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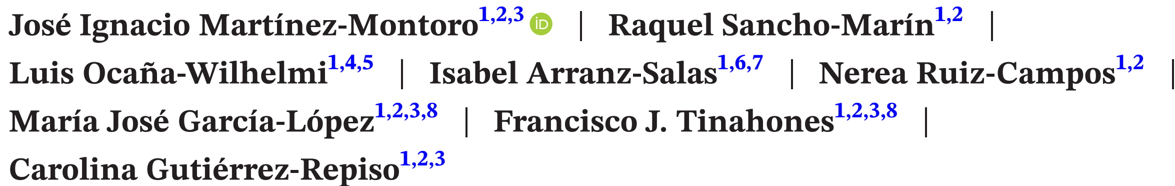
Gastric microbiota-specific signatures in adults with obesity and *Helicobacter pylori*-negative gastritis



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Abstract

Background: The role of the gastric microbiome in the pathophysiology of gastritis beyond *Helicobacter pylori* (HP) infection is poorly understood and has remained unexplored in patients with obesity. The aim of this study was to analyse gastric mucosa-associated microbiota in patients with obesity and nonatrophic chronic gastritis in the absence of HP infection or history of HP eradication.

Methods: This was a case–control study conducted at Virgen de la Victoria University Hospital in Malaga, performed in patients with severe obesity (body mass index ≥40 kg/m^2) undergoing sleeve gastrectomy, without HP infection and no history of HP eradication. Gastric biopsy specimens were collected at surgery and were analysed by 16S rRNA sequencing. Participants were divided into two groups according to the histological evaluation: nonatrophic chronic gastritis and nongastritis. An exploratory prospective analysis to determine the influence of gastritis on short-term outcomes after surgery was also performed.

Results: Sixty-seven participants (38 in the gastritis and 29 in the nongastritis group) were included. A lower alpha diversity (evenness and Shannon diversity indexes) and beta diversity (weighted Unifrac distance) were shown in the gastritis group. Higher relative abundances in the families *Micrococcaceae*, *Streptococcaceae* and *Leuconostocaceae* and the genera *Streptococcus*, *Weissella*

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and *Cryptobacterium* were observed in the gastritis group, compared with the nongastritis group. An enrichment in pathways involved in toluene degradation, heterolactic fermentation and secondary metabolites biosynthesis, such as ergothioneine and terpenoids, was found in the gastritis group. Also, higher total cholesterol levels 1 year after the surgery were observed in the gastritis group compared with the nongastritis group, although no within-group differences from baseline to 1 year were detected in this parameter.

Conclusion: Our results suggest a relationship between the gastric microbiome and nonatrophic chronic gastritis in obesity, beyond HP infection.

KEYWORDS

16S rRNA, gastric microbiota, nonatrophic chronic gastritis, obesity

1 | INTRODUCTION

Obesity is a chronic disease associated with a myriad of comorbidities, including gastrointestinal complications.[1] Therefore, an increased risk for several conditions, such as gastroesophageal reflux disease, gallstone disease, diverticular disease, colonic polyps and several types of gastrointestinal cancers, has been reported in people living with obesity.[1] Also, obesity has been shown to be a risk factor for gastritis.[2–5] In this regard, nonatrophic chronic gastritis, characterized by a mononuclear infiltration of the gastric mucosa, has been involved in the first steps of the natural history of gastric cancer according to Correa's gastric precancerous cascade, and may eventually progress to more advanced lesions, such as atrophic gastritis or intestinal metaplasia.[6] On the other hand, despite the fact that *Helicobacter pylori* (HP) is considered the most common cause of gastritis in the general population,[7] some studies have found a lower prevalence of HP infection in subjects with obesity.[8,9] Indeed, although HP eradication therapy has contributed to reduce the overall prevalence of this infection in the general population, a parallel decline in the prevalence of gastritis has not been shown.[10] Therefore, other agents, such as bile reflux or nonsteroidal anti-inflammatory drugs use, may play a part.[10] Moreover, additional factors, such as the gastric microbiome, may have an influence on the development of gastritis.

In the last few years, the gut microbiota has emerged as a key player in human health and disease.[11] However, the knowledge about different microbial niches, such as the stomach, is still limited. Recent evidence supports that the gastric microbiota may play a role in the pathophysiology of different upper gastrointestinal diseases.[12] In this regard, the 16S ribosomal RNA (rRNA) sequencing has enabled researchers to reach a closer approach to the gastric microbiome and to identify potential bacteria that may be involved in these diseases.[12] Previous research has shown that the gastric microbiota is influenced by several factors, including HP infection, antibiotics or proton pump inhibitors (PPIs).[13,14] Indeed, several studies conducted in patients with gastritis investigated the role of HP in the alterations of the gastric microbiota.[15,16] Also, some studies have reported alterations and/or partial restoration of the gastric microbiome after HP eradication.[17–20] Nevertheless, it should be noted that only a few studies have evaluated the gastric microbiota composition in patients with HP-negative gastritis, including a very limited number of participants with these characteristics,[21–24] and some of them did not consider adjusting for potential confounders, such as PPIs use.

On the other hand, the only clinical evidence on the gastric microbiota composition in obesity comes from our previous study conducted in 41 participants living with this disease who underwent sleeve gastrectomy (SG).[25] We showed that the gastric mucosa-associated microbiota of participants without HP infection or PPI use presented a predominance of the phyla Firmicutes, Bacteroidetes and Proteobacteria, the families *Streptococcaceae*, *Bacteroidaceae* and *Prevotellaceae*, and the genus *Streptococcus*, *Bacteroides* and *Prevotella*.[25] Moreover, significant differences in diversity and in gastric microbiota composition were found between participants with and without HP in gastric biopsy specimens, and the use of PPIs also affected the gastric microbiota of this population.[25]

It could be speculated that the gastric microbiome might also be involved in the pathophysiology of gastritis in people living with obesity. However, to our knowledge, no previous studies have evaluated the gastric microbiota of patients with obesity and chronic gastritis in the absence of HP. Therefore, in this study, we aimed to assess the potential differences between the gastric mucosa-associated microbiota of patients with obesity with HP-negative nonatrophic chronic gastritis and patients with obesity without gastritis or HP infection.

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2 | METHODS

2.1 | Participants

This study was conducted from 2019 to 2023, and included patients with severe obesity undergoing SG at Virgen de la Victoria University Hospital (Málaga, Spain). This study was reviewed and approved by the Ethics Research Committee of Málaga, and was conducted according to the principles of the Declaration of Helsinki All participants gave their written informed consent to participate in this study.

The inclusion criteria comprised patients with a body mass index (BMI) ≥ 40 kg/m^2 who underwent laparoscopic SG and tested stool antigen-negative for HP infection before surgery.

The exclusion criteria included cardiovascular disease, acute inflammatory disease, infectious disease or history of HP eradication therapy. Moreover, the use of antibiotics, probiotics or prebiotic agents in the previous 3 months was a reason for exclusion. Patients were removed from the study if the presence of HP was detected in the histological analysis and/or 16S rRNA gene sequencing.

A total of 75 patients met the criteria. Of them, eight patients were removed from the study because they showed a relative abundance of *H. pylori* >.1 based on 16S rRNA gene sequencing.

2.2 | Gastric sample collection and histological evaluation

During bariatric surgery, gastric samples were obtained. Gastric biopsies were frozen in liquid nitrogen and maintained at −80°C until gastric microbiota analysis. Resected partial stomach specimens were examined for any histopathologic alterations. Tissue samples were formalin-fixed and paraffin-embedded, sectioned, stained with haematoxylin–eosin and assessed by light microscopy. The presence of HP and histological alterations were evaluated using the Modified Sydney System, whose final report combines the type, intensity and extent of gastric pathology in addition to the possible aetiology.[26] The degree of mononuclear cell infiltration, polymorphonuclear cell infiltration, atrophy and intestinal metaplasia was classified into four grades: 0 'normal', 1 'mild', 2 'moderate' and 3 'marked' Scores ≥1 were considered to be positive. Groups were defined based on histological criteria in the nongastritis group (with no histological alterations) and the gastritis group (≥1 for mononuclear infiltration with no atrophy or intestinal metaplasia), as shown in Figure S1.

2.3 | Anthropometric and laboratory measurements

Before surgery, patients underwent standardized anthropometric measurements. BMI was calculated as weight (kg)/height^2 (m^2). After an overnight fast, a blood sample was collected, and serum was separated by centrifugation and immediately frozen at −80°C until analysis.

Serum glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c) were analysed using an Advia Chemistry XPT autoanalyzer (Siemens Healthcare Diagnostics). Serum insulin levels were measured via immunoassay (ADVIA Centaur Autoanalyzer, Siemens Healthcare Diagnostics). The homeostasis model assessment of insulin resistance was calculated as follows: fasting insulin (μIU/mL) × fasting glucose (mmol/L)/22.5. These anthropometric and laboratory measurements were also recorded 1 year after surgery.

Blood pressure was measured twice with a sphygmomanometer, with 5 min of rest between measurements, and the average of the measurements was reported.

The use of proton pump inhibitors (PPIs), nonsteroidal anti-inflammatory drugs and treatment for type 2 diabetes (T2DM) was recorded.

2.4 | Analysis of gastric microbiota

Gastric samples obtained during the SG surgery were maintained at −80°C until analysis. Gastric mucosa was scraped, and DNA was extracted using the QIAamp PowerFecal Pro DNA kit (QIAGEN Science, Hilden, Germany) according to the manufacturer's instructions. Libraries were built using Ion 16S Metagenomics kit and Ion Plus Fragment Library kit (Thermo-Fisher Scientific Inc., Waltham, MA) as previously described.[25,27,28] Template preparation and chip loading were performed using Ion Chef™ system and sequencing of the amplicon libraries was performed using the Ion Torrent S5 system (Thermo-Fisher Scientific Inc., Waltham, MA) according to the manufacturer's instructions.

2.5 | Sequence data analysis

Base calling and run demultiplexing were performed using Torrent Suite TM Server software (Thermo-Fisher Scientific Inc., Waltham, MA), version 5.18.1, with default parameters for the 16S Target Sequencing (bead loading ≤30, key signal ≤30 and usable sequences ≤30), as previously described.[27,28] Quality sequences were analysed using QIIME2 2023.5 software (Quantitative Insights into

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Microbial Ecology). Unique amplicon sequence variants (ASVs) were calculated using DADA2. Taxonomic classification of features was based on SILVA version 138 database, at 99% clustering similarity. The SILVA reference sequence and taxonomy were obtained as pre-formatted file (https://docs.qiime2.org/2022.2/data-resources/) that was processed using RESCRIPt plugin from QIIME2.

Features with a count sum less than 10 across all samples and those presented in only one sample were removed from further analysis. ASVs classified as chloroplasts or mitochondria were also excluded from downstream analysis.

For diversity analysis, the core-metrics-phylogenetic plugin in QIIME2 was used after randomly subsampling the samples to get the same number of sequences. Alpha diversity of bacterial communities was calculated using Pielou's evenness, Faith's phylogenetic diversity, Shannon's entropy and Observed Feratures indexes. Differences in alpha diversity metrics between groups were analysed using ANOVA. Beta diversity was assessed using weighted UniFrac distance and unweighted UniFrac distance. Unweighted UniFrac measures beta diversity based on the presence or absence of taxa, while Weighted UniFrac combines phylogenetic relationships and taxa abundance. Principal coordinate analysis (PCoA), a dimensionality reduction method based on distance matrices, was performed to visualise the results. Permutational multivariate analysis of variance (ADONIS) test evaluated the difference in beta diversity among groups. All tests were controlled for PPIs treatment as a confounding factor. p-Values <.05 were considered statistically significantly different.

Differential abundance of amplicon sequence variants was performed at different taxa levels (phylum, family and genus) using Analysis of Composition of Microbiomes with Bias Correction 2 (ANCOM-BC2) package in R studio. All tests were adjusted for PPIs use. p-Values were adjusted for false discovery rate (FDR) of multiple tests via the Benjamini–Hochberg method. Features with FDR-corrected p-value $< .05$ were considered differentially represented between groups.

Functional profiles of the microbial communities were calculated using the Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt2) plugin in QIIME2. Metacyc pathways were analysed using the ANCOM-BC 2 package. Pathways with p-value $< .05$ were considered statistically significant.

2.6 | Statistical analysis

Continuous variables are presented as mean ± standard deviation, and categorical variables as absolute numbers. Differences between groups were analysed with the Mann–Whitney test for continuous variables, or chi-square test for categorical variables. Values were considered to be statistically significant when $p < .05$.

3 | RESULTS

Sixty-seven participants were included in this study. Patients were classified according to histological study. Twenty-nine subjects showed no histological alterations of gastric mucosa (nongastritis group) and thirty-eight subjects showed nonatrophic chronic gastritis (gastritis group). The main clinical, anthropometric and biochemical characteristics of the subjects included in the study are shown in Table 1. There were no statistically significant differences between groups in baseline characteristics.

3.1 | Gastric microbiota diversity

The analysis of α-diversity showed that Pielou's evenness and Shannon diversity indexes were significantly higher in the nongastritis group than in the gastritis group ($q < .001$ and $q = .02$, respectively) (Figure 1). Regarding β-diversity,

TABLE 1 Anthropometric and biochemical characteristics of the subjects included in the study.

	Nongastritis ($n = 29$)	Gastritis ($n = 38$)
Age (years)	44.07 ± 9.38	46 ± 9.88
Sex (Male/Female)	11/18	13/25
Weight (kg)	131.15 ± 21.45	137.97 ± 25.03
BMI (kg/m^2)	47.15 ± 5.98	48.25 ± 6.66
Glucose (mg/dL)	101.48 ± 16.13	109.24 ± 25.60
Insulin (μUI/mL)	21.16 ± 10.61	18.45 ± 13.13
HOMA-IR	5.39 ± 3.05	5.39 ± 5.29
Type 2 diabetes (yes/no)	13/16	15/23
Cholesterol (mg/dL)	171.25 ± 39.44	181.49 ± 41.48
Triglycerides (mg/dL)	131.89 ± 51.98	124.27 ± 58.41
HDL-cholesterol (mg/dL)	40.75 ± 10.55	46.59 ± 13.96
LDL-cholesterol (mg/dL)	104.11 ± 32.58	111.12 ± 34.66
Systolic blood pressure (mmHg)	130.79 ± 16.20	136.73 ± 16.42
Diastolic blood pressure (mmHg)	80.54 ± 10.79	81.24 ± 11.23
Proton pump inhibitors intake (yes/no)	9/20	12/26
NSAIDs intake (yes/no)	1/28	3/35

Abbreviations: HOMA-IR, homeostatic model assessment of insulin resistance, NSAIDS, nonsteroidal anti-inflammatory drugs.

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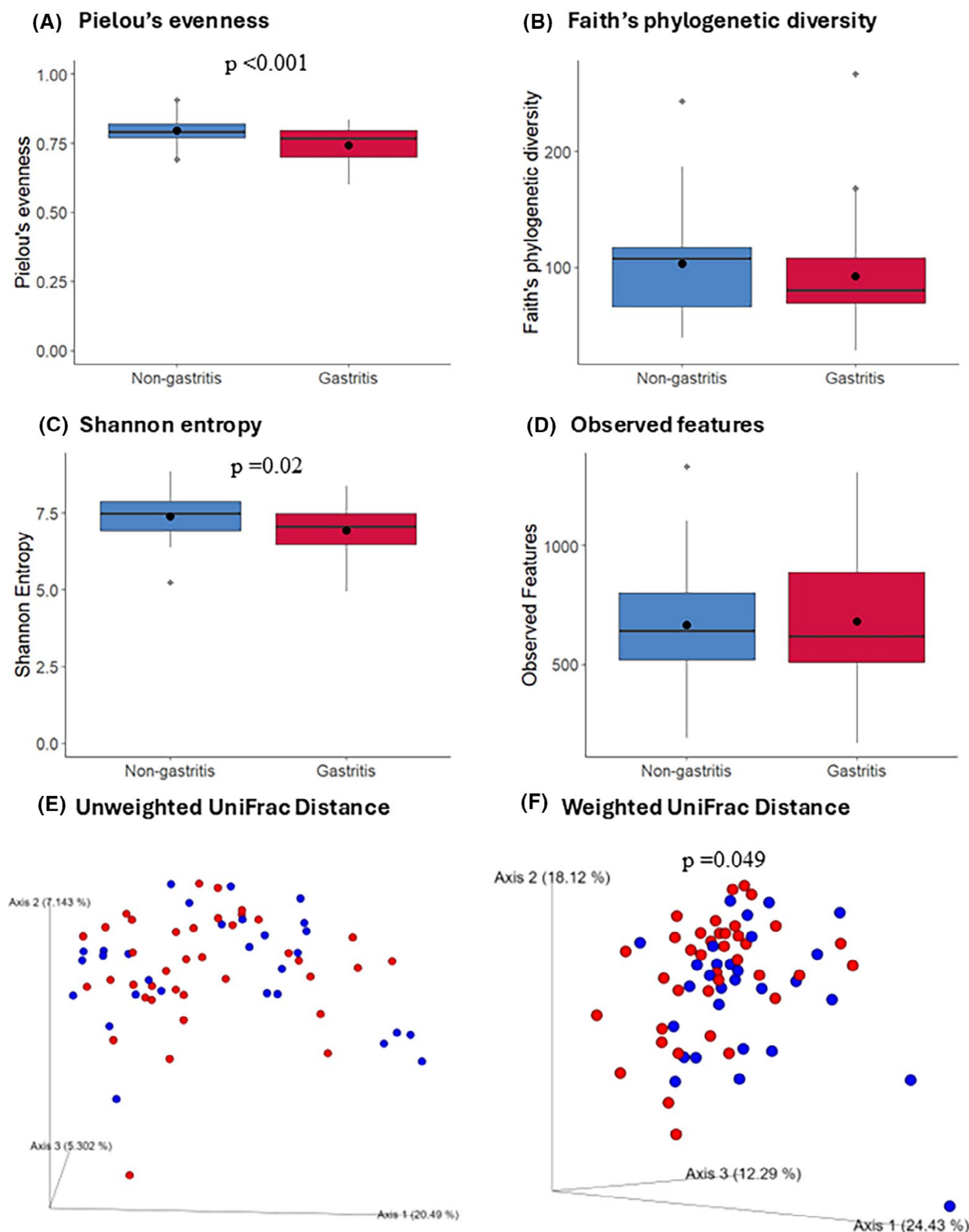

FIGURE 1 Gut microbiota diversity. (A) Pielou's evenness. (B) Faith's phylogenetic diversity. (C) Shannon entropy. (D) Observed features. (E) Principal coordinates analysis plot based on the unweighted UniFrac distance. The percentage of variation explained by PC1, PC2 and PC3 are indicated in the axis. Red circles: Gastritis group. Blue circles: Nongastritis group. (F) Principal coordinates analysis plot based on the weighted UniFrac distance. The percentage of variation explained by PC1, PC2 and PC3 are indicated in the axis. Red circles: Gastritis group. Blue circles: Nongastritis group. The statistically significant *p*-values ($p < .05$) are shown.

weighted UniFrac distance was shown to be significantly different ($q = .049$) (Figure 1).

3.2 | Gastric microbiota abundance

The gastritis group showed to be enriched in the families *Micrococcaceae*, *Streptococcaceae* and *Leuconostocaceae* and the genera *Streptococcus*, *Weissella* and *Cryptobacterium* (*q*-value < .05 in all cases) (Figure 2). The nongastritis group showed to be enriched in the families *Coriobacteriaceae*, *Pseudonocardiaceae*, [*Eubacterium*] *coprostanoligenes* group, *Yersiniaceae*, *Alteromonadaceae* and *Enterobacteriaceae*, and the genera *Collinsella*, *Lachnoclostridium*, [*Eubacterium*] *coprostanoligenes* group, *Pseudonocardia*, *Dechlorosoma*, *Serratia*, *Alishewanella*, *Kluyvera* and *Prevotellaceae-NK3B31* group (*q*-value < .05 in all cases) (Figure 2). A heatmap of the bacterial abundances according to the groups is also shown in Figure 3.

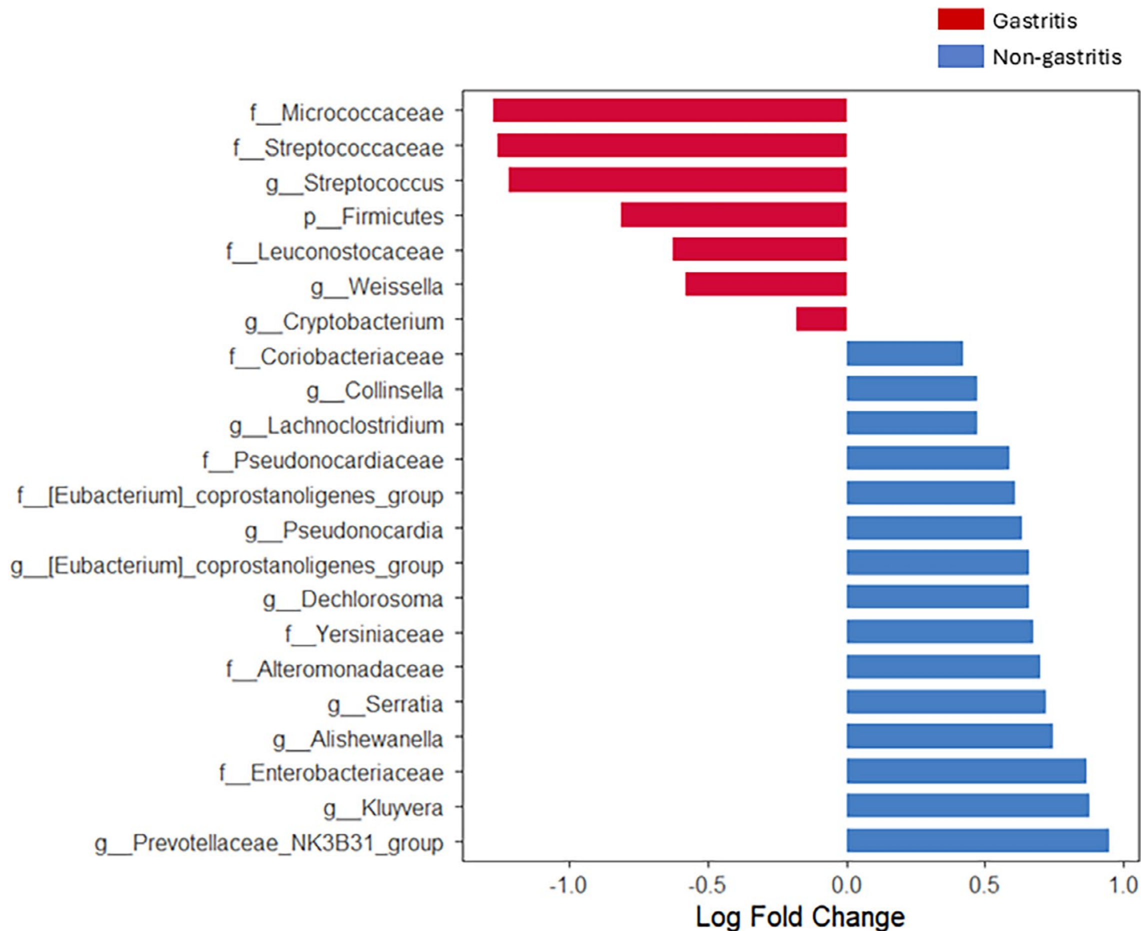

FIGURE 2 Log fold change of differentially abundant taxa identified by ANCOM-BC2 adjusted by PPIs intake (FDR-corrected *p*-value < .05).

3.3 | Functional prediction

Based on the PICRUSt2 functional prediction analysis, the gastritis group was shown to be enriched in pathways involved in toluene degradation (PWY-5180 and PWY-5182), heterolactic fermentation (P122-PWY) and secondary metabolites biosynthesis such as ergothioneine (PWY-7255) and terpenoids (PWY-922 and PWY-5910) (Figure 4).

On the other hand, the nongastritis group was enriched in pathways involved in the degradation of carbohydrates, aromatic compounds and the metabolism of inorganic nutrients, among others (Figure 4), as well as an enrichment in pathways involved in the fermentation to butyrate (CENTFERM-PWY, PWY-6590 and PWY-5676) and the biosynthesis of vitamin B12 (PWY-5009, PWY-6269 and PWY-7377).

3.4 | One-year bariatric surgery outcomes according to gastritis status

We evaluated different anthropometric and biochemical outcomes 1-year after sleeve gastrectomy in the gastritis group compared with the nongastritis group. In this regard, no between-group differences were observed in weight, BMI, glucose, insulin, HOMA-IR, HDL-cholesterol, LDL-cholesterol and triglyceride levels at this point (data not shown). On the other hand, higher total cholesterol levels were found in the gastritis group compared with the non-gastritis group (189.4 ± 31.3 vs. 164.2 ± 39.8 mg/dL, respectively, $p = .01$), although no within-group differences from baseline to 1 year were detected in this parameter.

4 | DISCUSSION

In this study, we compared two groups of patients with obesity based on histological criteria: nongastritis group (with no histological alterations in gastric biopsy) and gastritis group (with nonatrophic chronic gastritis), both without HP infection and no history of HP eradication. We reported a lower gastric microbiota diversity in subjects with obesity in the gastritis group, compared with the nongastritis group. Furthermore, our findings support the notion that the gastric microbiota composition differs between subjects with obesity with and without gastritis.

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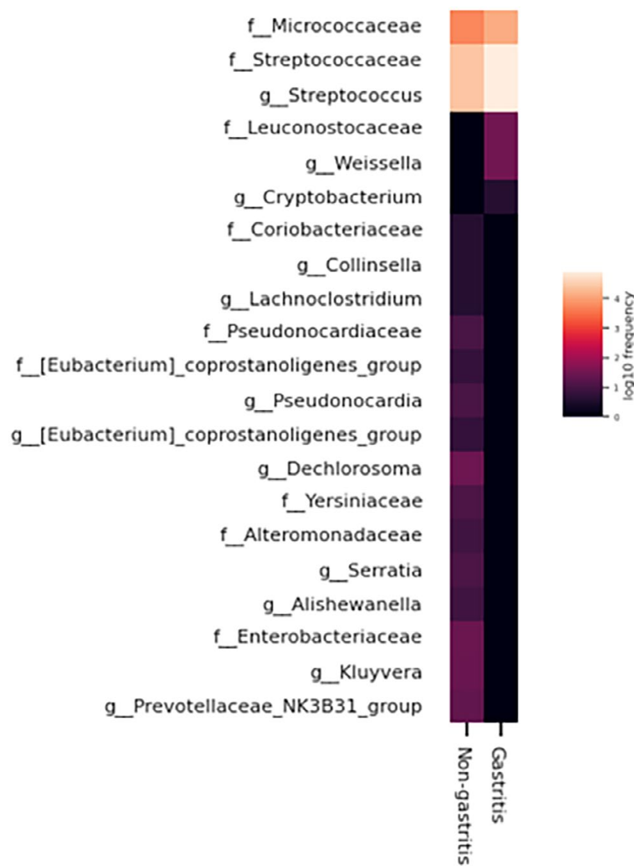

FIGURE 3 Heatmap of the bacterial abundances according to groups.

Given that no patients with HP infection (confirmed by 16S rRNA gene sequencing from gastric biopsy specimens) or history of HP eradication were included, these results may suggest a potential role of the gastric microbiota beyond HP in the pathophysiology of nonatrophic chronic gastritis in obesity.

To our knowledge, this is the first study to evaluate the gastric microbiome in subjects with obesity and gastritis without HP infection, a prevalent gastrointestinal comorbidity in this population. In fact, studies assessing the gastric-associated microbiota in individuals with obesity are lacking.[29] Previous research has shown that the gut microbiota is altered in patients with chronic gastritis, with and without HP infection.[30] However, it should be taken into account that stool samples may reflect an incomplete picture of the putative association between the microbiota and chronic gastritis, and more representative microbial niches (i.e. the gastric-associated microbiota) need to be considered.

The first works that profiled the gastric microbiota in subjects with HP-negative gastritis included biopsies from four and five patients with this condition, respectively.[21,22] On the one hand, Maldonado-Contreras et al. showed differences in the gastric microbiota of the included participants according to their HP status.[21] Additionally, Li et al. reported an increase in the genus *Streptococcus* abundance in patients with HP-negative gastritis compared with healthy controls, without differences in richness.[22] More recently, Gantuya et al. observed a different gastric microbiota composition among individuals with HP-positive/negative gastritis and healthy controls in a high-incidence gastric cancer area in Mongolia.[23] Also, a lower alpha and beta diversity were reported in individuals with HP-positive gastritis, with a similar diversity index between subjects with HP-negative gastritis and controls.[23] In this regard, previous evidence has systematically shown that HP significantly reduces gastric microbiota diversity, as other gastric bacteria are displaced by the dominant HP relative abundance.[19,31–33] However, it should be noted that only 11 patients with HP-negative gastritis were included in the aforementioned study.[23] On the other hand, Miftahussurur et al. profiled the gastric-associated microbiota in 137 gastric biopsy specimens from an Indonesian population with a low prevalence of HP, and compared the gastric microbiota of subjects with and without HP infection.[24] In this population, there were 22 samples from a subgroup of patients with nonatrophic gastritis (20 of them without HP infection). When only the HP-negative group was included in the analyses, the gastritis group showed a lower evenness and Shannon' diversity index compared with controls.[24] In line with this, we detected a significant decrease in alpha diversity (evenness and Shannon' diversity index) and beta diversity (weighted UniFrac distance) in the gastritis group, compared with the nongastritis group. Also, Miftahussurur et al. reported higher abundances of *Lactobacillus* sp., *Palludibacter* sp., *Dialister* sp. and *Scardovia* sp. in the gastritis group, compared with healthy subjects.[24] Nevertheless, although the authors excluded subjects with a history of HP eradication therapy, antibiotic use was not an exclusion criterion in this study, and analyses were not adjusted for PPIs use,[24] which may have had an impact on the results. Other studies assessed the gastric microbiota in different subjects without HP infection (with and without gastritis); however, they mainly included subjects with these characteristics after HP eradication therapy exposure.[17–20]

Significant differences in the gastric-associated microbiota between the gastritis and nongastritis group were shown in our study. Of note, similar to previous studies,[22–24] the relative abundances of the family *Streptococcaceae* and the genus *Streptococcus* were increased in the gastritis group compared with the nongastritis group. Recently, it has been demonstrated that *Streptococcus anginosus*, which primarily resides in the oral cavity, nasopharynx or gastrointestinal tract, is able

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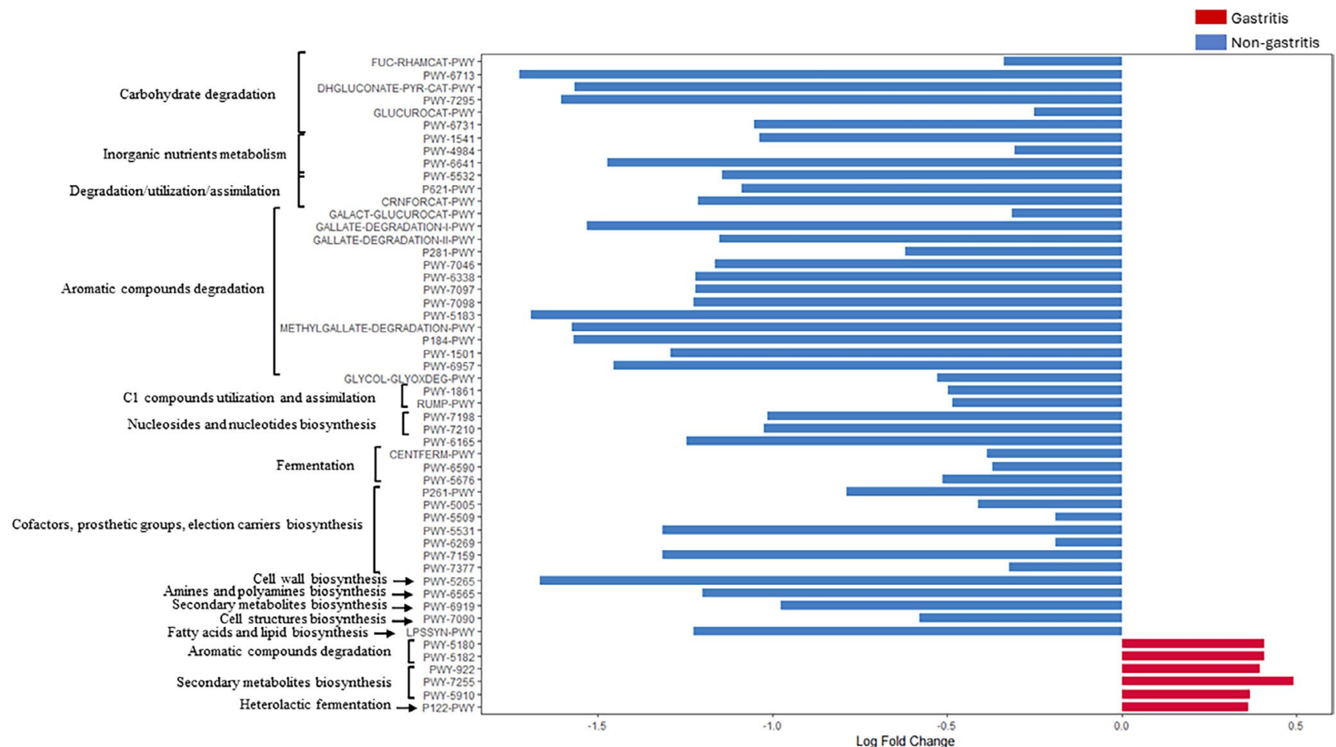

FIGURE 4 Log fold change of significant predictive metabolic pathways by PICRUSt2 identified by ANCOM-BC2 adjusted by PPIs intake ($p < .05$).

to induce acute and chronic gastritis, and accelerates gastric carcinogenesis in animal models.[34] A higher relative abundance of *Micrococcaceae* was also observed in the gastritis group. This family includes several genera (e.g. *Micrococcus* and *Staphylococcus*) that also colonize the oral cavity or the upper respiratory tract, similar to *Cryptobacterium*,[35] which was also enriched in the gastritis group. Therefore, these findings may suggest a role of bacteria from these locations in HP-negative gastritis. With regard to the higher relative abundance of *Weissella* in patients with gastritis, controversial roles have been attributed to this genus.[36]

We also explored the functional pathways according to the detected 16S sequences in our study population. Thus, heterolactic fermentation was enriched in the gastritis group. In this regard, it is known that the genus *Streptococcus* includes lactic acid-producing bacteria[37] and, together with other additional lactic acid-producing microbes, has been involved in the pathogenesis of gastric cancer.[38,39] According to our findings, this genus might also be implicated in earlier stages of the disease, such as nonatrophic chronic gastritis. Furthermore, the synthesis of ergothioneine, involved in the production of trimethylamine N-oxide (TMAO), was also increased in the gastritis group and might be linked to a pro-inflammatory state.[40–42] Additionally, the enrichment in toluene degradation observed in the gastritis group has been previously reported in patients with gastric cancer.[43] Moreover, terpenoid synthesis by the gut microbiome has been implicated in inflammation-mediated tumour growth in some gastrointestinal cancers.[44] Interestingly, pathways involved in the fermentation of butyrate were shown to be enriched in the nongastritis group, and this fact might be related to the higher relative abundance of some butyrate-producing bacteria, such as *Collinsella*, *Lachnoclostridium* or *Prevotellaceae-NK3B31*,[45–47] in this group. However, these results should be considered hypothesis-generating, and further specific studies are needed to fully unravel the potential microbial pathways related to gastritis in patients with obesity without HP infection.

Regarding the evaluation of short-term outcomes after surgery according to the gastritis status, we found higher total cholesterol levels in the gastritis group compared with the nongastritis group, although no within-group differences from baseline to 1 year were detected in this parameter. No between-group differences in other anthropometric or biochemical parameters after surgery were observed. Although these results might indicate that the presence of gastritis does not impact short-term surgery outcomes, these findings need to be further assessed in future longitudinal studies.

Some differences between the previous literature and our study may be highlighted. First, as we aimed to explore the role of the gastric microbiome in nonatrophic chronic gastritis in obesity, only patients with this condition were included. Thus, these findings add valuable

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information regarding an important population that had not been evaluated until now. Second, whereas previous studies assessing the gastric mucosa-associated microbiota were conducted in Asian participants, our study population comprised Spanish subjects. Also, while other studies classified their study population according to HP status, we decided to exclude participants with HP infection or history of HP eradication to focus on exploring the potential associations between obesity-related gastritis and the gastric microbiome beyond HP, which is known to be a key disruptor. Therefore, these points should also be taken into consideration for the interpretation of our results.

This study has some limitations. Therefore, considering that this is the first report assessing the association between the gastric microbiota and nonatrophic chronic gastritis in obesity, further longitudinal studies, also including a larger sample size, are needed to confirm these results. However, some important strengths should also be mentioned. Thus, a careful control for potential confounders was performed in this study, excluding patients with HP infection/eradication or recent use of antibiotics, and considering PPIs use for adjustment in all analyses.

In conclusion, a lower gastric microbial diversity is observed in patients with obesity and gastritis. Also, different signatures of gastric-associated microbiota can be found between patients with obesity and nonatrophic chronic gastritis and those without gastritis. Given that all participants in this study were HP-negative, our results suggest a relationship between the gastric microbiome and nonatrophic chronic gastritis in obesity, beyond HP infection.

AUTHOR CONTRIBUTIONS

JIMM was involved in conceptualization, formal analysis, visualization, writing-original draft, writing-review and editing. RSM, NRC and MJGL were involved in investigation. LOW and IAS were involved in investigation and resources. FJT was involved in conceptualization, writing-review and editing. CGR was involved in conceptualization, data curation, formal analysis, funding acquisition, methodology, supervision, visualization, writing-original draft, writing-review and editing. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

No potential conflicts of interests relevant to this article were reported.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding authors, upon reasonable request. Raw 16S rRNA sequencing data for all samples have been deposited in the NCBI short read archive under accession number PRJNA1249029.

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