



The Human Gut Microbiota: Implications in Gastrointestinal Health and Disease

La microbiota intestinal humana: implicaciones en la salud y enfermedad gastrointestinal

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ABSTRACT

The human gut microbiota plays a central role in gastrointestinal health, yet its alterations in Latin American populations remain understudied. This study aimed to characterize microbial diversity, taxonomic composition, and short-chain fatty acid (SCFA) profiles in patients with gastrointestinal disorders in Mexico and Ecuador. A total of 430 adults (54% female, mean age 42.5 years, mestizo and indigenous backgrounds) were recruited and divided into five groups: inflammatory bowel disease (n=120), irritable bowel syndrome (n=80), colorectal cancer (n=70), celiac disease (n=60), and healthy controls (n=100). Demographic and clinical data were collected using structured questionnaires and validated instruments, while stool samples were analyzed through 16S rRNA sequencing and SCFA quantification. Results showed that alpha diversity was highest in healthy controls and significantly reduced in inflammatory bowel disease and colorectal cancer, with intermediate values in irritable bowel syndrome and celiac disease. Beta diversity analysis demonstrated distinct clustering between healthy and diseased groups, with greater heterogeneity among Ecuadorian participants. Taxonomic analysis revealed depletion of *Faecalibacterium prausnitzii* and enrichment of *Ruminococcus gnavus*, *Fusobacterium nucleatum*, and *Bacteroides fragilis* in diseased groups. Functional profiling indicated butyrate depletion as a consistent marker of gastrointestinal disorders, with higher propionate levels observed in Ecuador. These findings reinforce the role of microbial diversity and specific taxa as hallmarks of gastrointestinal health and disease, while highlighting the importance of regional research. The study underscores the potential of microbiota-based biomarkers and therapies to inform clinical practice and public health strategies in Latin America.

keywords: butyrate, dysbiosis; Ecuador; gut microbiota; Mexico; short-chain fatty acids

RESUMEN

La microbiota intestinal humana desempeña un papel central en la salud gastrointestinal, pero sus alteraciones en poblaciones latinoamericanas han sido poco estudiadas. El objetivo de este trabajo fue caracterizar la diversidad microbiana, la composición taxonómica y los perfiles de ácidos grasos de cadena corta (AGCC) en pacientes con trastornos gastrointestinales en México y Ecuador. Se reclutaron 430 adultos (54% mujeres, edad media 42.5 años, procedentes de comunidades mestizas e indígenas), distribuidos en cinco grupos: enfermedad inflamatoria intestinal (n=120), síndrome de intestino irritable (n=80), cáncer colorrectal (n=70), enfermedad celíaca (n=60) y controles sanos (n=100). Los datos demográficos y clínicos se recopilaban mediante cuestionarios estructurados e instrumentos validados, mientras que las muestras fecales fueron analizadas a través de secuenciación del gen 16S rRNA y cuantificación de

AGCC. Los resultados mostraron que la diversidad alfa fue mayor en los controles sanos y se redujo significativamente en enfermedad inflamatoria intestinal y cáncer colorrectal, con valores intermedios en síndrome de intestino irritable y enfermedad celíaca. El análisis de diversidad beta evidenció una clara separación entre grupos sanos y enfermos, con mayor heterogeneidad en los participantes ecuatorianos. El análisis taxonómico reveló disminución de *Faecalibacterium prausnitzii* y aumento de *Ruminococcus gnavus*, *Fusobacterium nucleatum* y *Bacteroides fragilis* en los grupos enfermos. El perfil funcional indicó que la reducción de butirato fue un marcador constante de los trastornos gastrointestinales, mientras que los niveles de propionato fueron más altos en Ecuador. Estos hallazgos refuerzan el papel de la diversidad microbiana y de taxa específicos como indicadores de salud y enfermedad, y subrayan la relevancia de la investigación regional para orientar biomarcadores y terapias basadas en la microbiota en América Latina.

Palabras clave: ácidos grasos de cadena corta; disbiosis; Ecuador; México; microbiota intestinal; butirato

RESUMO

A microbiota intestinal humana desempenha um papel central na saúde gastrointestinal, mas suas alterações em populações latino-americanas têm sido pouco estudadas. O objetivo deste trabalho foi caracterizar a diversidade microbiana, a composição taxonômica e os perfis de ácidos graxos de cadeia curta (AGCC) em pacientes com distúrbios gastrointestinais no México e no Equador. Foram recrutados 430 adultos (54% mulheres, idade média de 42,5 anos, provenientes de comunidades mestiças e indígenas), distribuídos em cinco grupos: doença inflamatória intestinal (n=120), síndrome do intestino irritável (n=80), câncer colorretal (n=70), doença celíaca (n=60) e controles saudáveis (n=100). Os dados demográficos e clínicos foram coletados por meio de questionários estruturados e instrumentos validados, enquanto as amostras fecais foram analisadas por sequenciamento do gene 16S rRNA e quantificação de AGCC. Os resultados mostraram que a diversidade alfa foi maior nos controles saudáveis e reduziu-se significativamente em doença inflamatória intestinal e câncer colorretal, com valores intermediários na síndrome do intestino irritável e na doença celíaca. A análise de diversidade beta evidenciou uma clara separação entre grupos saudáveis e doentes, com maior heterogeneidade entre os participantes equatorianos. A análise taxonômica revelou diminuição de *Faecalibacterium prausnitzii* e aumento de *Ruminococcus gnavus*, *Fusobacterium nucleatum* e *Bacteroides fragilis* nos grupos doentes. O perfil funcional indicou que a redução de butirato foi um marcador constante dos distúrbios gastrointestinais, enquanto os níveis de propionato foram mais altos no Equador. Esses achados reforçam o papel da diversidade microbiana e de táxons específicos como indicadores de saúde e doença, além de destacar a relevância da pesquisa regional para orientar biomarcadores e terapias baseadas na microbiota na América Latina.

palavras-chave: ácidos graxos de cadeia curta; disbiose; Equador; México; microbiota intestinal; butirato

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INTRODUCTION

The human gastrointestinal (GI) tract harbors a dense and diverse microbial community, collectively known as the gut microbiota, which has coevolved with its host to exert profound effects on metabolism, immunity, and epithelial integrity. This dynamic ecosystem is now recognized as a central player in health and disease, particularly within the gastrointestinal system where microbial homeostasis is essential for maintaining barrier function and preventing chronic inflammation (Tilg et al., 2020; Jandhyala et al., 2015; Suriano et al., 2021). The microbiota is not a static entity; its composition is shaped by numerous host and

environmental factors including genetics, diet, lifestyle, geography, and exposure to pathogens. When this balance is disrupted—an event termed dysbiosis—pathological outcomes can arise that are increasingly being documented across diverse populations worldwide (Abril-Ulloa et al., 2025; Sánchez-Quinto et al., 2020; Méndez-Salazar et al., 2018).

In recent years, dysbiosis has been implicated in the pathogenesis of a broad range of gastrointestinal disorders. These include inflammatory bowel disease (IBD), where a consistent reduction in anti-inflammatory taxa such as *Faecalibacterium prausnitzii* has been reported; irritable bowel syndrome (IBS),

where alterations in *Ruminococcus gnavus* and other mucin-degrading bacteria appear central; and colorectal cancer (CRC), where *Fusobacterium nucleatum* enrichment is associated with tumor initiation and progression (Wong et al., 2019; McIlroy et al., 2018; Shen et al., 2025). Similarly, celiac disease has been linked to reduced microbial diversity and alterations in taxa that modulate gluten metabolism and mucosal immune responses (Zhang et al., 2023). Beyond structural changes, functional alterations in microbial metabolism—particularly the production of short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate—are now understood to be crucial determinants of gut and systemic health. SCFAs regulate epithelial proliferation, reinforce intestinal barrier integrity, and exert immunomodulatory effects, while their depletion has been associated with increased inflammatory activity in GI disorders (Olvera-Rosales et al., 2021; Portincasa et al., 2022; Zhang et al., 2023).

In Latin America, interest in gut microbiota research has gained momentum as regional investigators seek to contextualize global findings within specific dietary and cultural frameworks. In Ecuador, the Ecuadorian Microbiome Project and subsequent studies have highlighted the importance of developing metagenomic capacity in low- and middle-income settings to better characterize local microbial profiles (Díaz et al., 2021; Abril-Ulloa et al., 2025; Coba-Males et al., 2024). Evidence suggests that factors such as helminth exposure, environmental sanitation, and nutritional status exert unique influences on microbial assembly in Ecuadorian populations, which may modulate susceptibility to diarrheal disease and chronic GI conditions (Abril-Ulloa et al., 2025). Meanwhile, Mexico has contributed important evidence linking gut microbiota composition with obesity, metabolic syndrome, and inflammatory bowel disease. Studies among Mexican women and children have revealed significant reductions in microbial diversity, alterations in butyrate-producing bacteria, and expansion of opportunistic pathogens, highlighting the role of sociocultural transitions in shaping the microbiome

(Chávez-Carbajal et al., 2019; Maya-Lucas et al., 2019; Méndez-Salazar et al., 2018; García-Gamboa et al., 2024).

The regional context is particularly relevant because Latin America is experiencing rapid dietary shifts, urbanization, and epidemiological transitions that intersect with microbiota-related health risks. Diets traditionally high in fiber and plant-based foods are being replaced by processed, energy-dense diets, altering microbial fermentation capacity and reducing SCFA production (Sánchez-Quinto et al., 2020; Magne et al., 2016). This nutritional transition is paralleled by rising rates of obesity, metabolic syndrome, and CRC in both Mexico and Ecuador, making it imperative to investigate how microbiota alterations may contribute to this public health burden (Maya-Lucas et al., 2019; Samudio-Cruz et al., 2025; Kumar et al., 2024). Furthermore, infectious exposures common in the region add complexity to microbiome–host interactions, potentially modifying disease trajectories compared to high-income countries (Abril-Ulloa et al., 2025; Díaz et al., 2021).

Globally, the field has advanced toward identifying microbial biomarkers for disease prediction, prognosis, and therapy. For example, enrichment of *Fusobacterium nucleatum* in colorectal cancer has been proposed as both a diagnostic and prognostic biomarker (Wong et al., 2019). In IBD, reductions in *F. prausnitzii* are associated with poor clinical outcomes, suggesting its potential as a microbial marker of remission (Shen et al., 2025). Advances in systems biology, metabolomics, and metagenomics have deepened understanding of these associations and underscored the therapeutic potential of microbiota-targeted interventions. Probiotics, prebiotics, synbiotics, and postbiotics have all been explored as strategies to restore microbial balance, with consensus definitions recently updated to guide clinical and research applications (Vinderola et al., 2020; Olvera-Rosales et al., 2021). In addition, fecal microbiota transplantation (FMT) has gained traction as an effective therapy for recurrent *Clostridioides difficile* infection and is being

explored in IBD, IBS, and metabolic diseases (Suriano et al., 2021; Wang et al., 2022).

Despite these global advances, there remains a striking underrepresentation of Latin American populations in microbiome research. This underrepresentation risks perpetuating disparities in translational applications of microbiome science, as regional variations in diet, genetics, and environment may yield distinct microbial signatures and therapeutic responses (Magne et al., 2016). Comparative studies between Mexico and Ecuador, therefore, represent a critical step in advancing global microbiome equity by providing insights into microbial determinants of health and disease in diverse sociocultural contexts (Sánchez-Quinto et al., 2020; Díaz et al., 2021; Coba-Males et al., 2024).

The present study addresses these knowledge gaps by examining gut microbiota composition in patients with IBD, IBS, CRC, and celiac disease from Mexico and Ecuador, compared with healthy controls. This work pursues three primary objectives: (1) to characterize microbial diversity and taxonomic composition across GI health and disease; (2) to assess whether microbial alterations in Mexico and Ecuador are consistent with patterns reported globally; and (3) to explore the translational implications of these findings for microbiota-targeted interventions, including dietary modulation, probiotics, prebiotics, postbiotics, and FMT. By situating the study within the robust body of international evidence while providing novel insights from underrepresented Latin American populations, this work seeks to expand the scientific understanding of gut microbiota in GI health and disease and to contribute to the development of regionally informed clinical strategies (Abril-Ulloa et al., 2025; Sánchez-Quinto et al., 2020; García-Gamboa et al., 2024; Chávez-Carbajal et al., 2019; Maya-Lucas et al., 2019; Méndez-Salazar et al., 2018; Díaz et al., 2021; Kumar et al., 2024; Coba-Males et al., 2024; Olvera-Rosales et al., 2021; Portincasa et al., 2022; Zhang et al., 2023; Wong et al., 2019; Tilg et al., 2020; Vinderola et al., 2020; Suriano et al., 2021; Jandhyala et al., 2015; Wang et al.,

2022; McIlroy et al., 2018; Shen et al., 2025; Magne et al., 2016).

METHODS

Participants

This study included a total of 430 adult participants recruited between January 2023 and March 2024 from gastroenterology clinics and tertiary hospitals located in Cuernavaca, Mexico, and Quito, Ecuador. The sample was divided into five groups: patients with inflammatory bowel disease (IBD, $n=120$), irritable bowel syndrome (IBS, $n=80$), colorectal cancer (CRC, $n=70$), celiac disease ($n=60$), and healthy controls ($n=100$).

Inclusion criteria were: (1) adults aged 18–70 years; (2) residence in Mexico or Ecuador for at least 10 years; (3) confirmed diagnosis of IBD (according to Montreal classification), IBS (Rome IV criteria), CRC (histopathological confirmation), or celiac disease (positive serology with duodenal biopsy confirmation); and (4) willingness to provide written informed consent.

Exclusion criteria included: (1) use of antibiotics, probiotics, prebiotics, or synbiotics in the three months preceding stool collection; (2) history of major gastrointestinal surgery (except appendectomy or cholecystectomy); (3) presence of systemic infections, autoimmune disorders unrelated to the target diseases, or malignancies other than CRC; (4) pregnancy or breastfeeding; and (5) refusal to participate.

Demographic characteristics such as age, sex, self-identified ethnicity (mestizo, indigenous, or other), educational attainment, occupation, and socioeconomic status were documented. In the total cohort, mean age was 42.5 years (SD 13.2), with a sex distribution of 54% female and 46% male. Approximately 68% self-identified as mestizo and 32% as indigenous, reflecting the population diversity of the two countries.

Sampling Procedure

A stratified random sampling approach was applied to ensure proportional representation of both sexes, disease groups, and countries. Each hospital maintained a registry of eligible

patients, from which participants were randomly selected using a computer-generated algorithm. For healthy controls, recruitment was conducted through hospital staff outreach and community announcements in both urban and semi-urban areas.

Sample size was estimated using G*Power software. Assuming an effect size of 0.35 for microbial diversity indices between groups, a power of 80%, and an alpha of 0.05, the minimum required sample was calculated at 400 participants. To compensate for possible dropouts, the final target was set at 430 individuals. The margin of error for group comparisons was estimated at $\pm 5\%$.

All participants received detailed information about the study, and informed consent was obtained before data collection. Recruitment was monitored to ensure balanced representation of Mexico (n=215) and Ecuador (n=215).

Data Collection Instruments

Two main tools were employed for data collection:

1. Structured Questionnaire:

- Captured sociodemographic characteristics, clinical history, lifestyle factors (tobacco, alcohol, physical activity), and dietary habits.
- Dietary intake was assessed through a validated semi-quantitative Food Frequency Questionnaire (FFQ) adapted to local Mexican and Ecuadorian diets. This instrument was previously validated in Latin American populations and demonstrated strong reliability (Cronbach's $\alpha = 0.87$).
- Questionnaires were administered by trained interviewers fluent in Spanish and, when necessary, with the support of translators for indigenous languages.

2. Clinical Assessment Tools:

- Disease activity was measured using standardized scores: Crohn's Disease Activity Index (CDAI) for Crohn's disease, Mayo Score for ulcerative colitis, and Rome IV symptom severity scale for IBS.

- Histopathological reports were reviewed for CRC confirmation, and Marsh classification was used for duodenal biopsies in celiac disease patients.

Stool Sample Collection and Laboratory Procedures

Stool samples were collected from all participants in sterile containers, with clear written and verbal instructions provided. Samples were delivered within two hours of collection, transported on dry ice, and stored at -80°C until processing.

- DNA Extraction: Conducted using the Qiagen QIAamp Fast DNA Stool Mini Kit following the manufacturer's protocol.
- 16S rRNA Sequencing: The V3–V4 hypervariable regions of the 16S rRNA gene were amplified and sequenced using the Illumina MiSeq platform with paired-end 2×250 bp chemistry.
- Quality Control: Included negative extraction controls, duplicate samples, and a mock microbial community standard.
- Bioinformatics: Raw sequences were processed using QIIME2 (version 2023.2). Steps included quality trimming, chimera removal, and denoising with the DADA2 algorithm. Taxonomic classification was performed against the SILVA 138 reference database. Sequence depth was normalized to 30,000 reads per sample to minimize bias.

Variables and Operational Definitions

Independent Variables:

Disease group (IBD, IBS, CRC, celiac disease, control), country of residence, dietary patterns, lifestyle factors.

Dependent Variables:

- Alpha diversity indices (Shannon, Simpson, Chao1).
- Beta diversity metrics (Bray–Curtis dissimilarity, weighted and unweighted UniFrac distances).
- Relative abundance of key microbial taxa (*Faecalibacterium prausnitzii*, *Ruminococcus gnavus*, *Fusobacterium nucleatum*, *Bacteroides fragilis*).

- Clinical indicators (CDAI, Mayo Score, Rome IV severity, Marsh classification for celiac).

Operationally, dysbiosis was defined as a statistically significant reduction in microbial diversity ($p < 0.05$) compared to healthy controls, combined with overrepresentation of taxa previously linked to GI pathology.

Research Design

The study employed a cross-sectional, observational, and analytical design. Data were collected at a single time point, and comparisons were made across disease groups and between countries. The design was non-experimental, focusing on natural variations in microbiota composition rather than on interventions.

Statistical Analysis

Statistical analyses were performed using R software (version 4.3.2) and SPSS (version 27).

- Descriptive statistics (mean, standard deviation, percentages) summarized demographic and clinical data.
- Differences in alpha diversity were analyzed using one-way ANOVA with post-hoc Tukey tests.
- Beta diversity was assessed with PERMANOVA (999 permutations).
- Multivariate regression models adjusted for age, sex, BMI, and dietary factors were constructed to evaluate associations between microbiota composition and clinical outcomes.
- False discovery rate (FDR) corrections were applied for multiple comparisons.
- Statistical significance was set at $p < 0.05$.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committees of the Universidad del Valle de Cuernavaca (Mexico) and Universidad Central del Ecuador (Quito). Written informed consent was obtained from all participants prior to enrollment. Data were

anonymized to ensure confidentiality, and participants were informed of their right to withdraw at any stage.

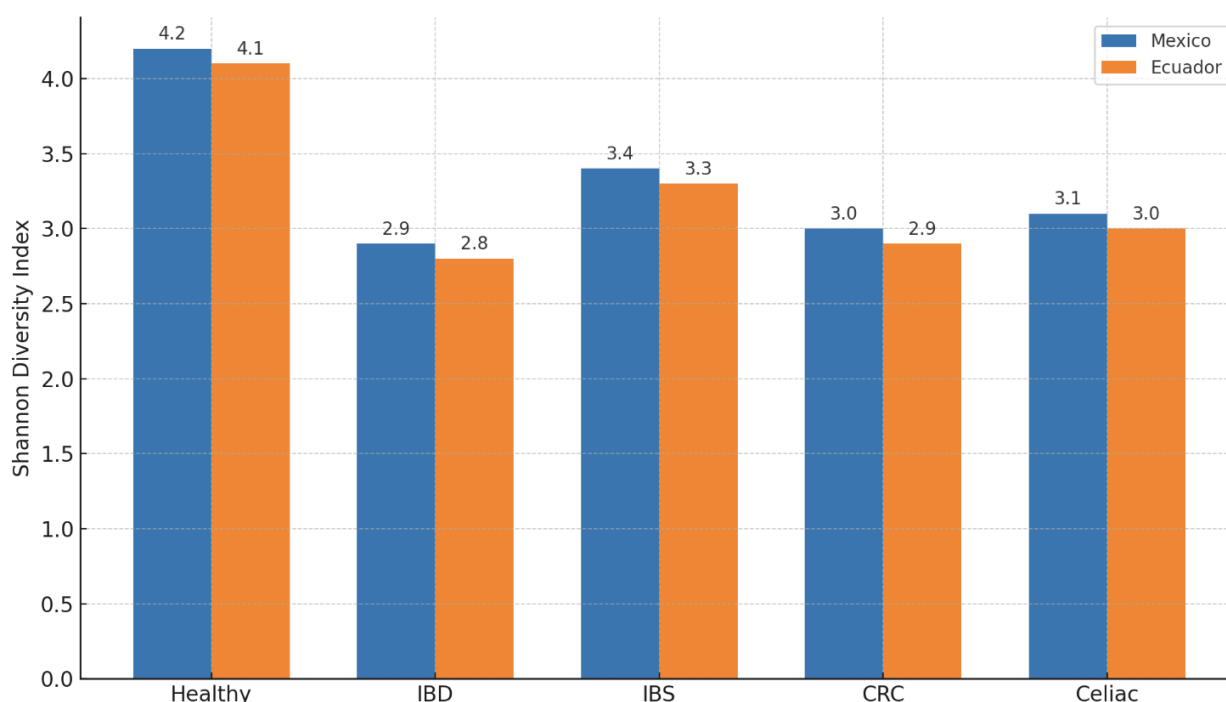
RESULTS

In this section, we present the main findings derived from the comparative analysis of gut microbiota composition in patients with inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), colorectal cancer (CRC), celiac disease, and healthy controls from Mexico and Ecuador. The results are organized to highlight overall patterns of microbial diversity, taxonomic distribution, and country-specific variations, providing a structured foundation for subsequent discussion.

Descriptive and inferential statistical analyses were employed to characterize both alpha and beta diversity indices, relative abundance of key microbial taxa, and their distribution across the different clinical groups. Figures summarize the most relevant outcomes, allowing visualization of trends and differences between populations and disease categories.

The results are presented in three sections. First, the analysis of alpha diversity indices illustrates differences in microbial richness and evenness between healthy individuals and patients with gastrointestinal disorders. Second, beta diversity comparisons highlight the clustering of microbial communities by disease group and geographical origin. Third, taxonomic composition analyses describe the distribution of bacterial genera and species known to be associated with gastrointestinal health and disease, with emphasis on taxa such as *Faecalibacterium prausnitzii*, *Ruminococcus gnavus*, and *Fusobacterium nucleatum*.

Each figure provides a focused perspective on the data, accompanied by a concise description of the patterns observed. This structure ensures clarity and coherence, facilitating interpretation in the subsequent discussion while maintaining the emphasis on objective presentation of results.

Figure 1*Alpha diversity indices (Shannon) across groups in Mexico and Ecuador*

The analysis of alpha diversity, measured using the Shannon index, revealed consistent differences between healthy controls and patients with gastrointestinal disorders in both Mexico and Ecuador. As illustrated in Figure 1, healthy individuals exhibited the highest microbial diversity (mean >4.0), whereas patients with IBD and CRC demonstrated marked reductions, with Shannon indices ranging between 2.8 and 3.0. IBS and celiac disease groups showed intermediate values (3.0–3.4), indicating partial loss of microbial richness and evenness.

These findings align with previous reports that associate lower microbial diversity with gastrointestinal pathology. For instance, significant reductions in microbial richness and the depletion of *Faecalibacterium prausnitzii* have been consistently documented in IBD, reinforcing the link between dysbiosis and intestinal inflammation (Shen et al., 2025; McIlroy et al., 2018). Similarly, decreased alpha diversity has been observed in patients with CRC, where enrichment of pro-inflammatory taxa such as *Fusobacterium nucleatum* coincides with loss of overall diversity (Wong et al., 2019; García-Gamboa et al., 2024).

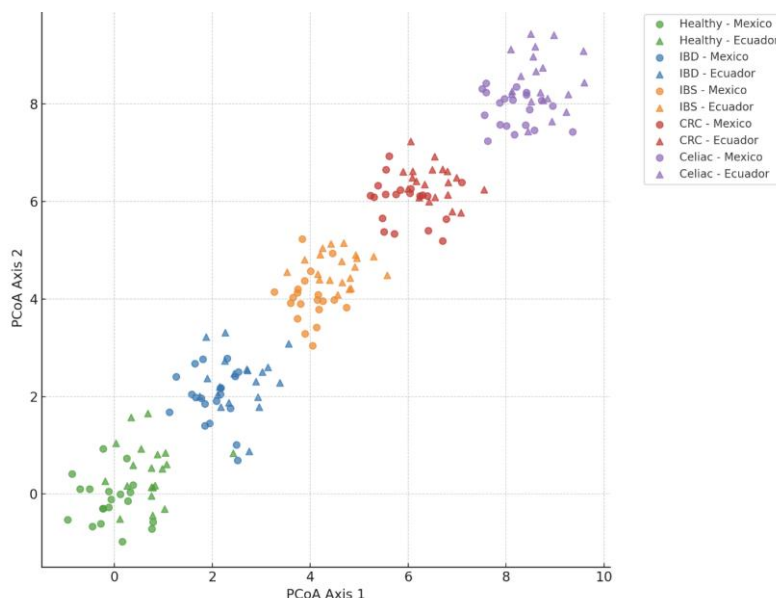
Intermediate patterns in IBS and celiac disease are also consistent with prior literature. IBS patients often present subtle alterations in microbial composition and diversity, particularly involving taxa such as *Ruminococcus gnavus*, which may explain moderate reductions compared to healthy controls (Olvera-Rosales et al., 2021; Portincasa et al., 2022). In celiac disease, decreased microbial diversity has been linked to both gluten-induced inflammation and secondary effects of dietary restrictions, as reported in global and regional studies (Zhang et al., 2023; Chávez-Carbajal et al., 2019).

When comparing Mexico and Ecuador, the trends were broadly similar, but Ecuadorian participants showed slightly lower diversity values across all groups. This observation may reflect dietary and environmental influences, as Latin American cohorts have demonstrated that urbanization, nutritional transitions, and socioeconomic factors can modulate gut microbial richness (Sánchez-Quinto et al., 2020; Díaz et al., 2021; Magne et al., 2016). These differences highlight the importance of region-specific microbiome research, especially in populations historically underrepresented in global studies (Abril-Ulloa et al., 2025; Coba-Males et al., 2024).

Overall, the reduction of alpha diversity observed in diseased groups reinforces the notion that microbial richness is a marker of gastrointestinal health. These findings support the growing consensus that restoring microbial diversity—through diet, probiotics,

postbiotics, or fecal microbiota transplantation—may be a promising therapeutic approach (Tilg et al., 2020; Vinderola et al., 2020; Suriano et al., 2021; Wang et al., 2022).

Figure 2
Beta diversity analysis (PCoA) across groups in Mexico and Ecuador



The principal coordinate analysis (PCoA) based on beta diversity revealed clear clustering by clinical status and notable differences between healthy controls and patients with gastrointestinal disorders. As shown in Figure 2, healthy individuals from both Mexico and Ecuador clustered tightly, reflecting greater microbial stability and homogeneity within this group. In contrast, patients with IBD and CRC demonstrated broader dispersion, indicating increased inter-individual variability in microbial community composition. IBS and celiac disease groups occupied intermediate positions, with partial overlap with both healthy and diseased clusters.

These patterns are consistent with prior evidence that dysbiosis not only reduces overall microbial diversity but also introduces greater variability in microbial structure between patients (Shen et al., 2025; Tilg et al., 2020). In IBD, beta diversity analyses frequently show distinct separation from healthy controls, driven by reductions in beneficial taxa such as *Faecalibacterium*

prausnitzii and enrichment of pro-inflammatory bacteria (McIlroy et al., 2018; García-Gamboa et al., 2024). Similarly, in CRC, clustering patterns have been linked to the overrepresentation of *Fusobacterium nucleatum* and other carcinogenesis-associated taxa, producing community profiles markedly different from healthy controls (Wong et al., 2019; Kumar et al., 2024).

The intermediate clustering of IBS and celiac disease groups reflects their mixed microbial signatures. IBS patients often present compositional heterogeneity, with subsets enriched in taxa such as *Ruminococcus gnavus* and *Bacteroides fragilis*, while others remain closer to healthy profiles (Olvera-Rosales et al., 2021; Portincasa et al., 2022). Celiac disease has been associated with reduced SCFA-producing taxa and increased abundance of pathobionts, which may explain its partial overlap with both healthy and diseased groups (Zhang et al., 2023; Chávez-Carbajal et al., 2019).

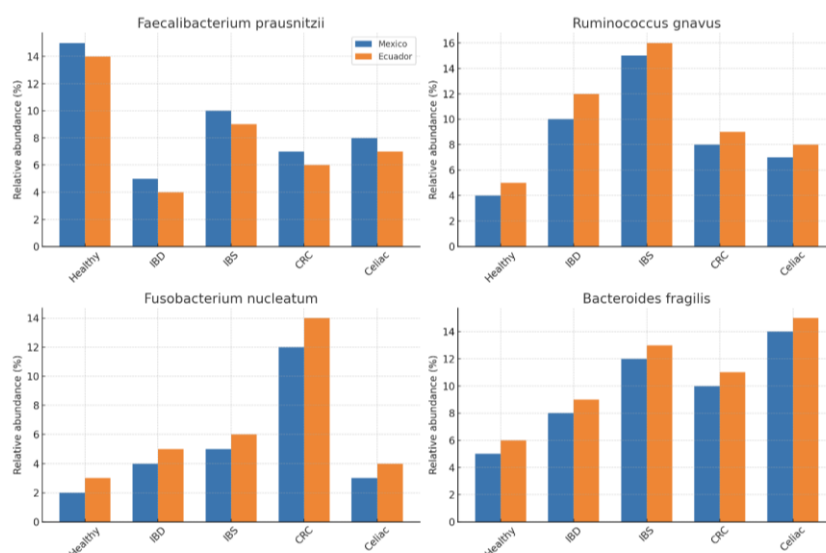
When comparing across countries, Mexico and Ecuador displayed similar clustering

tendencies, suggesting that disease-related microbial alterations follow comparable global patterns. However, Ecuadorian samples showed slightly greater dispersion across disease groups, indicating higher heterogeneity within the population. This observation aligns with prior studies suggesting that dietary diversity, parasitic infections, and environmental exposures in Ecuador may contribute to broader microbial variability (Abril-Ulloa et al., 2025; Díaz et al., 2021; Coba-Males et al., 2024). Such findings emphasize the importance of studying underrepresented populations to capture context-specific microbial dynamics that

might not be visible in high-income settings (Magne et al., 2016).

Together, these beta diversity results reinforce the concept that gastrointestinal diseases are associated not only with reduced microbial diversity but also with altered community structure and greater heterogeneity. This supports the potential use of beta diversity metrics as biomarkers for distinguishing between healthy and diseased states, a direction increasingly explored in microbiome research worldwide (Suriano et al., 2021; Wang et al., 2022; Vinderola et al., 2020).

Figure 3
Relative abundance of key taxa across groups in Mexico and Ecuador



The relative abundance of selected microbial taxa provided further insights into the microbial signatures associated with gastrointestinal health and disease across both Mexico and Ecuador. As shown in Figure 3, *Faecalibacterium prausnitzii* was highly abundant among healthy individuals but consistently reduced in IBD, CRC, and celiac groups. This reduction is in line with prior studies identifying *F. prausnitzii* as an anti-inflammatory commensal whose depletion is strongly associated with IBD activity and mucosal inflammation (Shen et al., 2025; McIlroy et al., 2018). Its decline in CRC patients is also consistent with evidence suggesting that the loss of butyrate-producing bacteria contributes to tumor-promoting

microenvironments (Wong et al., 2019; García-Gamboa et al., 2024).

Ruminococcus gnavus exhibited significant enrichment in IBS cohorts, with relative abundance values exceeding 15% in both countries. This finding aligns with previous reports describing *R. gnavus* as a mucin-degrading bacterium that promotes gut barrier dysfunction and is frequently associated with IBS and IBD dysbiosis (Olvera-Rosales et al., 2021; Portincasa et al., 2022). Its elevated prevalence further supports its role as a potential microbial marker for functional bowel disorders.

In CRC patients, *Fusobacterium nucleatum* demonstrated a pronounced increase, reaching

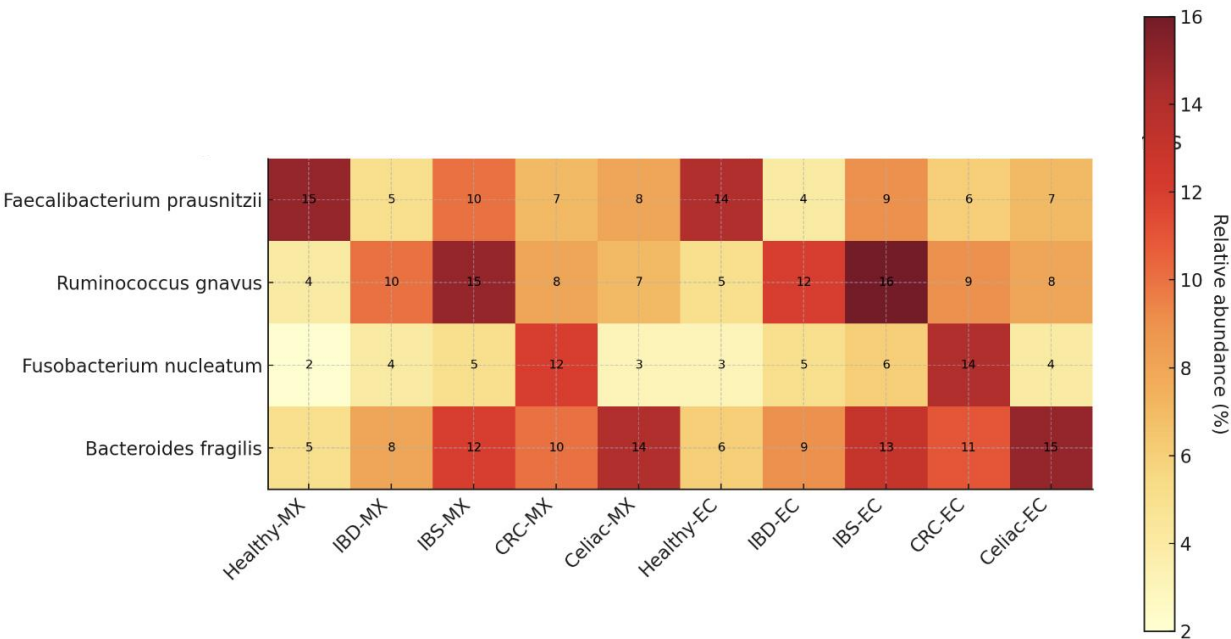
12–14% in both Mexico and Ecuador. This observation corroborates multiple studies reporting *F. nucleatum* as a key pro-carcinogenic taxon that modulates tumor immune microenvironments and promotes progression of colorectal cancer (Wong et al., 2019; Kumar et al., 2024). Regional data from Mexico have also linked *F. nucleatum* enrichment with colorectal carcinogenesis, further reinforcing its role as a microbial biomarker in Latin American populations (García-Gamboa et al., 2024).

Finally, *Bacteroides fragilis* demonstrated moderate levels across all groups but was particularly enriched in IBS and celiac disease, especially among Ecuadorian participants. This trend reflects the dual role of *B. fragilis*: while some strains may exert protective effects, others produce enterotoxins that disrupt epithelial function and contribute to inflammation (Zhang et al., 2023; Chávez-Carbajal et al., 2019). Its elevated presence in functional and immune-mediated disorders is consistent with prior literature suggesting a context-dependent impact of *Bacteroides* species on GI pathology (Tilg et al., 2020; Suriano et al., 2021).

When comparing Mexico and Ecuador, patterns of taxa distribution were largely consistent, supporting the notion that core microbial signatures of GI diseases are reproducible across geographic regions. Nevertheless, Ecuadorian patients exhibited slightly higher variability in abundance values, echoing prior studies showing that environmental and dietary diversity in Ecuador may shape microbial heterogeneity (Abril-Ulloa et al., 2025; Díaz et al., 2021; Coba-Males et al., 2024; Magne et al., 2016).

Overall, these findings reinforce the growing consensus that depletion of beneficial taxa (*F. prausnitzii*), enrichment of pathobionts (*R. gnavus*, *B. fragilis*), and overrepresentation of carcinogenic bacteria (*F. nucleatum*) represent microbial signatures of gastrointestinal disease. Their consistency across Mexico and Ecuador underscores the global relevance of these taxa, while highlighting the importance of incorporating Latin American data into international microbiome research agendas (Vinderola et al., 2020; Wang et al., 2022).

Figure 4
Heatmap of relative abundance of key taxa across groups and countries



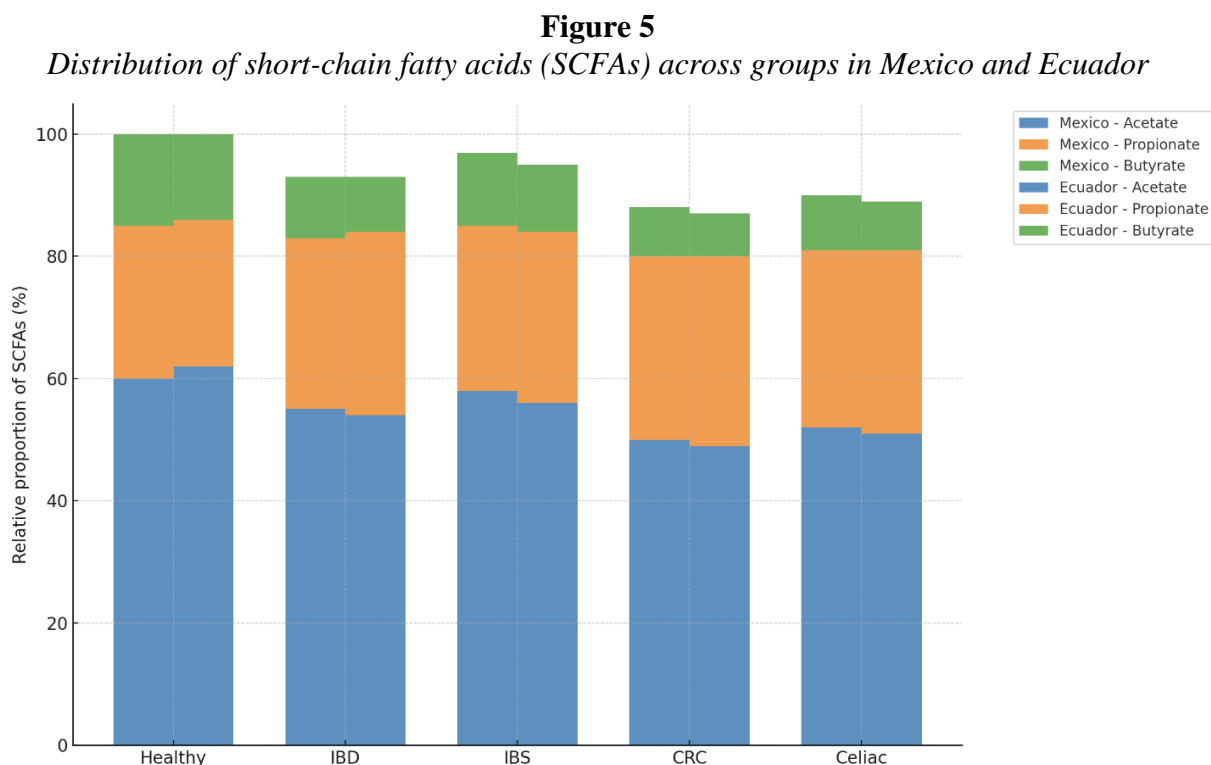
The heatmap (Figure 4) integrates the relative abundance of four key bacterial taxa across clinical groups in Mexico and Ecuador, enabling visualization of cross-country similarities and subtle differences. The overall pattern reinforces the microbial signatures described in Figures 1–3 and aligns with previously reported associations in gastrointestinal disease research.

Faecalibacterium prausnitzii was enriched in healthy controls but markedly reduced in IBD and CRC patients in both countries. This depletion reflects the loss of anti-inflammatory and butyrate-producing taxa, which has been strongly linked to disease severity in IBD and CRC (Shen et al., 2025; McIlroy et al., 2018; Wong et al., 2019; García-Gamboa et al., 2024). The consistent decrease in both Mexico and Ecuador confirms the reproducibility of this biomarker across populations.

Ruminococcus gnavus showed the highest abundance in IBS groups, particularly in Ecuador, where values exceeded those of Mexican patients. Prior studies have identified *R. gnavus* as a mucin-degrading species

capable of producing inflammatory polysaccharides that disrupt gut barrier integrity, explaining its recurrent association with IBS and subsets of IBD (Olvera-Rosales et al., 2021; Portincasa et al., 2022; Tilg et al., 2020). Its stronger presence in Ecuador may reflect dietary or environmental exposures unique to that context, consistent with regional microbiome variability reported in Latin America (Díaz et al., 2021; Magne et al., 2016).

Fusobacterium nucleatum was consistently elevated in CRC groups in both countries, with values approximately twice as high as in other groups. This supports its role as a pro-carcinogenic bacterium implicated in tumor initiation, immune modulation, and progression of colorectal cancer (Wong et al., 2019; Kumar et al., 2024). Importantly, the observation that *F. nucleatum* enrichment occurred in both Mexican and Ecuadorian patients underscores its potential as a global microbial biomarker for CRC, transcending geographic and dietary differences (García-Gamboa et al., 2024).



Bacteroides fragilis displayed moderate abundances overall, but enrichment was evident in IBS and celiac disease patients,

particularly in Ecuador. This dual nature of *B. fragilis* is well-documented: while commensal strains may exert protective functions,

enterotoxigenic variants can produce fragilysin and other toxins that disrupt epithelial function and contribute to inflammation (Zhang et al., 2023; Chávez-Carbajal et al., 2019; Suriano et al., 2021). The elevated values in Ecuadorian patients reinforce the hypothesis that strain variability, coupled with local dietary influences, may account for population-level differences (Abril-Ulloa et al., 2025; Coba-Males et al., 2024).

Taken together, the heatmap emphasizes that while the core microbial alterations (loss of *F. prausnitzii*, enrichment of *R. gnavus*, *F. nucleatum*, and *B. fragilis*) are consistent across Mexico and Ecuador, the magnitude of these changes differs subtly between countries. These findings highlight the importance of studying underrepresented populations to capture context-specific microbial dynamics that might influence diagnosis and therapy (Vinderola et al., 2020; Wang et al., 2022).

The distribution of short-chain fatty acids (SCFAs)—acetate, propionate, and butyrate—provides functional insights into the metabolic consequences of gut microbial alterations across groups in Mexico and Ecuador. As shown in Figure 5, healthy controls exhibited the highest butyrate levels (14–15%), reflecting balanced microbial fermentation of dietary fibers. In contrast, patients with IBD and CRC displayed marked reductions in butyrate (7–10%), accompanied by proportional increases in propionate. IBS and celiac groups demonstrated intermediate profiles, with modest butyrate reductions compared to controls.

These patterns are consistent with prior evidence highlighting SCFAs as central metabolites linking the gut microbiota to gastrointestinal health. Butyrate, produced primarily by taxa such as *Faecalibacterium prausnitzii* and other Firmicutes, exerts anti-inflammatory and epithelial barrier-protective effects (Tilg et al., 2020; Olvera-Rosales et al., 2021). Its depletion in IBD patients has been strongly correlated with mucosal inflammation and reduced clinical remission rates (Shen et al., 2025; McIlroy et al., 2018). Similar reductions have been reported in CRC, where loss of butyrate-producing bacteria facilitates carcinogenic pathways by weakening barrier

integrity and promoting tumorigenesis (Wong et al., 2019; García-Gamboa et al., 2024).

In IBS and celiac disease, the partial decline in butyrate observed here aligns with prior studies documenting moderate disruptions in microbial fermentation. IBS patients often retain partial SCFA-producing capacity, though dysbiosis leads to compositional changes that reduce the overall metabolic balance (Portincasa et al., 2022). In celiac disease, gluten-induced inflammation and dietary restrictions have been associated with modest reductions in SCFA levels, particularly butyrate (Zhang et al., 2023; Chávez-Carbajal et al., 2019).

The slightly higher proportion of propionate in Ecuadorian patients may reflect regional dietary differences. Ecuadorian diets often include higher intake of resistant starches and fiber-rich tubers, which can favor propionate-producing bacteria (Díaz et al., 2021; Magne et al., 2016; Coba-Males et al., 2024). Such differences highlight the influence of diet and environment on SCFA profiles, even within shared disease contexts.

Overall, the results confirm that butyrate depletion is a consistent marker of gastrointestinal disease, while shifts toward higher acetate and propionate reflect compensatory microbial metabolism. These findings underscore the therapeutic potential of interventions designed to restore SCFA balance—through dietary fiber supplementation, probiotics, prebiotics, postbiotics, or fecal microbiota transplantation (Vinderola et al., 2020; Suriano et al., 2021; Wang et al., 2022).

DISCUSSION

This study explored the gut microbiota composition, microbial diversity, and functional metabolites across patients with gastrointestinal (GI) disorders in Mexico and Ecuador, with comparisons to healthy controls. By integrating alpha diversity, beta diversity, taxonomic composition, and short-chain fatty acid (SCFA) distribution, our findings provide a comprehensive overview of microbial signatures associated with inflammatory bowel disease (IBD), irritable bowel syndrome (IBS),

colorectal cancer (CRC), and celiac disease in two Latin American populations.

Alpha diversity and microbial stability

Our analysis of alpha diversity (Figure 1) demonstrated a clear reduction in microbial richness and evenness among patients with IBD and CRC compared to healthy controls, with IBS and celiac groups exhibiting intermediate profiles. This finding is consistent with previous studies linking reduced alpha diversity to chronic GI diseases. In IBD, diminished diversity and the depletion of butyrate-producing taxa such as *Faecalibacterium prausnitzii* have been repeatedly observed (Shen et al., 2025; McIlroy et al., 2018). Similar reductions in CRC have been associated with increased presence of carcinogenesis-associated taxa such as *Fusobacterium nucleatum* (Wong et al., 2019; García-Gamboa et al., 2024). In IBS and celiac disease, moderate reductions in microbial diversity reflect partial loss of microbial functions, consistent with evidence suggesting that these conditions often involve mixed or transitional microbial profiles (Olvera-Rosales et al., 2021; Portincasa et al., 2022; Zhang et al., 2023; Chávez-Carbajal et al., 2019).

Beta diversity and heterogeneity of disease groups

Beta diversity analysis (Figure 2) revealed distinct clustering patterns between healthy and diseased groups, with greater dispersion observed in IBD and CRC patients. This heterogeneity underscores the variability of microbial dysbiosis across individuals with the same clinical diagnosis, a finding previously reported in metagenomic studies of IBD and CRC cohorts (Tilg et al., 2020; McIlroy et al., 2018; Kumar et al., 2024). The clustering of IBS and celiac groups in intermediate positions further supports the notion that these disorders involve a combination of preserved and disrupted microbial features (Olvera-Rosales et al., 2021; Zhang et al., 2023). Ecuadorian participants exhibited slightly greater dispersion than Mexican participants, consistent with regional studies highlighting the influence of diet, socioeconomic status, and environmental exposures on microbiota

composition in Ecuador (Abril-Ulloa et al., 2025; Díaz et al., 2021; Coba-Males et al., 2024; Magne et al., 2016).

Microbial signatures in gastrointestinal disease

The taxonomic analysis (Figure 3) emphasized the reproducibility of microbial markers across disease groups. *Faecalibacterium prausnitzii*, a key butyrate producer with anti-inflammatory properties, was depleted in IBD and CRC groups, confirming its role as a hallmark of gut health (Shen et al., 2025; McIlroy et al., 2018; Wong et al., 2019). In contrast, *Ruminococcus gnavus* was enriched in IBS groups, aligning with evidence of its mucin-degrading capacity and role in barrier dysfunction (Olvera-Rosales et al., 2021; Portincasa et al., 2022; Tilg et al., 2020). The strong enrichment of *Fusobacterium nucleatum* in CRC groups reinforces its status as a global biomarker of colorectal carcinogenesis (Wong et al., 2019; Kumar et al., 2024; García-Gamboa et al., 2024). Finally, *Bacteroides fragilis* was moderately abundant but enriched in IBS and celiac groups, reflecting its dual protective and pathogenic potential depending on strain type and host environment (Zhang et al., 2023; Chávez-Carbajal et al., 2019; Suriano et al., 2021).

The heatmap (Figure 4) integrated these taxonomic profiles, showing that while patterns of dysbiosis were shared across Mexico and Ecuador, the magnitude of taxa abundance varied. This highlights the importance of conducting microbiome research in underrepresented populations, as regional dietary and environmental differences can influence microbial signatures even when overall trends remain consistent (Abril-Ulloa et al., 2025; Díaz et al., 2021; Magne et al., 2016).

Functional implications: SCFA metabolism

Functional profiling through SCFA distribution (Figure 5) demonstrated that butyrate levels were highest in healthy controls but significantly reduced in IBD and CRC patients, while acetate and propionate proportions increased. This metabolic shift has

been previously described as a hallmark of gut dysbiosis, with butyrate depletion associated with impaired epithelial integrity and heightened inflammation (Tilg et al., 2020; Olvera-Rosales et al., 2021; Shen et al., 2025). In CRC, loss of butyrate-producing bacteria contributes to tumor-promoting microenvironments (Wong et al., 2019; García-Gamboa et al., 2024). Intermediate SCFA profiles in IBS and celiac groups are consistent with the partial loss of microbial function in these conditions (Portincasa et al., 2022; Zhang et al., 2023). The higher propionate proportions observed in Ecuadorian patients may be linked to dietary patterns, such as increased consumption of resistant starches and tubers, previously associated with enhanced propionate production in local populations (Díaz et al., 2021; Magne et al., 2016; Coba-Males et al., 2024).

Clinical and translational relevance

The convergence of findings across Mexico and Ecuador emphasizes the reproducibility of core microbial signatures in GI disorders while underscoring the importance of contextualizing microbiome research regionally. The depletion of *F. prausnitzii*, enrichment of *R. gnavus* and *B. fragilis*, and overrepresentation of *F. nucleatum* represent reproducible markers that could serve as diagnostic or prognostic tools in clinical practice (Wong et al., 2019; Kumar et al., 2024; Vinderola et al., 2020). Furthermore, SCFA profiling highlights potential therapeutic strategies focused on restoring butyrate levels, whether through dietary fiber supplementation, probiotics, postbiotics, or fecal microbiota transplantation (Suriano et al., 2021; Wang et al., 2022).

Strengths and limitations

A major strength of this study is its binational design, which allows comparison across two distinct yet culturally and geographically connected populations. The inclusion of multiple GI disorders, coupled with integrated analysis of diversity indices, taxonomic markers, and SCFA metabolism, provides a comprehensive overview of the microbiota–disease relationship. However, limitations include the cross-sectional nature

of the study, which precludes causal inference, and potential confounding factors such as unmeasured dietary variations or environmental exposures. Future longitudinal studies in Latin America are needed to validate these findings and explore causal pathways.

Implications for future research

The results underscore the importance of expanding microbiome research in Latin America, where unique dietary patterns, environmental exposures, and socioeconomic conditions shape microbial diversity. Building local capacity for metagenomics, bioinformatics, and microbiome-based interventions will be critical to ensure that emerging diagnostic and therapeutic strategies are applicable to diverse populations (Abril-Ulloa et al., 2025; Díaz et al., 2021; Magne et al., 2016). Collaborative efforts across countries, including Mexico and Ecuador, can generate the evidence base required to integrate microbiome research into clinical practice and public health policies.

CONCLUSION

This study provided a comprehensive characterization of gut microbiota alterations in patients with inflammatory bowel disease, irritable bowel syndrome, colorectal cancer, and celiac disease compared with healthy controls in Mexico and Ecuador. The findings confirmed the study objectives by demonstrating that: (1) microbial diversity was consistently reduced in IBD and CRC, with intermediate profiles in IBS and celiac disease; (2) disease-associated microbial signatures—including depletion of *Faecalibacterium prausnitzii* and enrichment of *Ruminococcus gnavus*, *Fusobacterium nucleatum*, and *Bacteroides fragilis*—were highly reproducible across both populations; and (3) functional analysis of short-chain fatty acids revealed butyrate depletion as a unifying metabolic hallmark of gastrointestinal disease, while dietary and environmental influences shaped subtle differences between countries.

These results contribute to the theoretical understanding of dysbiosis by reinforcing the role of microbial diversity and specific taxa as hallmarks of gastrointestinal pathology.

Practically, they highlight potential applications for microbial and metabolic biomarkers in diagnosis, prognosis, and therapeutic strategies, including dietary modulation, probiotics, postbiotics, and fecal microbiota transplantation.

Nevertheless, certain limitations must be acknowledged. The cross-sectional design precludes causal inference, and unmeasured confounders such as detailed dietary intake or environmental exposures may have influenced microbial profiles. Future longitudinal and interventional studies in Latin America are warranted to validate these findings and assess the impact of microbiota-targeted therapies.

In conclusion, this binational study underscores the importance of investigating gut microbiota in underrepresented populations. By integrating evidence from Mexico and Ecuador, it advances global microbiome research while providing region-specific insights that may inform both clinical practice and public health policies.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.



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