Original Article
SAGE Open Medicine

# Association between the presence of Helicobacter pylori and the development of de novo anemia in adults undergoing sleeve gastrectomy

SAGE Open Medicine
Volume 12: 1-9

© The Author(s) 2024
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/20503121241275340
journals.sagepub.com/home/smo



Tammy S Carrillo-Levin<sup>1</sup>, Maria F Jaramillo-Ocharan<sup>1</sup>, Gustavo Salinas-Sedo<sup>2</sup> and Carlos J Toro-Huamanchumo<sup>3,4,5</sup>

### **Abstract**

**Background:** Sleeve gastrectomy has gained prominence in obesity treatment, yet it is not without complications, such as the development of anemia in the medium term. Given the high prevalence of *Helicobacter pylori* infection in Peru, it is imperative to explore its potential association with this postoperative complication.

**Objective:** To evaluate the association between the presence of *Helicobacter pylori* and the development of anemia 12 months after sleeve gastrectomy.

**Methods:** A retrospective cohort study was carried out based on an analysis of secondary data from a private clinic in Lima, Peru, which included two groups of people over 18 years of age who had undergone sleeve gastrectomy between 2010 and 2020. We considered the subjects who had the previous diagnosis of *Helicobacter pylori* as well as those who did not have the infection, according to the detection of the bacteria by endoscopy before surgery.

**Results:** A total 313 individuals were analyzed, and it was found that the prevalence of *Helicobacter pylori* was 46.0% and the incidence of anemia 12 months after sleeve gastrectomy was 18.2%. The presence of *Helicobacter pylori* increased the risk of de novo anemia (Relative Risk = 1.56; 95% confidence intervals: 1.02–2.41; p = 0.043). When stratifying by sex, the association was maintained only for the male group (Relative Risk = 2.84; 95% confidence intervals: 1.02–7.02; p = 0.047).

**Conclusions:** It was identified that the presence of *Helicobacter pylori* had a significant association with the development of de novo anemia, mainly in male subjects, I year after undergoing sleeve gastrectomy.

### **Keywords**

Bariatric surgery, sleeve gastrectomy, Helicobacter pylori, anemia

Date received: 28 March 2024; accepted: 29 July 2024

### **Highlights**

- To our knowledge, this study is the first to investigate whether the presence of *Helicobacter pylori* had an association with the development of de novo anemia in adults who underwent bariatric surgery in the Latin American population.
- The presence of H. Pylori had a significant association with the development of de novo anemia, mainly in male subjects, 1 year after undergoing sleeve gastrectomy.
- Considering the high prevalence of *H. pylori* infection in Peru, ranging from 50% to 70%, this research fills a critical data void and explores the potential impact

of this infection on the development of complications following sleeve gastrectomy in Latin populations.

<sup>1</sup>School of Medicine, Universidad Peruana de Ciencias Aplicadas, Lima, Peru <sup>2</sup>Clínica Avendaño, Lima, Peru

<sup>3</sup>Unidad de Investigación para la Generación y Síntesis de Evidencias en Salud, Universidad San Ignacio de Loyola, Lima, Peru

<sup>4</sup>OBEMET Center for Obesity and Metabolic Health, Lima, Peru <sup>5</sup>Nutrition and Health Innovation Research Institute, School of Medical and Health Sciences, Edith Cowan University, Joondalup, Western Australia, Australia

### Corresponding author:

Carlos J Toro-Huamanchumo, Universidad San Ignacio de Loyola, Avenue la Fontana 550, La Molina, Lima I 5024, Peru. Email: ctoro@usil.edu.pe

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

• This study emphasizes the importance of screening for *H. pylori* before bariatric surgery and suggests that for those patients who test positive, ensuring timely treatment, proper follow-up, and confirming the eradication of the infection is crucial.

### Introduction

Bariatric surgery, defined as a set of procedures aimed at reducing and preventing excess weight through surgical modification of the stomach and/or intestines, has gained significant prominence in the last two decades due to its well-documented effectiveness in treating obesity and its associated comorbidities, as well as its impact on psychosocial aspects and individual quality of life. 1,2 Specifically, sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) have become the most commonly performed interventions. While RYGB has long been recognized as the gold standard, 3 in recent times, SG has gained ground due to its efficacy as a standalone bariatric procedure and its lower technical complexity, resulting in reduced operative time. 4 This procedure involves resecting 70%–80% of the greater gastric curvature, reducing its storage capacity. 5

Despite its efficiency and a mortality rate close to 1%, SG is not exempt from complications, with an overall morbidity that can reach up to 17.5%.<sup>6</sup> In the short term, common complications include bleeding and staple line leaks.<sup>7</sup> In the medium term, anemia emerges as a significant nutritional problem, affecting approximately 17% of patients, potentially prolonging hospital stays and increasing the risk of hospitalization.<sup>8</sup> It is relevant to mention that new nutritional deficiencies may arise, or pre-existing ones may worsen after bariatric surgery.<sup>9</sup>

Various factors could be associated with these complications, including *Helicobacter pylori*. A study involving 260 patients demonstrated that its presence increases the risk of postoperative marginal ulcers, with approximately a quarter of infected patients experiencing ulcer hemorrhage. 10 Another study, involving 98 patients, showed an increase in ferritin deficiency in 6% of them and a decrease of around 1 g/dL in hemoglobin levels 1-year post-surgery. 9 In contrast, a systematic review of seven studies did not find a significant association between post-bariatric complications and H. pylori infection. However, it is important to consider that these results may be limited by the variability in study samples, diagnostic methods, and the scope of follow-up.<sup>2</sup> Additionally, this potential relationship has not yet been explored in the Latin American population, which tends to exhibit higher post-surgical complications and a higher surgical mortality rate compared to other populations. 11

Considering the high prevalence of *H. pylori* infection in Peru, ranging from 50% to 70%, <sup>12</sup> it is essential to explore the potential impact of this infection on the development of complications following SG. This topic gains even more significance, given the 39% increase in bariatric surgeries

in Latin America between 2011 and 2013, <sup>13</sup> with Peru ranking among the top three countries in SG operations by 2019. <sup>14</sup>

The objective of this study was to assess the association between the presence of *H. pylori* and the development of de novo anemia in adults undergoing SG. As a secondary objective, we evaluated the association between *H. pylori* and the variation in hemoglobin values at 12 months post-SG.

### **Methods**

### Study design and population

A retrospective cohort study was conducted based on a secondary data analysis of patients who attended Clínica Avendaño, a bariatric center in Lima, Peru, and underwent SG between the years 2010 and 2020.

### Sample

For sample size calculation, a 95% confidence level, 80% power, and a relative risk (RR) to detect equal to 2 were considered. Additionally, an N2/N1 ratio of 1 (consistent with the reality observed in patients undergoing SG at the clinic) and an incidence of anemia at 12 months in the H. pylorinegative group equal to 15.7% were considered. 10 With these data, a minimum required sample size of 228 was obtained. Despite the clinic having a protocol for postoperative followup of bariatric patients, there was a possibility that some laboratory or clinical data (important confounders in the association) might not be adequately documented in the follow-up and would need to be excluded from the analysis. Therefore, a 20% loss rate was considered. Following this conservative scenario, the required sample size was increased to 286 patients. However, to maximize the study's power and ensure robust results, we aimed to include all eligible patients meeting the selection criteria. Consequently, the final sample size analyzed in this study was 313 patients.

### Selection criteria

The exposed group included adults (≥18 years old) who underwent SG during the period 2010–2020 with a diagnosis of *H. pylori* through biopsy. The non-exposed group included adults who underwent the same type of surgery during the same period without a prior diagnosis of *H. pylori* within at least 1 year before surgery. Both groups included patients with a body mass index (BMI) greater than or equal to  $30 \, \text{kg/m}^2$ . Patients were excluded if they had undergone previous bariatric surgery or had been diagnosed with anemia in the last month before bariatric surgery. Additionally, patients with self-perceived harmful consumption of alcohol, tobacco, and/or drugs in the last month before bariatric surgery according to medical history were also excluded.

### Definition of variables

Outcome variable: De novo anemia.

This variable was defined as a reduction in hemoglobin concentration compared to age- and sex-specific normal values in the 12-month postoperative period. It was dichotomized as yes or no.

Exposure variable: H. pylori infection

This variable was defined as the condition of being diagnosed with *H. pylori* infection before surgery by endoscopy. It was dichotomized as yes or no.

### Other variables

The following variables were also included in the analysis: age (in years), sex (male, female), alcohol consumption (yes, no), tobacco consumption (yes, no), hypertension (yes, no), type 2 diabetes mellitus (yes, no), insulin resistance (yes, no), baseline hemoglobin level (g/dL), hemoglobin level at 1 year postoperative (g/dL), number of H. pylori crosses (negative, 1+, 2+, 3+), weight (kg) and height (m) before surgery, preoperative BMI (kg/m²), weight (kg) and height (m) at 1 year post-surgery, and BMI at 1 year post-surgery (kg/m²).

### Data collection

This study conducted a secondary analysis of data sourced from a private bariatric center in Peru. To collect the study population, all patients who met the proposed inclusion and exclusion criteria were considered. The information used included clinical, laboratory, and imaging data.

For this study, endoscopy-guided biopsy was considered the gold standard for confirming *H. pylori* infection. This procedure was performed before surgery, followed by post-operative controls at 3, 6, 9, and 12 months. Patients were required to have a minimum of 8 h of fasting for these analyses. These controls were performed using an Olympus CV-190 endoscope. The endoscopy procedure involved the exploration of the esophagus, stomach, and duodenum to search for anomalies and the presence of *H. pylori*.

Additionally, the clinic conducted a laboratory evaluation to assess the development of de novo anemia. This evaluation was carried out at 3, 6, 9, and 12 months after bariatric surgery. To ensure that it was indeed de novo anemia, the preoperative hemoglobin value was also considered.

### Statistical analysis

The clinic's database was exported as a Microsoft Excel spreadsheet for quality control. This process involved identifying missing and/or implausible values. When such cases were found, the entire physical and/or electronic medical record was reviewed. Subsequently, the data were coded following a variable dictionary constructed for the purpose of this study. This coding process was conducted independently

by two individuals, and once completed, the coded datasets were cross-checked to detect coding errors. After this process, the dataset was imported into the statistical package Stata v17.0 (StataCorp LCC, College Station, TX, USA).

For descriptive analysis, numerical variables were presented with their mean and standard deviation (SD) or with their median and 25–75th percentile, depending on the presence or absence of normality. Normality was assessed by considering kurtosis and skewness values, as well as graphically through histograms and quantile—quantile plots. Additionally, the Shapiro—Wilk test was used as a reference for assessing normality. Categorical variables were presented as absolute and relative frequencies.

For bivariate analysis, sample characteristics were evaluated based on the development of de novo anemia (yes/no) and the presence of *H. pylori* (yes/no). For this purpose, when crossing with a numerical variable, the *t*-test or Mann–Whitney *U* test was used to identify significant differences. When crossing with a categorical variable, the Fisher's Exact Test or Chi-squared test was used, depending on the number of expected values.

To assess the association between H. pylori presence and de novo anemia, generalized linear models with a Poisson family, a logarithmic link function, and robust variances were constructed to calculate crude relative risk (cRR) and adjusted relative risk (aRR). For the multivariable model, an epidemiological approach was followed. Initially, the adjustment variables considered were age, sex, cardiometabolic comorbidity (defined as having hypertension, diabetes mellitus, and/or insulin resistance), baseline hemoglobin, and BMI. However, after evaluating the linearity assumption, it was evident that it was not met for the hemoglobin and BMI variables. Therefore, hemoglobin was categorized into terciles and BMI was converted into morbid obesity (yes: BMI ≥40 kg/m<sup>2</sup>, no: BMI <40 kg/m<sup>2</sup>). It is important to note that linearity was assessed using Anscombe residuals and residual component plots. Additionally, a model comparison was conducted (model 1: considering the quadratic term of the numerical variable, model 2: adjusting the original model). The absence of statistical multicollinearity was verified using the variance inflation factor (VIF), with all values being less than 4.

To assess the secondary objective (the association between *H. pylori* presence and the variation in hemoglobin values at 12 months post-SG), we first subtracted the baseline hemoglobin from the hemoglobin at 12 months. Subsequently, a variable representing the percentage change in hemoglobin was constructed to facilitate interpretation. This was achieved by subtracting the baseline hemoglobin from the hemoglobin at 12 months, dividing this value by the baseline hemoglobin, and then multiplying it by 100: [(baseline hemoglobin–hemoglobin at 12 months)/ baseline hemoglobin] × 100. Following an epidemiological criterion, sex, age, and cardiometabolic comorbidity were initially considered as adjustment variables. Since the outcome now involved a change, we believed that the weight-related variable should also represent this change. Therefore, we decided to work

with the percentage of excess weight loss (%EWL) instead of BMI. This variable was constructed using the formula: [(baseline weight (kg)-weight at 12 months (kg)/(baseline weight (kg)-ideal body weight (kg))]  $\times$  100. The ideal body weight was constructed based on gender. For men: [Height (cm)-100]-([Height (cm)-100] $\times 0.10$ ), and for women: [Height (cm)-100]–([Height (cm)–100]  $\times$  0.15). In the original model, we decided to include the baseline hemoglobin variable because, although it is contained in the construction of the outcome (percentage change in hemoglobin), we considered that the baseline hemoglobin level could influence how much the hemoglobin varies over the year. In other words, people with higher baseline hemoglobin levels may have more "room" for a change in their hemoglobin levels compared to those with lower levels. Additionally, a sensitivity analysis was conducted where baseline hemoglobin was not considered in the multivariable model.

The association between *H. pylori* presence and the percentage change in hemoglobin at 12 months was evaluated using bivariable and multivariable ordinary least squares (OLS) linear regression models, calculating crude (βc) and adjusted (βa) coefficients, respectively. As mentioned earlier, for the multivariable model, adjustments were made for age, sex, cardiometabolic comorbidity, baseline hemoglobin in terciles, and %EWL. Compliance with the assumptions of linearity and normality was verified using standardized residuals, while homoscedasticity was assessed using the Breusch–Pagan/Cook–Weisberg test. The presence of collinearity was also evaluated with the VIF, obtaining values less than four in all cases.

Finally, all the aforementioned models were presented stratified by sex. This was not due to an effect modification assessment but rather followed an epidemiological criterion, taking into account the differences in both the prevalence and cutoff points for anemia in men and women. It should be noted that all estimates were reported with their respective 95% confidence intervals (CI), and values with p < 0.05 were considered significant.

### **Ethics**

This research project was reviewed and approved by the Ethics Committee of the Universidad Peruana de Ciencias Aplicadas (#FCS-SCEI/181-03-23). The information obtained from the database was exclusively handled by the researchers of this study.

### **Results**

### General characteristics of the study population

The information of a total of 313 patients was analyzed. 67.4% were female, and the mean age was  $37.2 \pm 10.8$  years. The prevalence of *H. Pylori* was 46.0% (n=144; 25.2% with 1+, 14.7% with 2+, and 6.1% with 3+), and the incidence of de novo anemia at 12 months post-SG was 18.2% (n=57). The remaining clinical, anthropometric, and laboratory data are presented in Table 1.

**Table 1.** General characteristics of the study population (n=313).

Characteristics	n (%)			
Age (years)	$37.2 \pm 10.8^{a}$			
Sex				
Male	102 (32.6)			
Female	211 (67.4)			
Basal weight (kg)	100.4 [89–116.2] <sup>b</sup>			
Weight per year (kg)	$72.8 \pm 15.8^{a}$			
Baseline BMI (kg/m²)	36.9 [33.3 <del>-4</del> 1.3] <sup>b</sup>			
BMI per year (kg/m <sup>2</sup> )	$26.4 \pm 4.5^{a}$			
Basal Hb (gr/dl)	$14 \pm 1.3^{a}$			
Hb per year (gr/dl)	$13.3 \pm 1.6^{a}$			
HTN				
Yes	74 (23.6)			
No	239 (76.4)			
T2DM				
Yes	21 (6.7)			
No	292 (93.3)			
Insulin resistance				
Yes	68 (21.7)			
No	245 (78.3)			
H. pylori				
Yes	144 (46)			
No	169 (54)			
De novo anemia				
Yes	57 (18.2)			
No	256 (81.8)			

BMI: body mass index; Hb: hemoglobin; HTN: arterial hypertension; T2DM: type 2 diabetes mellitus.

### Characteristics of the population according to the development of anemia at 12 months

In Table 2, it is observed that the incidence of de novo anemia was significantly higher in female patients (23.7% versus 6.9%; p < 0.001) and those without arterial hypertension (21.3% versus 8.11%; p = 0.010). The means of weight at 12 months (66.3 versus 74.2; p = 0.001), BMI at 12 months (24.9 versus 26.7; p = 0.008), baseline hemoglobin (12.8 versus 14.2; p < 0.001), and hemoglobin at 12 months (11.2 versus 13.8; p < 0.001) were significantly lower in patients who developed de novo anemia. The median of baseline weight was also significantly lower in those who developed anemia (95 kg versus 102.6 kg; p = 0.008).

## Characteristics of the population according to the presence of H. Pylori

The presence of *H. pylori* was significantly higher in male patients (56.9% versus 40.8%; p=0.007). There were no differences between groups for the rest of the variables (Table 3).

 $<sup>{}^{</sup>a}Mean \pm SE.$ 

<sup>&</sup>lt;sup>b</sup>Median [p25-p75].

Table 2. Characteristics of the study population according to development of anemia at 12 months.

Characteristics	De novo anemia	p Value		
	Yes (n = 57)	No (n=256)		
Age (years) <sup>a</sup>	36.I ± 10.4	37.4 ± 10.9	0.416 <sup>b</sup>	
Sex			<0.001e	
Male	7 (6.9)	95 (93.1)		
Female	50 (23.7)	161 (76.3)		
Basal weight (kg) <sup>c</sup>	95 [87–104.2]	102.6 [89.5–118]	0.008 <sup>d</sup>	
Weight per year (kg) <sup>a</sup>	$66.3 \pm 9.1$	$74.2\pm16.6$	0.001 <sup>b</sup>	
Baseline BMI (kg/m²) <sup>c</sup>	36.8 [32.8–39.6]	36.9 [33.4-41.9]	0.216 <sup>d</sup>	
BMI per year (kg/m²) <sup>a</sup>	$24.9 \pm 3.4$	$26.7 \pm 4.7$	0.008 <sup>b</sup>	
Basal Hb (g/dL) <sup>a</sup>	$12.8\pm0.9$	$14.2\pm1.2$	<0.001 <sup>b</sup>	
Hb per year (g/dL) <sup>a</sup>	$11.2 \pm 1.1$	$13.8\pm1.3$	<0.001 <sup>b</sup>	
HTN			0.010e	
Yes	6 (8.1)	68 (91.9)		
No	51 (21.3)	188 (78.7)		
T2DM	. ,	, ,	0.141 <sup>f</sup>	
Yes	I (4.8)	20 (95.2)		
No	56 (19.2)	236 (80.8)		
Insulin resistance	, ,	,	0.353°	
Yes	15 (22.1)	53 (77.9)		
No	42 (17.1)	203 (82.9)		
H. pylori	` '	, ,	0.267°	
Yes	30 (20.8)	114 (79.2)		
No	27 (16)	142 (84)		

BMI: body mass index; Hb: hemoglobin; HTN: arterial hypertension; T2DM: type 2 diabetes mellitus.

### Association between H. Pylori and de novo anemia at 12 months

In the adjusted model (Table 4), after controlling for age, sex, cardiometabolic comorbidity, baseline hemoglobin, and morbid obesity, it was evident that the presence of H. pylori increased the risk of de novo anemia at 12 months post-SG (RR=1.56; 95% CI: 1.02–2.41; p=0.043). When stratified by sex, the association remained significant only for the male group (RR=2.84; 95% CI: 1.02–7.02; p=0.047).

## Association between H. Pylori and percentage change in hemoglobin at 12 months

In the adjusted model (Table 5), after controlling for age, sex, cardiometabolic comorbidity, baseline hemoglobin, and percentage of excess weight lost, it was evident that patients with *H. pylori* had, on average, a 1.71% decrease in their hemoglobin levels at 12 months post-SG, compared to those without *H. pylori* ( $\beta$ =-1.71; 95% CI: -3.33 to -0.08; p=0.039). When stratified by sex, it was evident that male

patients with *H. pylori* had, on average, a 2.91% decrease in their hemoglobin levels at 12 months compared to their peers without *H. pylori* ( $\beta$ =-2.91; 95% CI: -5.28 to -0.54; p=0.017).

In the sensitivity analysis (Supplemental material Table S1), adjusting for the same variables except baseline hemoglobin, the direction of the effect remained the same but was marginally significant ( $\beta$ =-1.61; 95% CI: -3.27 to -0.06; p=0.059). In the stratified analysis, both the direction and statistical significance remained for male patients ( $\beta$ =-2.86; 95% CI: -5.27 to -0.45; p=0.020).

### **Discussion**

We found that the presence of *H. pylori* was associated with a higher risk of developing de novo anemia during the year following SG. Despite women having a higher incidence of de novo anemia after the procedure, when evaluating the association with *H. pylori* infection and stratifying by sex, it was observed that the increased risk attributed to the bacterium was only present in the group of male patients.

 $<sup>{}^{</sup>a}Mean \pm SD.$ 

<sup>&</sup>lt;sup>b</sup>Student *t*-test.

<sup>&</sup>lt;sup>c</sup>Median [p25-p75].

dMann-Whitney U test.

<sup>&</sup>lt;sup>e</sup>Chi-square test.

Fisher's exact test.

Table 3. Characteristics of the study population according to the presence of H. Pylori.

Characteristics	H. Pylori	p Value		
	Yes (n = 144)	No (n=169)		
Age (years) <sup>a</sup>	36.9 ± 10.8	37.4 ± 10.8	0.708 <sup>b</sup>	
Sex			0.007e	
Male	58 (56.9)	44 (43.1)		
Female	86 (40.8)	125 (59.2)		
Basal weight (kg) <sup>c</sup>	102.1 [90–119.2]	99.3 [87.6–114.2]	0.105 <sup>d</sup>	
Weight per year (kg) <sup>a</sup>	74.1 ± 15.8	$71.1 \pm 15.7$	0.187 <sup>b</sup>	
Baseline BMI (kg/m <sup>2</sup> ) <sup>c</sup>	38 [33.7–41.9]	36.3 [32.9-41]	0.105 <sup>d</sup>	
BMI per year (kg/m <sup>2</sup> ) <sup>a</sup>	26.9 ± 4.4	$26.1 \pm 4.6$	0.111 <sup>b</sup>	
Basal Hb (gr/dl) <sup>a</sup>	$14.1 \pm 1.4$	$13.8 \pm 1.2$	0.071 <sup>b</sup>	
Hb per year (gr/dl) <sup>a</sup>	$13.4\pm1.7$	$13.2 \pm 1.5$	0.566 <sup>b</sup>	
HTN			0.430e	
Sí	37 (50)	37 (50)		
No	107 (44.8)	132 (55.2)		
T2DM		, ,	0.544e	
Sí	11 (52.4)	10 (47.6)		
No	133 (45.6)	159 (54.5)		
Insulin resistance	, ,	,	0.455e	
Sí	34 (50)	34 (50)		
No	110 (44.9)	135 (55.1)		
De novo anemia	, ,	` ,	0.267 <sup>d</sup>	
SÍ	30 (52.6)	27 (47.4)		
No	114 (44.5)	142 (55.5)		

BMI: body mass index; Hb: hemoglobin; HTN: arterial hypertension; T2DM: type 2 diabetes mellitus.

**Table 4.** Association between *H. pylori* and the development of anemia 12 months after sleeve gastrectomy.

Exposure: H. Pylori	Crude mod	el		Adjusted model <sup>a</sup>			
	cRR	95% CI	p Value	aRR	95% CI	p Value	
All the sample							
No	Ref.			Ref.			
Yes	1.30	0.81-2.09	0.269	1.56	1.02-2.41	0.043	
Males							
No	Ref.			Ref.			
Yes	1.90	0.38-9.40	0.433	2.84	1.02-7.92	0.047	
Females							
No	Ref.			Ref.			
Yes	1.45	0.90-2.36	0.129	1.47	0.93-2.34	0.102	

<sup>&</sup>lt;sup>a</sup>Model adjusted for age, sex, cardiometabolic comorbidity, baseline hemoglobin, and morbid obesity.

In our study, 18.2% of patients developed de novo anemia 1 year after bariatric surgery. Findings related to the association between *H. pylori* and the development of anemia after bariatric surgery are varied in the literature. A study conducted in Italy in 2017 revealed a 17% prevalence of anemia

in patients undergoing SG, similar to our findings.<sup>8</sup> Another study in Poland in 2019 suggested that bariatric surgery can lead to or even exacerbate nutritional deficiencies, such as iron and vitamin B12 deficiency.<sup>9</sup> In contrast, a 2019 Canadian study that focused on patients with normal iron

 $<sup>{}^{</sup>a}Mean \pm SD.$ 

<sup>&</sup>lt;sup>b</sup>T-student test.

<sup>&</sup>lt;sup>c</sup>Median [p25–p75].

<sup>&</sup>lt;sup>d</sup>Mann–Whitney *U* test. <sup>e</sup>Chi-square test.

<sup>95%</sup> CI: 95% confidence interval; RR: relative risk.

Table 5.	Association	between	H. pylori and the	variation in	hemoglobin	values	12 months after	sleeve gastrectomy.	

Exposure: H. Pylori	Crude mod	lel		Adjusted model <sup>a</sup>			
	сβ	95% CI	p Value	aβ	95% CI	p Value	
All the sample							
No	Ref.			Ref.			
Yes	-1.04	-2.72 to 0.63	0.221	-1.71	-3.33 to -0.08	0.039	
Males							
No	Ref.			Ref.			
Yes	-2.86	-5.27 to -0.45	0.020	-2.91	-5.28 to -0.54	0.017	
Females							
No	Ref.			Ref.			
Yes	-0.77	-2.96 to 1.43	0.491	-1.23	-3.38 to -0.91	0.257	

<sup>a</sup>Model adjusted for age, sex, cardiometabolic comorbidity, baseline hemoglobin, and excess weight loss (EWL). β: beta coefficient; 95% CI: 95% confidence interval.

levels before the surgery did not observe an increase in the incidence of iron deficiency 1 year after SG.<sup>15</sup> Additionally, in Canada, another study conducted in 2023 found a low rate of *H. pylori* infection confirmed by histology in severely obese patients eligible for bariatric surgery.<sup>16</sup>

Regarding the association between a prior diagnosis of *H. pylori* infection and the development of de novo anemia, a 2018 Slovenian study described that a history of infection with this bacterium increased the risk of iron-deficiency anemia and immune thrombocytopenic purpura. Similarly, a retrospective study in China found that the prevalence of anemia was significantly higher in individuals with *H. pylori* compared to those without the infection, after adjusting for factors such as age, gender, underlying diseases and BMI. In contrast, a 2014 study conducted in the Middle East evaluated 682 patients and suggested that *H. pylori* infection was not significantly associated with complications after SG. It is worth mentioning that in this study, the number of infected patients before surgery was limited (20.5%), and it represents a different population from the Latin population. 19

Iron deficiency is one of the main causes of de novo anemia after bariatric surgery. This deficiency arises due to changes in the gastrointestinal tract, such as the resection of up to 80% of the greater curvature of the stomach, which reduces acidity and, consequently, iron absorption. Additionally, removing a large part of the stomach decreases ghrelin production decreases, leading to a reduced appetite. <sup>20</sup> Another potential consequence is vitamin B12 or cobalamin deficiency, as many parietal cells, which produce the intrinsic factor essential for the absorption of this vitamin in the distal ileum, are lost. <sup>21</sup>

After gastric surgery, the intragastric microenvironment undergoes significant changes. The pH increases, concentrations of ascorbic acid decrease, and oxygen radicals increase due to inflammation. These changes can contribute to novo anemia since a basic environment hinders iron absorption. <sup>22</sup> Furthermore, *H. pylori* induces chronic gastritis, affecting iron absorption due to gastric hypochlorhydria, resulting in

less iron conversion from ferric to ferrous form. An acidic gastric pH is essential for dietary iron absorption in its ferrous form, and *H. pylori* interferes with this process. Additionally, this altered environment favors the survival of *H. pylori*, as the gastric flora can produce the enzyme betalactamase, which generates resistance and reduces the effectiveness of drugs aimed at eradicating *H. pylori*.<sup>23</sup>

Regarding gender differences in post-bariatric surgery complications, it has been shown that men tend to attend medical check-ups less frequently and seek medical attention less often, influencing the development of postoperative anemia.<sup>24</sup> On the other hand, literature reports that both estrogen and progestogen have antibacterial properties in vitro and in vivo against various bacteria, including *H. pylori*. It is suggested that these hormones may interact with the cholesterol-binding site on bacterial cell membranes, producing bacteriostatic or even bactericidal effects.<sup>25</sup> Such interaction could mitigate the effects of *H. pylori* on the gastric wall in women, acting as a protective factor against decreased iron absorption, unlike in men.

Our results emphasize the importance of screening for *H*. pylori in patients undergoing bariatric surgery due to the risk of developing anemia. This condition, besides causing fatigue, also reduces the patient's quality of life. Iron deficiency, for example, has been linked to hair loss, specifically diffuse alopecia.<sup>26</sup> Furthermore, long-term nutritional deficiencies, including iron, ferritin, and vitamin B12, are common following SG, significantly impacting the patient's overall health.<sup>27</sup> De novo anemia in patients with preexisting comorbidities, such as type 2 diabetes mellitus, can lead to long-term complications. A positive relationship has been found between iron-deficiency anemia and elevated glycosylated hemoglobin (A1C) levels, as well as the development of diabetic nephropathy, oxidative stress, and decreased high-density lipoprotein (HDL) function. Additionally, anemia has a direct effect on the kidneys and heart through fibrogenic mechanisms related to the expression of growth factors linked to diabetic microvascular disease.<sup>28</sup>

Given the increased risk of post-bariatric surgery anemia observed, it is essential to promote adherence to nutritional supplementation in patients who require it. Additionally, due to the identified association between *H. pylori* and the development of de novo anemia, preoperative screening should be emphasized, especially in male patients. Their follow-up should be particularly rigorous, considering their greater predisposition to gastric cancer development, as the presence of this bacterium is a major risk factor for the disease.<sup>29</sup>

This study has some limitations. First, there is a possibility that some laboratory, anthropometric, and/or clinical variables may have measurement errors, which could introduce information bias or residual confounding bias in the case of adjustment variables. However, the clinic where the study was conducted follows standardized procedures for obtaining information from bariatric surgery candidates, so any errors, if they exist, would be expected to be minimal. Second, the study population consists of patients treated at a private clinic, mainly from middle to high socioeconomic backgrounds, limiting the external validity to this specific demographic. Third, some variables could not be considered due to their unavailability, such as adherence to post-surgery supplements, which introduces the potential for unmeasured confounding bias. Fourth, there was no information available regarding compliance with treatment after diagnosing H. pylori before surgery, and there is also no information related to bacterial eradication.

### **Conclusion**

This study suggests an association between *H. pylori* infection and the development of de novo anemia following SG, particularly in male subjects. Given the high prevalence of *H. pylori* infection in Latin America and the significant complications that anemia can cause in patients' quality of life and health, it is essential to emphasize the importance of screening for *H. pylori* before bariatric surgery. Furthermore, for those patients who test positive, ensuring timely treatment, proper follow-up, and confirming the eradication of the infection is crucial.

### **Acknowledgements**

Carlos J. Toro-Huamanchumo is supported by the Forrest Research Foundation Scholarship and the Edith Cowan University Higher Degree by Research Scholarship.

#### **Author contribution**

T.S.C.-L.: Conceptualization, Investigation, Writing—Original Draft.

M.F.J.-O.: Conceptualization, Investigation, Writing—Original Draft.

G.S.-S.: Conceptualization, Investigation, Writing—Original Draft. C.J.T.-H.: Conceptualization, Methodology, Supervision, Writing—Review & Editing.

### **Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### **Funding**

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was self-funded.

### **Ethics approval**

Ethical approval for this study was obtained from Ethics Committee of the Universidad Peruana de Ciencias Aplicadas (#FCS-SCEI/181-03-23).

### Informed consent

Informed consent was not sought for the present study because it was a retrospective study based on a secondary data analysis. So it is not applicable.

### **Trial registration**

None.

### **ORCID iD**

Carlos J Toro-Huamanchumo https://orcid.org/0000-0002-4664-2856

### Supplemental material

Supplemental material for this article is available online.

### References

- Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. Cochrane Database Syst Rev 2014; 2014(8): CD003641.
- 2. Mocanu V, Dang JT, Switzer N, et al. The effect of *Helicobacter pylori* on postoperative outcomes in patients undergoing bariatric surgery: a systematic review and meta-analysis. *Obes Surg* 2018; 28(2): 567–573.
- Berbiglia L, Zografakis JG and Dan AG. Laparoscopic Rouxen-Y gastric bypass: surgical technique and perioperative care. Surg Clin North Am 2016; 96(4): 773–794.
- 4. Chung AY, Thompson R, Overby DW, et al. Sleeve gastrectomy: surgical tips. *J Laparoendosc Adv Surg Tech A* 2018; 28(8): 930–937.
- 5. Yehoshua RT, Eidelman LA, Stein M, et al. Laparoscopic sleeve gastrectomy—volume and pressure assessment. *Obes Surg* 2008; 18(9): 1083–1088.
- Ali M, El Chaar M, Ghiassi S, et al. American Society for Metabolic and Bariatric Surgery updated position statement on sleeve gastrectomy as a bariatric procedure. Surg Obes Relat Dis 2017; 13(10): 1652–1657.
- Kassir R, Debs T, Blanc P, et al. Complications of bariatric surgery: presentation and emergency management. *Int J Surg* 2016; 27: 77–81.
- 8. Lupoli R, Lembo E, Saldalamacchia G, et al. Bariatric surgery and long-term nutritional issues. *World J Diabetes* 2017; 8(11): 26–32.

 Antoniewicz A, Kalinowski P, Kotulecka KJ, et al. Nutritional deficiencies in patients after Roux-en-Y gastric bypass and sleeve gastrectomy during 12-month follow-up. *Obes Surg* 2019; 29(10): 3277–3284.

- Rasmussen JJ, Fuller W and Ali MR. Marginal ulceration after laparoscopic gastric bypass: an analysis of predisposing factors in 260 patients. Surg Endosc 2007; 21(7): 1090–1094.
- Eguia E, Cobb AN, Kirshenbaum EJ, et al. Racial and ethnic postoperative outcomes after surgery: the Hispanic paradox. J Surg Res 2018; 232: 88–93.
- Pareja Cruz A, Navarrete Mejía PJ and Parodi García JF. Seroprevalencia de infección por *Helicobacter pylori* en población adulta de Lima, Perú 2017. *Horiz Med* 2017; 17(2): 55–58.
- Lutfi R, Palermo M and Cadiere GB. Global bariatric surgery. Berlin, Germany: Springer, 2019.
- International Federation for the Surgery of Obesity and Metabolic Disorders. *The IFSO Global Registry 2019*. Italy: IFSO, 2019.
- Enani G, Bilgic E, Lebedeva E, et al. The incidence of iron deficiency anemia post-Roux-en-Y gastric bypass and sleeve gastrectomy: a systematic review. Surg Endosc 2020; 34(7): 3002–3010.
- Baillargeon D, Greenblatt M, Côté M, et al. Prevalence of Helicobacter pylori infection in bariatric surgery patients. Obes Surg 2023; 33(7): 2132–2138.
- 17. Pintar T, Kaliterna N and Carli T. The need for a patient-tailored *Helicobacter pylori* eradication protocol prior to bariatric surgery. *J Int Med Res* 2018; 46(7): 2696–2707.
- Xu MY, Cao B, Yuan BS, et al. Association of anaemia with Helicobacter pylori infection: a retrospective study. Sci Rep 2017;7(1): 13434.
- Almazeedi S, Al-Sabah S, Alshammari D, et al. The impact of *Helicobacter pylori* on the complications of laparoscopic sleeve gastrectomy. *Obes Surg* 2014; 24(3): 412–415.

- Bužga M, Zavadilová V, Holéczy P, et al. Dietary intake and ghrelin and leptin changes after sleeve gastrectomy. Wideochirurgia I Inne Techniki Maloinwazyjne 2014; 9(4): 554–561.
- Majumder S, Soriano J, Louie Cruz A, et al. Vitamin B12 deficiency in patients undergoing bariatric surgery: preventive strategies and key recommendations. Surg Obes Relat Dis 2013; 9(6): 1013–1019.
- Gasmi A, Bjørklund G, Mujawdiya PK, et al. Micronutrients deficiences in patients after bariatric surgery. *Eur J Nutr* 2022; 61(1): 55–67.
- Lin YS, Chen MJ, Shih SC, et al. Management of Helicobacter pylori infection after gastric surgery. World J Gastroenterol 2014; 20(18): 5274–5282.
- Dugan N, Thompson KJ, Barbat S, et al. Male gender is an independent risk factor for patients undergoing laparoscopic sleeve gastrectomy or Roux-en-Y gastric bypass: an MBSAQIP® database analysis. Surg Endosc 2020; 34(8): 3574–3583.
- Fong P and Wang QT. Protective effect of oral contraceptive against Helicobacter pylori infection in US adult females, NHANES 1999–2000. Epidemiol Infect 2021; 149: e120.
- DeLoughery TG. Iron deficiency anemia. Med Clin North Am 2017; 101(2): 319–332.
- Mulita F, Lampropoulos C, Kehagias D, et al. Long-term nutritional deficiencies following sleeve gastrectomy: a 6-year single-centre retrospective study. *Prz Menopauzalny* 2021; 20(4): 170–176.
- Soliman AT, De Sanctis V, Yassin M, et al. Iron deficiency anemia and glucose metabolism. *Acta Biomed* 2017; 88(1): 112–118.
- Rawla P and Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. *Prz Gastroenterol* 2019; 14(1): 26–38.