesterol levels were significantly lower among obese participants ($p < 0.001$).

Table 3: Gut Microbiota Characteristics and Correlation with Body Mass Index

Variable	Obese Group (n=45)	Non-Obese Group (n=45)	Correlation with BMI (r)	Test Used	p-value
Firmicutes abundance (%)	58.4 ± 9.6	42.8 ± 8.5	0.55	Independent t-test / Spearman's correlation	<0.001
Bacteroidetes abundance (%)	24.6 ± 7.2	38.5 ± 8.1	-0.48	Independent t-test / Spearman's correlation	<0.001
Firmicutes/Bacteroidetes ratio	2.4 ± 0.8	1.1 ± 0.4	0.59	Independent t-test / Spearman's correlation	<0.001
Proteobacteria abundance (%)	9.6 ± 3.1	5.8 ± 2.2	0.41	Independent t-test / Spearman's correlation	<0.001
Actinobacteria abundance (%)	7.4 ± 2.8	9.2 ± 3.0	-0.32	Independent t-test / Spearman's correlation	0.004
Microbial diversity index	2.8 ± 0.6	3.9 ± 0.7	-0.54	Independent t-test / Spearman's correlation	<0.001
Leptin (ng/ml)	32.8 ± 10.6	12.4 ± 4.8	0.68	Spearman's correlation	<0.001
Ghrelin (pg/ml)	486.5 ± 92.4	612.8 ± 105.6	-0.52	Spearman's correlation	<0.001
GLP-1 (pmol/L)	18.6 ± 4.5	24.8 ± 5.2	-0.49	Spearman's correlation	<0.001
Peptide YY (pg/ml)	78.4 ± 16.8	102.6 ± 18.5	-0.45	Spearman's correlation	<0.001
HOMA-IR	5.2 ± 1.8	2.1 ± 0.8	0.71	Spearman's correlation	<0.001

Discussion

The obese group demonstrated significantly higher Firmicutes abundance, Firmicutes/Bacteroidetes ratio, Proteobacteria abundance, leptin levels, and HOMA-IR compared to the non-obese group. Conversely, Bacteroidetes abundance, Actinobacteria abundance, microbial diversity index, ghrelin, GLP-1, and peptide YY levels were significantly lower among obese participants. BMI showed a significant positive correlation with leptin levels, HOMA-IR, and Firmicutes/Bacteroidetes ratio, whereas significant negative correlations were observed with ghrelin, GLP-1, peptide YY, and microbial diversity index. In the present study, the mean age of participants in the obese group was 43.8 ± 9.6 years compared to 41.2 ± 8.9 years in the non-obese group, with no statistically significant difference between the groups ($p = 0.18$). Males constituted 53.3% of the obese group and 48.9% of the non-obese group.

These findings suggested that both groups were comparable with respect to age and sex distribution. The present study showed that obese participants had significantly higher weight (89.6 ± 11.8 vs 63.5 ± 8.7), BMI (33.8 ± 3.2 vs 22.4 ± 1.9), waist circumference (108.4 ± 10.6 vs 84.3 ± 8.4),

waist-hip ratio (0.98 ± 0.07 vs 0.84 ± 0.05), systolic blood pressure (136.8 ± 14.2 vs 122.6 ± 10.8), and diastolic blood pressure (86.4 ± 8.6 vs 78.5 ± 7.2) compared to non-obese individuals ($p < 0.001$). These findings were consistent with studies showing that obesity is associated with central adiposity, hypertension, and increased cardiometabolic risk. The elevated waist circumference and waist-hip ratio observed in our study suggested greater visceral adiposity, which is metabolically active and contributes to insulin resistance and systemic inflammation [26]. In the present study, fasting blood glucose (112.6 ± 18.4 vs 91.8 ± 11.5), HbA1c (6.4 ± 0.9 vs 5.4 ± 0.5), serum insulin (18.7 ± 5.8 vs 9.6 ± 3.2), and HOMA-IR (5.2 ± 1.8 vs 2.1 ± 0.8) were significantly higher in obese participants compared to non-obese controls ($p < 0.001$). Similarly, total cholesterol (212.5 ± 34.8 vs 176.4 ± 28.6), triglycerides (186.2 ± 48.5 vs 121.6 ± 36.8), and LDL cholesterol (136.4 ± 28.7 vs 102.5 ± 24.6) were significantly elevated, whereas HDL cholesterol (38.6 ± 7.2 vs 48.8 ± 8.4) was significantly lower among obese participants ($p < 0.001$).These findings were in agreement with previous literature showing that obesity is strongly associated with insulin resistance, impaired glucose metabolism, and dyslipidemia. Visceral adiposity promotes chronic inflammation and altered lipid metabolism, thereby increasing the risk of metabolic syndrome and cardiovascular disease [26]. The present study demonstrated significantly higher serum leptin levels in the obese group compared to the non-obese group (32.8 ± 10.6 ng/ml vs 12.4 ± 4.8 ng/ml; $p < 0.001$). Furthermore, leptin showed a strong positive correlation with BMI ($r = 0.68$, $p < 0.001$).These findings were comparable with the study by Adeyemi et al., who reported median leptin levels of 38 ng/ml in obese individuals compared to 5.6 ng/ml in lean controls ($p < 0.0001$). Al-Sultan et al. also reported that serum leptin increased significantly with obesity and correlated positively with BMI and hip circumference. Similarly, Perakakis et al. observed that circulating leptin levels reflect body fat mass and are markedly elevated in obesity, indicating a state of leptin resistance. Our findings support the concept that hyperleptinemia is a hallmark of obesity and may contribute to persistent hunger and impaired energy expenditure due to leptin resistance [27]. In the present study, ghrelin (486.5 ± 92.4 vs 612.8 ± 105.6 pg/ml), GLP-1 (18.6 ± 4.5 vs 24.8 ± 5.2 pmol/L), and peptide YY levels (78.4 ± 16.8 vs 102.6 ± 18.5 pg/ml) were significantly lower in obese individuals compared to non-obese controls ($p < 0.001$). Ghrelin showed a significant negative correlation with BMI ($r = -0.52$), while GLP-1 and peptide YY also showed inverse correlations with BMI ($r = -0.49$ and -0.45, respectively).These findings were consistent with previous studies showing that obesity is associated with impaired satiety signaling and altered gastrointestinal hormone secretion. Steinert et al. reported that ghrelin, GLP-1, and peptide YY are major regulators of appetite, meal size, and postprandial glucose metabolism. Abou-Samra et al. found that normal-weight individuals had significantly higher ghrelin levels than obese individuals. Wilbrink et al. proposed that obesity is associated with attenuated concentrations of GLP-1 and peptide YY, thereby contributing to reduced satiety and increased caloric intake. Furthermore, recent reviews have highlighted that gut hormones such as GLP-1 and PYY play a fundamental role in regulating energy metabolism and appetite through gut-brain communication pathways [28]. In the present study, obese participants demonstrated significantly higher Firmicutes abundance (58.4 ± 9.6% vs 42.8 ± 8.5%), Firmicutes/Bacteroidetes ratio (2.4 ± 0.8 vs 1.1 ± 0.4), and Proteobacteria abundance (9.6 ± 3.1% vs 5.8 ± 2.2%) compared to non-obese controls ($p < 0.001$). Conversely, Bacteroidetes abundance (24.6 ± 7.2% vs 38.5 ± 8.1%), Actinobacteria abundance (7.4 ± 2.8% vs 9.2 ± 3.0%), and microbial diversity index (2.8 ± 0.6 vs 3.9 ± 0.7) were significantly lower among obese participants. These findings were in line with the observations of Koliada et al., who reported that obese individuals had significantly higher Firmicutes levels and lower Bacteroidetes levels compared to lean controls. Magne et al. and Tseng et al. also suggested that an increased Firmicutes/Bacteroidetes ratio is commonly observed in obesity and may reflect enhanced energy extraction from the diet. However, some meta-analyses have reported inconsistent associations between the Firmicutes/Bacteroidetes ratio and obesity status, suggesting that microbial diversity and specific bacterial taxa may be more important markers than the ratio alone. Reduced microbial diversity observed in our study was also consistent with recent reviews demonstrating that obesity is associated with decreased microbial richness and altered gut microbial composition [29]. The present study showed that BMI had a positive correlation with Firmicutes/Bacteroidetes ratio ($r = 0.59$, $p < 0.001$) and a negative correlation with microbial diversity index ($r = -0.54$, $p < 0.001$). These findings suggested that obesity-related dysbiosis may contribute to altered appetite regulation and metabolic dysfunction. Asadi et al. reported that gut bacteria can modify the secretion of ghrelin, GLP-1, peptide YY, and leptin, thereby influencing hypothalamic neuroendocrine pathways involved in appetite and satiety. Similarly, SCFAs derived from microbial fermentation have been shown to stimulate the release of GLP-1 and peptide YY from enteroendocrine cells. Recent reviews also emphasized that the gut-brain axis plays an

important role in regulating appetite, glucose metabolism, and energy homeostasis through interactions among gut microbiota, gastrointestinal hormones, and neural signaling pathways [30].

Conclusion:-

Overall findings: The present study demonstrated that obesity was associated with significant alterations in gastrointestinal hormones, gut microbiota composition, insulin resistance, dyslipidemia, and inflammatory status. Obese individuals showed higher leptin levels, lower ghrelin, GLP-1, and peptide YY levels, increased Firmicutes abundance, higher Firmicutes/Bacteroidetes ratio, and reduced microbial diversity compared to non-obese controls. These changes were significantly associated with higher BMI and adverse metabolic parameters. The findings suggested that dysregulation of the gut–brain axis played an important role in the pathogenesis of obesity and its metabolic complications. Therefore, gastrointestinal hormones and gut microbiota may serve as potential biomarkers and therapeutic targets for obesity management.

Limitation

The present study had certain limitations. First, the sample size was relatively small, which may have limited the generalizability of the findings. Second, the cross-sectional design of the study did not allow assessment of causal relationships between gut microbiota, gastrointestinal hormones, and obesity. Third, dietary intake, physical activity, sleep pattern, and psychological factors, which could influence hormonal levels and gut microbial composition, were not evaluated in detail. In addition, microbiota analysis was limited to major bacterial phyla and did not assess species-level variations or functional microbial metabolites. Finally, long-term follow-up was not performed to determine the temporal relationship between gut–brain axis alterations and metabolic outcomes.

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