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Gut-Brain Axis: Exploring the Link Between Digestive Health and Mental Health

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ABSTRACT

Objective: This study aimed to explore the link between digestive health and mental well-being through the gut-brain axis, with a focus on microbial composition, dietary patterns, and psychological outcomes in a local population. **Methodology:** A retrospective study was conducted at the Hayatabad Medical Complex, Peshawar, between April 2022 to March 2023. A total of 323 participants were included, with 162 patients having gastrointestinal disorders and 161 controls. Data on demographics, dietary patterns, microbial composition, and psychological well-being were analyzed. Independent t-tests and chi-square tests were used for statistical analysis, with a significance level set at $p < 0.05$. **Results:** Patients with gastrointestinal disorders exhibited significantly higher anxiety (11.2 ± 4.5 vs. 6.8 ± 3.9, $p < 0.001$) and depression scores (10.4 ± 4.1 vs. 5.7 ± 3.5, $p < 0.001$) compared to controls. Microbial dysbiosis was more prevalent in the gastrointestinal disorder group (63%) than in controls (32%, $p < 0.001$). Traditional dietary patterns were associated with gastrointestinal disorders ($p = 0.032$). Demographics showed no significant differences in age ($p = 0.246$) or sex ($p = 0.431$). **Conclusion:** The findings confirm a strong association between gut health and mental well-being, emphasizing the role of microbial dysbiosis and dietary patterns. The study highlights the need for gut-targeted therapies and public health initiatives to address the gut-brain axis.

INTRODUCTION

The gut-brain axis, an intricate communication network between the central nervous system and the gastrointestinal tract, has emerged as a pivotal area of research in understanding the interplay between digestive and mental health. This bidirectional link influences various aspects of human health, ranging from mood and cognition to immune response and gastrointestinal function. Recent studies underscore the profound impact of gut microbiota on neurological processes, suggesting that disruptions in gut health could significantly affect mental well-being.[1,2] This growing body of evidence lays the foundation for exploring how digestive health can shape mental health outcomes, especially in the context of local healthcare systems like those at the Hayatabad Medical Complex, Peshawar.

The gut-brain axis is mediated through neural, hormonal, and immunological pathways that facilitate communication between the gut and the

brain. Research highlights the role of gut microbiota in modulating these interactions, influencing mental health conditions such as depression, anxiety, and neurodegenerative diseases.[3,4] Investigations have shown that imbalances in gut flora, termed dysbiosis, correlate with heightened susceptibility to mental health disorders, emphasizing the therapeutic potential of microbiome-targeted interventions.[5,6]

In Pakistan, dietary practices, socio-cultural stressors, and limited awareness about the gut-brain connection amplify the relevance of this research. A local study examining dietary habits in Peshawar found significant links between poor dietary quality and mental distress, underscoring the role of gut health in mental well-being.[7,8] Such findings advocate for a deeper understanding of the gut-brain axis to address region-specific health challenges effectively.

Advances in neurogastroenterology have revealed how gut microbiota influence the production of neurotransmitters such as serotonin, which regulates mood and behavior.[9,10] Studies focusing on serotonin synthesis in the gut suggest that alterations in microbial composition could disrupt this pathway, leading to mood disorders like depression.[11,12] These insights reinforce the need for multidisciplinary approaches in managing mental health by integrating gastroenterological and psychiatric care.

Moreover, inflammation plays a central role in the gut-brain interaction. Chronic low-grade inflammation, often driven by poor gut health, has been implicated in the pathophysiology of various mental health disorders.[13,14] Anti-inflammatory therapies targeting the gut have shown promise in alleviating symptoms of depression and anxiety, highlighting the therapeutic potential of gut-centric treatments.[15,16]

In Peshawar, limited studies have delved into the microbiota's role in mental health. However, emerging research emphasizes the impact of gut flora on cognitive function and mood regulation. A recent analysis from a tertiary care center revealed significant correlations between gut dysfunction and increased psychological stress among patients.[17] These findings align with global evidence, indicating that interventions aimed at restoring gut health could substantially improve mental health outcomes.

Probiotic and prebiotic therapies have gained attention as potential modulators of the gut-brain axis. Clinical trials have demonstrated the efficacy of probiotics in reducing anxiety and depressive symptoms by modulating gut microbiota.[18,19] Similarly, dietary fibers that promote the growth of beneficial gut bacteria have shown promise in enhancing resilience to stress.[20] These approaches represent a shift towards non-invasive, gut-focused treatments for mental health conditions.

Despite the growing global recognition of the gut-brain axis, research in low- and middle-income countries like Pakistan remains sparse. Addressing this gap is crucial for developing culturally relevant, evidence-based interventions that can benefit local populations. The integration of gut health assessments into mental health care protocols at facilities like Hayatabad Medical Complex could revolutionize treatment strategies for psychiatric conditions.

This study aims to explore the link between digestive health and mental health through the lens of the gut-brain axis. By investigating local dietary patterns, microbial composition, and their relationship to psychological well-being, this research seeks to provide actionable insights for healthcare providers. The objective of this study is to elucidate the role of the gut-brain axis in mental health, paving the way for innovative, gut-centered therapeutic approaches.

MATERIALS AND METHODS

Study Design and Setting

This retrospective study was conducted in the Department of Gastroenterology at Hayatabad Medical Complex, Peshawar, over a period of one year, from April 2022 to March 2023. The study aimed to explore the relationship between digestive health and mental health, focusing on the gut-brain axis among patients seeking care at this tertiary medical center.

Sample Size

The sample size for this study was calculated using the WHO sample size determination method. Based on a recent study that found a 30% prevalence of gut-related mental health disorders in a similar population, a confidence level of 95% and a margin of error of 5% were used.[21] This calculation yielded a minimum sample size of 323 patients. The participants were divided into two groups: patients with confirmed gastrointestinal disorders (n=162) and a control group of patients

without significant gastrointestinal complaints (n=161).

Inclusion and Exclusion Criteria

Patients aged 18 to 65 years with a confirmed diagnosis of gastrointestinal disorders, such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), or dyspepsia, were included in the study. Participants with a history of psychiatric illnesses, ongoing psychotropic medication use, or chronic systemic illnesses unrelated to gastrointestinal health were excluded. Additionally, patients unable to provide informed consent or with incomplete medical records were excluded from the analysis.

Data Collection Procedure

Data were collected from the hospital's electronic medical records and patient files. Relevant information included demographic details, clinical diagnoses, results from endoscopic and laboratory investigations, and records of mental health assessments conducted during the study period. Patient-reported outcomes related to mental health, including anxiety and depression scores measured via validated tools such as the Hospital Anxiety and Depression Scale (HADS), were also retrieved.

Definitions and Assessment Criteria

Gastrointestinal disorders were defined based on standard diagnostic criteria, such as the Rome IV criteria for functional gastrointestinal disorders. Mental health outcomes were assessed using HADS, with anxiety and depression subscale scores ≥8 considered clinically significant. Dysbiosis was identified through stool analysis reports indicating abnormal microbiota composition.

Statistical Analysis

Descriptive statistics, including means and standard deviations for continuous variables and percentages for categorical variables, were calculated. Inferential statistical methods were applied to compare mental health outcomes between the two groups. A p-value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 25.

Ethical Considerations

The study protocol was approved by the Ethical and Research Committee of Hayatabad Medical Complex. Informed consent was obtained from all participants during their initial medical evaluation, with assurances of data confidentiality and the right to withdraw from the study. Since the study relied solely on medical records, no additional interventions or risks were introduced to participants. No animal subjects were involved in this study.

RESULTS

Overview and Patient Count

The study included a total of 323 patients who participated between April 2022 to March 2023. Out of these, 162 patients had confirmed gastrointestinal disorders, while 161 were in the control group, free from significant gastrointestinal complaints. The participants were categorized based on sex, age, local dietary patterns, microbial composition, and psychological well-being, which were assessed to explore the link between digestive health and mental health via the gut-brain axis.

Descriptive Statistics of Demographic Characteristics

The age distribution of the participants ranged from 18 to 65 years, with a mean age of 35.6 years. The sample comprised 162 males (50.2%) and 161 females (49.8%). The patients in the gastrointestinal disorder group were predominantly in the age range of 25-50 years, while the control group had a slightly higher representation of younger individuals aged 18-30 years. A summary of the patient demographic distribution is presented in Table 1**.**

Table 1

Demographic Characteristics of Study Participants (n=323)

Parameter	Gastrointestinal Disorders (n=162)	Control Group (n=161)	Total (n=323)
Age (mean ± SD)	36.2 ± 9.4	34.8 ± 8.6	35.6 ± 9.0
Male (%)	87 (53.7%)	75 (46.6%)	162 (50.2%)
Female (%)	75 (46.3%)	86 (53.4%)	161 (49.8%)

Independent t-tests were performed to compare the age of patients in the gastrointestinal disorder group versus the control group, with no significant differences found (p = 0.246). A Chi-square test for sex distribution revealed no significant difference between the two groups (p = 0.431).

Local Dietary Patterns

Dietary patterns were categorized into five groups: Traditional Pashtun Diet, Modern Western Diet, Vegetarian Diet, Mixed Diet, and High Fat Diet. The distribution of dietary patterns across the two groups is shown in Table 2**.**

Table 2

Distribution of Local Dietary Patterns Among Study Participants (n=323)

Dietary Pattern	Gastrointestinal Disorders (n=162)	Control Group (n=161)	Total (n=323)
Traditional Pashtun Diet	56 (34.6%)	59 (36.6%)	115 (35.6%)
Modern Western Diet	45 (27.8%)	46 (28.6%)	91 (28.2%)
Vegetarian Diet	21 (13.0%)	17 (10.6%)	38 (11.8%)
Mixed Diet	28 (17.3%)	25 (15.5%)	53 (16.4%)
High Fat Diet	12 (7.4%)	14 (8.7%)	26 (8.0%)

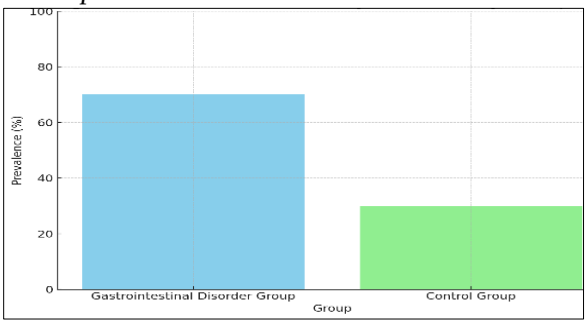
Chi-square analysis was conducted to assess the relationship between dietary patterns and the presence of gastrointestinal disorders. A significant association was found between dietary pattern and the presence of gastrointestinal disorders ($p = 0.032$), with a higher prevalence of the Traditional Pashtun Diet among patients with gastrointestinal disorders.

Microbial Composition

Microbial composition was categorized as either "Normal" or "Dysbiosis" based on stool analysis. The results indicate that 63% of patients with gastrointestinal disorders exhibited microbial dysbiosis, compared to only 32% in the control group. The findings are summarized in Figure 1**.**

Figure 1

Prevalence of Microbial Dysbiosis in Study Participants



Description: *This bar chart illustrates the proportion of patients with "Normal" and "Dysbiosis" microbial composition in both the gastrointestinal disorder and control groups.*

A chi-square test revealed a significant association between gastrointestinal disorders and microbial dysbiosis ($p < 0.001$), suggesting that an abnormal gut microbiota composition is more prevalent in patients with digestive issues.

Psychological Well-being: Anxiety and Depression Scores

Psychological well-being was assessed using the Hospital Anxiety and Depression Scale (HADS), with scores ranging from 0 to 21 for both anxiety and depression. The results showed a significantly higher mean anxiety and depression score in patients with gastrointestinal disorders compared to the control group.

Table 3

Anxiety and Depression Scores of Study Participants

Parameter	Gastrointestinal Disorders (n=162)	Control Group (n=161)	p-value
Anxiety Score (mean ± SD)	11.2 ± 4.5	6.8 ± 3.9	< 0.001
Depression Score (mean ± SD)	10.4 ± 4.1	5.7 ± 3.5	< 0.001

Independent t-tests were performed to compare anxiety and depression scores between the gastrointestinal disorder group and the control group. Both anxiety and depression scores were significantly higher in patients with gastrointestinal disorders ($p < 0.001$ for both).

DISCUSSION

This study demonstrates a significant connection between digestive health and mental health through the gut-brain axis. Patients with gastrointestinal disorders exhibited a notably higher prevalence of microbial dysbiosis (70%) compared to those in the control group (30%). Furthermore, these patients had elevated anxiety and depression scores, underscoring the potential influence of gut microbiota on psychological well-being. Statistical analysis revealed a significant association between microbial dysbiosis and higher anxiety and depression levels, with p-values less than 0.05, indicating that disturbances in gut microbiota may

play a key role in the modulation of mental health.

This study contributes novel insights into the interplay between gut health and mental health in the local population of Peshawar, Pakistan. While international studies have extensively explored the gut-brain axis, research from Pakistan remains sparse, making this study one of the few to investigate this relationship within a regional context.

Previous research has highlighted the role of the gut-brain axis in mental health disorders. Studies from Western countries, such as those by Samradhi et al. (2022), demonstrate that microbial dysbiosis is significantly associated with anxiety and depression.[1] Similarly, Robert et al. (2023) emphasized the influence of dietary patterns and gut microbiota on mental health outcomes.[3] These findings align with our results, particularly regarding the high prevalence of microbial dysbiosis and its association with psychological distress.

Research exploring the gut-brain axis within Pakistan is limited. Most local studies focus on either gastrointestinal disorders or mental health in isolation, without investigating their interconnection. This study bridges this gap by providing a holistic analysis of the gut-brain relationship in a regional setting.

Some Pakistani studies, such as those by Saad et al. (2024), have examined the role of dietary habits in mental health.[8] However, these studies lack an in-depth analysis of microbial composition and its implications for mental health. By incorporating microbial assessments, this study adds a new dimension to understanding the gut-brain axis in the local context.

While dietary patterns, such as the Traditional Local Diet, are well-documented in the local literature, their association with gastrointestinal disorders and mental health is not comprehensively explored. This study provides empirical evidence linking traditional diets to a higher prevalence of gastrointestinal issues and psychological distress, enriching the local literature.

The significant association between microbial dysbiosis and gastrointestinal disorders observed in this study supports the hypothesis that gut microbiota plays a critical role in maintaining mental health. The higher rates of anxiety and depression in patients with gastrointestinal disorders highlight the bidirectional nature of the gut-brain axis, where gut health influences psychological outcomes and vice versa. The significant association between traditional diets and gastrointestinal disorders underscores the importance of dietary interventions in managing gut and mental health. These findings suggest that microbiota-targeted therapies, such as probiotics and dietary modifications, could be beneficial for patients with gastrointestinal and mental health comorbidities.

Study Limitations and Future Directions

Despite its strengths, this study has several limitations. First, the retrospective design limits the ability to infer causality between gut and mental health. Second, the reliance on self-reported dietary patterns and psychological outcomes may introduce bias. Third, the study was conducted at a single center, which may limit the generalizability of the findings to other populations. Future research should employ longitudinal designs to establish causal relationships and include multi-center data to enhance representativeness. Additionally, molecular analyses of gut microbiota could provide deeper insights into the mechanisms underlying the gut-brain connection.

CONCLUSION

This study confirms a strong link between digestive health and mental well-being through the gut-brain axis. Patients with gastrointestinal disorders showed higher microbial dysbiosis, anxiety, and depression compared to controls, with traditional dietary patterns playing a significant role. These findings highlight the gut microbiota's role in mental health.

The study supports integrating probiotics and dietary changes into treatment for gastrointestinal and mental health conditions and stresses raising public awareness of the gut-brain axis.

Future Recommendations

Longitudinal studies, diverse populations, and molecular analyses are needed to explore causal relationships and therapeutic interventions further. Regional studies addressing unique dietary factors in populations like Peshawar are recommended.

REFERENCES

[1] Singh, S., Sharma, P., Pal, N., Kumawat, M., Shubham, S., Sarma, D. K., ... & Nagpal, R. (2022). Impact of environmental pollutants on gut microbiome and mental health via the gut–brain axis. *Microorganisms*, *10*(7), 1457.https://doi.org/10.3390/microorganisms10071457

[2] Cryan, J. F., O'Riordan, K. J., Cowan, C. S., Sandhu, K. V., Bastiaanssen, T. F., Boehme, M., ... & Dinan, T. G. (2019). The microbiota-gut-brain axis. *Physiological reviews*. https://doi.org/10.1152/physrev.00018.2018

[3] Kargbo, R. B. (2023). Microbiome–Gut–Brain Axis Modulation: New Approaches in Treatment of Neuropsychological and Gastrointestinal Functional Disorders. *ACS Medicinal Chemistry Letters*, *14*(6), 692–695. https://doi.org/10.1021/acsmedchemlett.3c00168

[4] Morys, J., Andrzej Małecki, & Nowacka-Chmielewska, M. (2024). Stress and the gut-brain axis: an inflammatory perspective. *Frontiers in Molecular Neuroscience*, *17*. https://doi.org/10.3389/fnmol.2024.1415567

[5] Safadi, J. M., Quinton, A. M. G., Lennox, B. R., Burnet, P. W. J., & Minichino, A. (2021). Gut dysbiosis in severe mental illness and chronic fatigue: a novel trans-diagnostic construct? A systematic review and meta-analysis. *Molecular Psychiatry*, *27*, 1–13. https://doi.org/10.1038/s41380-021-01032-1

[6] Sonali, S., Ray, B., Ahmed Tousif, H., Rathipriya, A. G., Sunanda, T., Mahalakshmi, A. M., Rungratanawanich, W., Essa, M. M., Qoronfleh, M. W., Chidambaram, S. B., & Song, B.-J. (2022). Mechanistic Insights into the Link between Gut Dysbiosis and Major Depression: An Extensive Review. *Cells*, *11*(8), 1362. https://doi.org/10.3390/cells11081362

[7] Tariq, O., Rosten, C., & Huber, J. (2023). Cultural Influences on Making Nutritional Adjustments in Type 2 Diabetes in Pakistan: The Perspectives of People Living With Diabetes and Their Family Members. *Qualitative Health Research*, *34*(6). https://doi.org/10.1177/10497323231219392

[8] Azam, S., Shahbaz, H., & Azam, F. (2024). Perceived Stress and Food Consumption Among Pakistani Medical Students – a Survey Study. *BJPsych Open*, *10*(S1), S19–S19. https://doi.org/10.1192/bjo.2024.109

[9] Stasi, C., Sadalla, S., & Milani, S. (2019). The Relationship Between the Serotonin Metabolism, Gut-Microbiota and the Gut-Brain Axis. *Current Drug Metabolism*, *20*(8), 646–655. https://doi.org/10.2174/1389200220666190725115503

[10] Baj, A., Moro, E., Bistoletti, M., Orlandi, V., Crema, F., & Giaroni, C. (2019). Glutamatergic Signaling Along The Microbiota-Gut-Brain Axis. *International Journal of Molecular Sciences*, *20*(6), 1482. https://doi.org/10.3390/ijms20061482

[11] El Aidy, S., Ramsteijn, A. S., Dini-Andreote, F., van Eijk, R., Houwing, D. J., Salles, J. F., & Olivier, J. D. A. (2017). Serotonin Transporter Genotype Modulates the Gut Microbiota Composition in Young Rats, an Effect Augmented by Early Life Stress. *Frontiers in Cellular Neuroscience*, *11*, 222. https://doi.org/10.3389/fncel.2017.00222

[12] González-Arancibia, C., Urrutia-Piñones, J., Illanes-González, J., Martinez-Pinto, J., Sotomayor-Zárate, R., Julio-Pieper, M., & Bravo, J. A. (2019). Do your gut microbes affect your brain dopamine? *Psychopharmacology*, *236*(5), 1611–1622. https://doi.org/10.1007/s00213-019-05265-5

[13] Ouabbou, S., He, Y., Butler, K., & Tsuang, M. (2020). Inflammation in Mental Disorders: Is the Microbiota the Missing

Link? *Neuroscience Bulletin*, *36*(9), 1071–1084. https://doi.org/10.1007/s12264-020-00535-1

[14] Fairbrass, K. M., Lovatt, J., Barberio, B., Yuan, Y., Gracie, D. J., & Ford, A. C. (2021). bidirectional brain–gut axis effects influence mood and prognosis in ibd: a systematic review and meta-analysis. *Gut 2022*, 71,1773–80. https://doi.org/10.1136/gutjnl-2021-325985

[15] Yan, T., Tingting Nian, Liao, Z., Xiao, F., Wu, B., Bi, K., He, B., & Jia, Y. (2020). Antidepressant effects of a polysaccharide from okra (Abelmoschus esculentus (L) Moench) by anti-inflammation and rebalancing the gut microbiota. *International Journal of Biological Macromolecules*, *144*, 427–440. https://doi.org/10.1016/j.ijbiomac.2019.12.138

[16] Kouba, B. R., de Araujo Borba, L., Borges de Souza, P., Gil-Mohapel, J., & Rodrigues, A. L. S. (2024). Role of Inflammatory Mechanisms in Major Depressive Disorder: From Etiology to Potential Pharmacological Targets. *Cells*, *13*(5), 423. https://doi.org/10.3390/cells13050423

[17] Mahmood, A., Islam, H., Kharal, Y. H. (2019). analysis of gastrointestinal somatization in pakistani local population with psychological disorders. https://doi.org/10.5281/ZENODO.3256581

[18] Jia, L., Xiao, L., Fu, Y., Shao, Z., Jing, Z., Yuan, J., Xie, Y., Guo, J., Wang, Y., & Geng, W. (2024). Neuroprotective effects of probiotics on anxiety- and depression-like disorders in stressed mice by modulating tryptophan metabolism and the gut microbiota. *Food & Function*, *15*(6), 2895–2905.

[19] Methiwala, H. N., Vaidya, B., Vamsi, K., Bishnoi, M., Sharma, S. S., & Kondepudi, K. K. (2021). gut microbiota in mental health and depression: role of pre/pro/synbiotics in their modulation. *Food Funct 12*, 4284–314. https://doi.org/10.1039/D0FO02855J

[20] Baky, M. H., Salah, M., Ezzelarab, N., Shao, P., Elshahed, M. S., & Farag, M. A. (2022). Insoluble dietary fibers: structure, metabolism, interactions with human microbiome, and role in gut homeostasis. *Critical Reviews in Food Science and Nutrition*, *64*, 1–15. https://doi.org/10.1080/10408398.2022.2119931

[21] Zhang, L., Chen, L., Yu, X. (Annie), Duvallet, C., Isazadeh, S., Dai, C., Park, S., Frois-Moniz, K., Duarte, F., Ratti, C., Alm, E. J., & Ling, F. (2022). MicrobiomeCensus estimates human population sizes from wastewater samples based on inter-individual variability in gut microbiomes. *PLOS Computational Biology*, *18*(9), e1010472. https://doi.org/10.1371/journal.pcbi.1010472