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ORIGINAL ARTICLE

Relationship between active *Helicobacter pylori* infection and anemia, iron deficiency, iron deficiency anemia: A cross-sectional study in a sub-Saharan setting

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Abstract

Background and Aim: There have been contradictory reports about the association between *Helicobacter pylori* infection and iron deficiency anemia (IDA). Based on the high frequency of *H. pylori* infection in Cameroon, we have evaluated the frequency of *H. pylori* infection as the cause of anemia, and IDA among dyspeptic patients in Cameroon.

Methods: This cross-sectional study enrolled 842 dyspeptic patients (472 women and 370 men) in two reference hospitals in Douala-Cameroon. Each participant gave a written consent, and the study was approved by the National Ethical Committee. Erythroid-related indices and markers of iron deficiency (ID) measurement were done for each participant as well as *H. pylori* detection. Data were analyzed using SSPS statistical package.

Results: The prevalence of anemia, ID, IDA, and *H. pylori* infection was 65.08%, 31.47%, 25.65%, and 80.88%, respectively. *H. pylori* infected individuals had a significantly lower mean value of hemoglobin ($P = 0.01$), hematocrit ($P = 0.04$), ferritin ($P = 0.03$) and coefficient of transferrin saturation (CTS) levels ($P = 0.04$) and a significantly higher mean value of mean corpuscular hemoglobin concentration (MCHC) ($P = 0.02$). Compared with *H. pylori* non-infected participants, *H. pylori* infected patients were 1.2938 (95% confidence interval [CI]: 0.9087–1.8421), 1.1851 (95% CI: 0.8122–1.7292), and 1.5636 (95% CI: 1.0206–2.3953) times at higher risk to develop anemia, ID, and IDA, respectively. A significant relationship was found between *H. pylori* infection and IDA ($P = 0.04$ and 0.04 for crude and age/sex-adjusted, respectively).

Conclusion: *H. pylori* infection seems to be associated with anemia, and IDA among dyspeptic patients in our milieu.

Introduction

Iron deficiency (ID) is the most common nutritional disorder in the world, and it is estimated that at least 500 million people have iron deficiency anemia (IDA) worldwide.[1] It is a global public health problem affecting both developing and developed countries, with major consequences for human health as well as social and economic development. The causes of ID anemia include inadequate iron intake, chronic blood loss, and impaired iron absorption. Blood loss from the gastrointestinal tract is the most common cause of ID in men and postmenopausal women.[2,3] Existing practice guidelines recommend that the upper and lower gastrointestinal tract be evaluated in patients with confirmed IDA to exclude lesions that can cause chronic gastrointestinal blood loss such as carcinoma, large adenomas, severe mucosal erosions, ulcer disease, and vascular lesions or other sources of occult bleeding like celiac disease.[4,5] Celiac disease results in malabsorption of iron and is a well-described cause of IDA, especially among persons from Northern Europe,[4] where 2–3% patients with IDA have celiac disease.[6] Despite this endoscopic evaluation, approximately 35% of IDA cases remain without a clear cause.[7,8]

Multiple studies on the association between *Helicobacter pylori* (*H. pylori*) infection and IDA have been documented.[4,5] *H. pylori* is a gram-negative pathogen that is widespread all over the world, infecting more than 50% of the world's population, with a predominant distribution in developing countries (up to 80%) compared with industrialized ones (20–50%).[9] *H. pylori* is etiologically associated with several important upper gastrointestinal tract conditions, including chronic gastritis, peptic ulcer disease, atrophic gastritis, mucosa-associated-lymphatic tissue

(MALT-lymphoma), and gastric adenocarcinoma. The mechanisms by which *H. pylori* may produce IDA such as to impair iron uptake and increase iron loss have been documented.[10,11] Peptic ulcer disease and malignancies caused by *H. pylori* infection can lead to gastrointestinal blood loss and eventually to IDA.[4,5] However, patients infected with *H. pylori* mostly have chronic gastritis, which is not associated with gastrointestinal bleeding.[12] Although gastritis is not associated with gastrointestinal blood loss, it may lead to chronic atrophic gastritis, which is associated with hypochlorhydria or achlorhydria.[13] Because gastric acid is critical for the absorption of iron, atrophic gastritis can cause malabsorption of iron and IDA.[13]

Meta-analyses showed that *H. pylori* eradication combined with iron administration was more effective than iron administration alone for the treatment of IDA.[14,15] Such observation may justify the recommendation of The British Society of Gastroenterology, which persistently insist on *H. pylori* eradication in patients with IDA and normal colonoscopy or esophagogastroduodenoscopy (EGD) (Grade of recommendation, C),[4] and that of the Maastricht IV Consensus on the management of *H. pylori* infection, which recommends testing and treatment for *H. pylori* infection in patients with unexplained IDA.[16]

Recent local and regional estimates show a considerable prevalence of *H. pylori* infection in Cameroon. The prevalence of *H. pylori* infection in the Littoral region was 64.34%,[9] 60% in Western region,[17] and 64.74% in the Centre region.[18]

Despite this high prevalence of *H. pylori* infection in Cameroon, its role in peptic ulcer and gastrointestinal malignancies, which can bleed and eventually lead to IDA, there is lack of published reports focused on ID and anemia status in relation to *H. pylori* infection or data on the frequency of *H. pylori* infection as the cause of IDA in the country.

Therefore, the aim of the present study was to explore the relationship between *H. pylori* infection and anemia, ID, and IDA among dyspeptic patients living in the Littoral region of Cameroon, an area with high prevalence for *H. pylori* infection.

The choice of the use of endoscopy with rapid test urease as *H. pylori* diagnostic method in this study is hinged on the detection of active infection with this pathogen and its probable link to anemia and iron depletion instead of serological testing, which does not indicate a current infection and only shows exposure to these bacteria. Endoscopic evaluation was performed with the view to exclude patients with blood loss from the gastrointestinal tract, a common cause of anemia and ID. On the other hand, our sample population included participants older than 15 years old and both sex in place of children or only women in reproductive age who have a relatively high iron requirement respectively to meet the demands of growth and menstrual blood loss,[19,20] making it difficult to determine whether *H. pylori* is the cause of IDA or whether this organism is just a bystander.

Methods

Selection of subjects. This study took place in two reference health facilities in the Littoral region of Cameroon; the Laquintinie Hospital and the General Hospital all in Douala metropolis from August 2014 to December 2016. All 15 years or older patients complaining of epigastric pain, epigastric burning, abdominal bloating, or nausea/vomiting and who have undergone upper endoscopy with normal EGD and colonoscopy (which did not show gastrointestinal blood loss) in the Gastroenterology Department of the selected health centers were enrolled in this study. We employed a consecutive sampling for data collection, requesting consent from all volunteer patients in the selected health facilities who fulfilled the eligibility criteria for the study during the study period. Were excluded from the study: (i) patients who have taken antibiotics 2 weeks before performing the gastroscopy or proton pump inhibitors (PPI) 6 weeks before; (ii) patients who frequently use non-steroidal anti-inflammatory drugs (NSAIDS) or aspirin; (iii) those in other conditions that cause anemia or interfere with erythropoiesis including malignancy, hematological diseases, celiac disease, chronic diseases (chronic renal failure, chronic liver disease, severe cardiac and respiratory disease); (iv) pregnant and breastfeeding women; (v) women with heavy menstrual flow and/or metrorrhagia; (vi) patients with obvious blood loss (melena, hematochezia, hematuria, recurrent epistaxis); and (vii) non-cooperative patients.

Variables. From the subjects, the following information were requested: age, sex, personal medical history (history of malignancy, hematological diseases, chronic renal failure, chronic liver disease, severe cardiac disease, respiratory disease), medication history including current and regular use of antibiotics, PPI, medication, which lead to hemostasis failure such as NSAIDs or aspirin in a structural questionnaire. For all participants, direct inquiry about blood loss symptoms, such as melena, hematochezia, hematuria, intestinal worm or hematophagous parasites, and recurrent epistaxis, was done by a resident physician. Endoscopic evaluation of the upper and lower gastrointestinal tract for all the recruited patients was also performed by a resident gastroenterologist during the EGD examination in order to identify a source of chronic gastrointestinal blood loss.[4,5] The clinical sign evocative of gastrointestinal blood loss included masses, ulcerations, villous blunting of the small bowel mucosa suggestive of celiac disease, colitis, vascular ectasia or arteriovenous malformation, inflammatory polyps, or large bleeding hemorrhoids. Endoscopic indications were recorded, and only patients with normal EGD and colonoscopy that did not show any sign of gastrointestinal blood loss were included in the study.

Gastric biopsies were collected from all the enrolled dyspeptic patients for *H. pylori* screening using the rapid urease test.

The blood sample was also collected from each patient for complete blood cell counts and for the determination of ferritin level, serum iron level, total iron-binding capacity (TIBC), and coefficient of transferrin saturation (CTS). The obtained value for all these parameters was compared in both groups of patients according to *H. pylori* status. Anemia was defined according to the World Health Organization (WHO) sex-based criteria, that is, hemoglobin level of <13 g/dL (130 g/L) in men and <12 g/dL (120 g/L) in women.[21]

IDA was defined according to the Guidelines and Protocols Advisory Committee British Columbia,[22] which considered IDA in the following case: (i) anemia combined with ferritin <20 ng/mL in women and <30 ng/mL in men; (ii) anemia combined with serum iron concentration below 10 μmol/L and CTS <0.15; (iii) microcytosis together with hypochromia.

Samples collection and analysis. During EGD examinations (FOGD), biopsy samples from the antrum, the fundus, and the angulus of the small gastric curvature were collected and analyzed for *H. pylori* detection using the rapid urease test.

About 5 mL of venous blood were collected from each subject, then 2.5 mL of it was transferred into a tube containing K3-ethylenediaminetetraacetic acid (K3-EDTA) for complete blood counts determination (hemoglobin level, hematocrit, red blood cell count, mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC]). The remaining 2.5 mL of the blood was emptied into disposable clean test tubes, and used for serum iron levels, ferritin concentration, and TIBC determination.

Determination of* H. pylori *status. Biopsy samples were analyzed for *H. pylori* detection using the rapid urease test commercial kit HelicotecUT®Plus (Strong Biotech Corporation, Taipei, Taiwan). The specimens were placed on the test disc according to the manufacturer's recommendations, and the results were read at 5–30 min and 1 h later. The change in the color of the edge of the disc test from yellow to red was considered as a positive result.

Complete blood cells counts. The complete blood cells counts were measured using an automated electronic counter (ABX Pentra XL 80 PLC, HORIBA ABX.SAS, France) in blood samples collected in K3-EDTA tube. Anemia was defined as a hemoglobin level of <130 g/L in men and <120 g/L in women.[21] Patients with anemia were further divided into three groups according to the severity of anemia: mild anemia (110 g/L ≤ hemoglobin < 119 g/L for women and 110 ≤ hemoglobin < 129 g/L for men); moderate anemia (hemoglobin <110 g/L for men and women); and severe anemia (hemoglobin <80 g/L). Other erythroid-related indices such as hematocrit, red blood cell count, MCV, MCH, and MCHC were also recorded, and patients were then divided according to reference range value of these indices into the following type of anemia: normocytic anemia (80 ≤ MCV ≤ 100 fl), microcytic anemia (MCV <80 fl), macrocytic anemia (MCV >100 fl), hypochromic anemia (MCHC <320 pg), and normochromic anemia (320 ≤ MCHC ≤ 360 pg).[23]

Ferritin dosage. Serum ferritin concentration was evacuated using AccuDiag™ ferritin ELISA kit (Diagnostic Automation/Cortez Diagnostics. Inc., USA). The ferritin quantitative test kit is based on a solid-phase enzyme-linked immunosorbent assay. The assay system utilizes one anti-ferritin antibody for solid-phase immobilization and another mouse monoclonal anti-ferritin antibody in the antibody–enzyme (horseradish peroxidase) conjugate solution. The test sample was allowed to react simultaneously with antibodies, resulting in the ferritin molecules being sandwiched between the solid-phase and enzyme-linked antibodies. After a 60-min incubation at room temperature, the wells were washed with water to remove unbound labeled antibodies. A solution of TMB was added and incubated for 20 min, resulting in the development of a blue color. The color development was stopped with the addition of 2 N HCl, and the color was changed to yellow and measured at 450 nm. The concentration of ferritin was directly proportional to the color intensity of the test sample. The absorbance value of each test sample was used to determine the corresponding concentration of ferritin from the standards curve obtained with the reference standard set provided with the kit. The minimum sensitivity of the test was 5.0 ng/mL and its specificity was 98.5%. Ferritin level <20 ng/mL in women and <30 ng/mL in men was considered as ferritin deficient or decreased ferritin level, while those >100 ng/mL were considered as high.

Serum iron dosage. Serum iron was detected using Ferrimat-Kit (Biomerieux, France). This kit test allows colorimetric determination of iron in human serum and plasma without deproteinization, in an acid medium, and in the presence of guanidine, using hydroxylamine as a reducing agent and FerroZine as indicator. In the test mixture, guanidine hydrochloride denatures the carrier protein, hydroxylamine reduces ferric iron to ferrous iron, which is then chelated with FerroZine to give a magenta-colored complex. The intensity of the coloration is proportional to the amount of iron present in the sample. The test sensitivity in terms of detection limit was equal to 4 µmol/L or 0.22 mg/L or 0.23 µg/dL. Ferrimat-Kit was used following manufacturer's procedure. The working solution was prepared by emptying the content of reagent 2 (guanidine) into reagent 3 (color reagent) and was gently mixed. Reagent 1 was a standard. Sterile plastic tubes were labeled; blank, standard blank, standard, sample blank, and sample, respectively. The working solution (1 mL) was put in each tube, and 200 µL of the standard was put in the tubes labeled standard blank and standard. The sample (200 µL) was put in the tubes labeled sample blank and sample. One drop of reagent 3 was put in the tubes labeled sample and standard. The tubes were vortexed for 1 mn and kept for 10 mn for the reaction to take place, the absorbance was read at 562 nm, and the iron concentration was calculated using the following formula:

$$\text{Sample concentration} = \frac{[(\text{Abs of sample} - \text{Abs of sample blank})/(\text{Abs of standard} - \text{Abs standard blank})]}{\times n.n : \text{concentration of standard.}}$$

Serum iron concentrations below 10 µmol/L were considered as low serum iron or decreased serum iron level, those between 10–30 µmol/L as normal, and those above 30 µmol/L as high.

TIBC determination. The TIBC was evaluated after saturation of transferrin by an iron solution and absorption of the excess iron on magnesium hydroxycarbonate. The determination of iron bound to transferrin is then performed using Ferrimat-Kit as described above. The test sensitivity in terms of detection limit was equal to 0.54 µmol/L or 0.03 mg/L or 3.0 µg/dL. TIBC (µmol/L) normal value was between 40 and 80 µM, and a TIBC value above 80 µM was considered as high TIBC or increased TIBC value.[24]

Percent of transferrin saturation and CTS determination. The CTS and the percent of transferrin saturation were calculated from the TIBC and serum iron concentration as follows:

$$\text{Percent of transferrin saturation} = [\text{Serum iron}\,(\mu\text{mol/L})/\text{TIBC}] \times 100,$$

$$\text{CTS} = \text{Serum iron}\,(\mu\text{mol/L})/\text{TIBC}\,(\mu\text{mol/L}).$$

CTS normal value was between 20% and 40%.[24] CTS values below 20% were considered as low CTS or decreased CTS level.

Statistical analysis. Statistical analyses were performed using Statistical Package for SPSS (Windows version 19.0). Continuous variables were expressed as mean ± SD. Categorical variables were expressed as *n* (%). The Fisher exact test or chi-square test was used for the analysis of categorical variables and the Student *t*-test was used for the analysis of continuous variables. Multivariable logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) on the association between *H. pylori* infection and anemia, ID, and IDA. A probability value of <0.05 was considered statistically significant.

Results

Characteristics of the study population. This study included 1465 consecutive dyspeptic subjects who underwent upper endoscopy in the Gastroenterology Department of the selected health facilities. Those having a history of antibiotics, PPI, NSAIDs, or aspirin consumption ($n = 323$), those with a history of chronic diseases ($n = 158$), and those with blood loss symptoms or endoscopic indications of gastrointestinal blood loss ($n = 142$) were excluded, resulting in a final sample of 842 subjects (Fig. 1). Of the 842 subjects, 472 (56.06%) were women and 370 (43.94%) were men: their mean age was 44 ± 17 years and ranged from 15 to 90 years old.

Distribution of erythroid-related indices in the study population. The mean value of hemoglobin level among our sample population was 11.64 ± 1.429 g/dL (range 6–17 g/dL). Hemoglobin level less than 12 g/dL in men and less than 13 g/dL in women was detected in 548 participants, giving an overall prevalence of anemia of 65.08% (548/842) in our sample population. Participants in the age groups less than 20 years old and those above 61 years old with an approximate prevalence of 70% were most affected by anemia compared with those of the other age groups, but the difference was not significant ($\chi^2 = 4.224$, $P = 0.51$). As far as gender is concerned, men were significantly more affected than women ($P < 0.0001$); anemia was detected in 80.54% of men *versus* 52.97% for women (Table 1).

Regarding the intensity of anemia, mild, moderate, and severe anemia was detected respectively among 44.77% (377/842), 19.24 (162/842), and 1.06% (9/842) of our sample population. Men were the predominant gender among any degree of anemia ($\chi^2 = 70.231$, $P < 0.0001$). Also, mild anemia was seen mostly in participants aged less than 20 and those in the age group of 41–50 years old, moderate in those aged above 61 years, and severe in the age group 31–40 ($\chi^2 = 5.310$, $P = 0.42$) (Table 1).

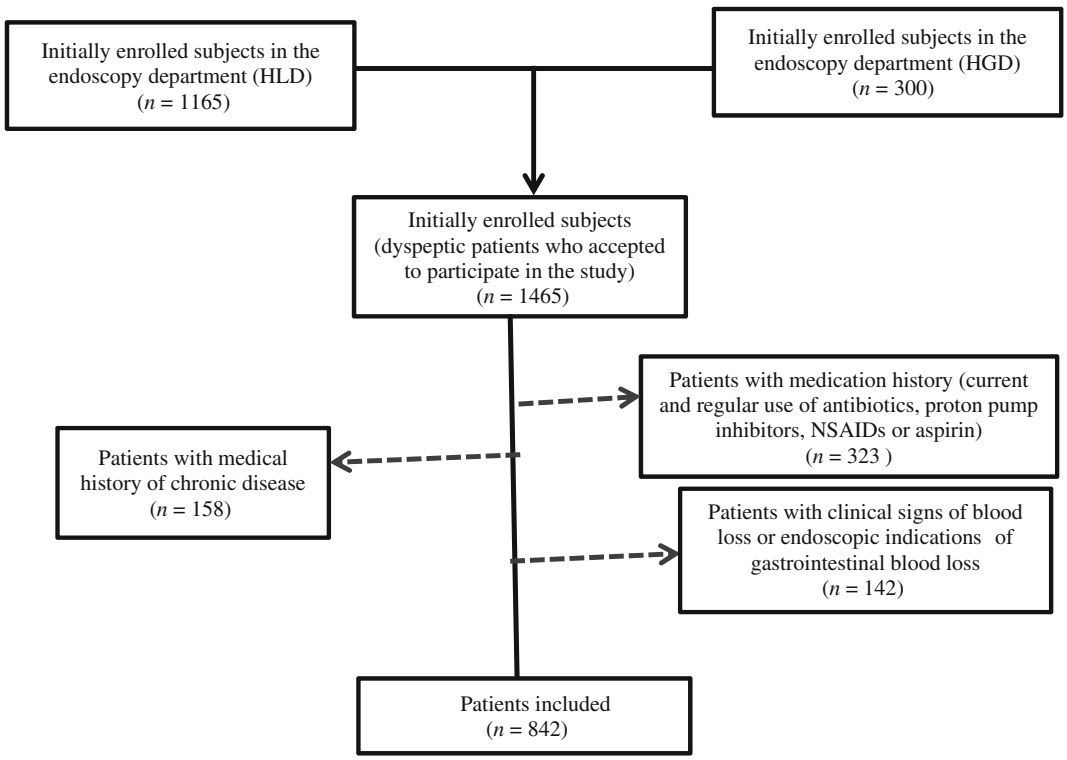

Figure 1 Sketch outlining the selection of our sample population

Table 1 Erythroid-related indices in the study population

Variable	*n*	Anemia status		Intensity of anemia			Type of anemia			
		Positive *n* = 548	Negative *n* = 294	Mild *n* = 377	Moderate *n* = 162	Severe *n* = 9	Hypochro *n* = 233	Normochro *n* = 609	Microcytic *n* = 122	Normocytic *n* = 720
Sex										
Women	472	250 (52.97)	222 (47.03)	170 (36.02)	77 (16.31)	3 (0.63)	124 (26.27)	348 (73.73)	75 (15.89)	397 (84.11)
Men	370	298 (80.54)	72 (19.46)	207 (55.94)	85 (22.97)	6 (1.62)	109 (29.46)	261 (70.54)	47 (12.70)	323 (87.30)
χ^2 (*P* value)		**(0.000)***		70.231 (**0.000**)*				(0.307)		(0.192)
Age (years)										
≤20	43	30 (69.77)	13 (30.23)	22 (51.16)	8 (18.60)	0 (0.00)	9 (20.93)	34 (79.07)	7 (16.28)	36 (83.72)
21–30	164	98 (59.76)	66 (40.24)	62 (37.80)	36 (21.95)	0 (0.00)	50 (30.49)	114 (69.51)	28 (17.07)	136 (82.93)
31–40	179	117 (65.36)	62 (34.64)	77 (43.02)	36 (20.11)	4 (2.23)	46 (25.70)	133 (74.30)	23 (12.85)	156 (87.15)
41–50	137	91 (66.42)	46 (33.58)	71 (51.82)	19 (13.87)	1 (0.73)	45 (32.85)	92 (67.15)	22 (16.06)	115 (83.94)
51–60	158	100 (63.29)	58 (36.71)	71 (44.93)	27 (17.09)	2 (1.26)	42 (26.58)	116 (74.42)	22 (13.92)	136 (86.07)
≥61	161	112 (69.56)	49 (30.44)	74 (45.96)	36 (23.36)	2 (1.24)	41 (25.46)	120 (74.53)	20 (12.42)	141 (87.58)
χ^2 (*P* value)		4.224 (0.517)		15.310 (0.429)			4.292 (0.508)		2.251 (0.813)	

*Significant.
N, n, Number; Hypochro, hypochromic; Normochro, normochromic; χ^2, chi-square.

Examining the type of anemia, microcytic anemia was detected in 14.49% (122/842) and normocytic anemia in 85.51% of participants. No case of macrocytic anemia was seen. Women and men were closely affected, 15.89% *versus* 12.70% for microcytosis and 84.1% *versus* 87.30% for normocytosis ($P = 0.19$). Participants aged less than 30 years old had the highest prevalence of microcytosis, while those aged above 51 years were found to have the highest prevalence of normocytosis ($P = 0.81$). Hypochromic and normochromic anemia was detected in 27.67% (233/842) and 72.33% (609/842) of participants, respectively. Men were slightly most affected by hypochromic anemia (29.46% compared with 26.27%) and women by normochromic anemia (73.73% compared with 70.54%). But the difference was not significant ($P = 0.30$). Participants in the age group of less than 20 years old had the highest prevalence of hypochromic anemia and the lowest prevalence of normochromic anemia ($P = 0.50$) (Table 1).

Distribution of markers of ID in the study population. The prevalence of iron parameters in the population was as follows (Table 2). The mean value of serum iron concentration among our sample population was 16.28 ± 5.63 µmol/L (range 6.08–40 µmol/L). When taking the threshold value for normal serum iron concentration (10–30 µmol/L), we noticed that 9.74% (82/842) of the participants had a decreased serum iron level. According to gender, decreased serum iron level rate of 9.96% (47/472) in women and 9.46% (35/370) in men was seen ($\chi^2 = 3.720$, $P = 0.15$). Concerning age, the lowest rate of decreased serum iron level (2.32%) was recorded among participants aged less than 20 years old, and the rate ranged from 8.69 to 11.73% in the other age groups. But the differences were not significant ($\chi^2 = 12.893$, $P = 0.22$).

The mean value of TIBC among our sample population was 57.858 ± 15.958 µmol/L (range 31.64 to 99.9 µmol/L). TIBC increased level was seen in 48.69% (410/842) of participants. Men (47.84%) and women (49.36%) were similarly concerned with TIBC increased level ($X^2 = 3.947$, $P = 0.13$). Nearly similar rate of TIBC increased level was recorded according to age of participant ($X^2 = 4.936$, $P = 0.89$).

The mean value of CST among our sample population was 21.70 ± 7.09% (range 2.00–45.00%). Decreased CST level was detected in 44.89% (378/842) of participants. A relatively similar rate of decreased CST level was seen in men (47.30%) and women (43.01%) ($\chi^2 = 1.680$, $P = 0.43$). As age is concerned, a lower rate of decreased CST level (38.41%) was seen in the age group of 21–30 years compared with the other age groups. However, the difference was not significant compared with the corresponding peer groups ($\chi^2 = 8.489$, $P = 0.58$).

The mean value of ferritin concentration among our sample population was 57.57 ± 37.11 ng/mL (range 10.00–221.00 ng/mL). Decreased ferritin level was seen in 26.65% (216/842) of participants. A significantly higher rate of decreased ferritin level was seen in men compared with women (41.89% in men *vs* 12.92% in women, $\chi^2 = 96.977$, $P < 0.0001$). Participants in the age group less than 20 years (39.53%) were more represented among subjects with decreased ferritin level. But the difference was non-significant ($\chi^2 = 15.301$, $P = 0.12$).

H. Pylori *infection and erythroid-related indices in the study population.* The prevalence of *H. pylori* in the study population was 80.88% (681/842): 80.51% (380/472) among women and 81.35% (301/370) among men, but the difference was not significant ($P = 0.75$). The rate of *H. pylori* infection with age was relatively constant with increasing age from less than 20 years to more than 61 years, and the difference was non-significant ($\chi^2 = 8.381$, $P = 0.13$) (Table 3).

The prevalence of anemia in the *H. pylori* positive group was higher than that in the negative group (82.30 [451] *vs* 17.70% [97]), even if the difference was not significant ($P = 0.15$). In addition, *H. pylori* infected individuals compared with *H pylori* uninfected ones had a significantly lower mean value of hemoglobin concentration (11.45 ± 0.048 *vs* 11.74 ± 0.125 g/dL, $t = 2.485$, $P = 0.01$) and hematocrit (35.82 ± 0.122 *vs* $36.68 \pm 0.317\%$, $t = 2.9$, $P = 0.04$) and a marginal lower value of red blood cell count (4.273 ± 0.020 *vs* 4.363 ± 0.520 10^9/l, $t = 1.863$, $P = 0.06$).

The strength of the association of *H. pylori* infection and anemia was analyzed by determining the OR and the corresponding 95% CI value. Our results show that compared with *H. pylori* negative patients, the OR of *H. pylori* status on anemia's prevalence was 1.2938 (95% CI: 0.9087–1.8421; $P = 0.15$). We also adjusted for age and sex in the logistic regression, and similar results were noticed (OR: 1.2907, 95% CI: 0.8912–1.8693, $P = 0.17$) (Table 4).

As far as the degree of anemia is concerned; mild, moderate, and severe anemia was detected respectively among 82.76%, 82.72%, and 55.55% of infected subjects compared with17.24%, 17.28%, and 44.45% in non-infected ones, but the difference was not significant ($\chi^2 = 6.279$, $P = 0.09$) (Table 3). Our results also show an OR of 1.2488 (95% CI: 0.8808–1.7704) for mild anemia and 1.1636 (95% CI: 0.7426–1.8234) for moderate anemia in the *H. pylori* positive group compared with *H. pylori* negative ones. This positive relationship persist even after adjusting with potential confounders (1.2339 [95% CI: 0.8637–1.7628]) and (1.1595 [95% CI: 0.7383–1.8211]) respectively (Table 4).

Regarding the type of anemia, hypochromic anemia, as well as microcytic anemia, was commonly found among *H. pylori* infected individuals compared with non-infected ones. But the difference was not significant ($P = 0.07$ and 0.40 for hypochromia and microcytosis, respectively). Concerning the mean value of other erythroid-related indices, a higher mean value of MCHC (32.82 ± 0.084 *vs* 32.23 ± 0.158 pg) with a significant difference ($t = 3.121$, $P = 0.02$), while a lower mean value of MCV (82.81 ± 0.192 *vs* 83.49 ± 0.462 fl) but with no significant difference ($t = 1.501$, $P = 0.13$) was noticed in *H. pylori* positive groups *versus* negative ones (Table 5). The strength of the association between *H. pylori* infection and the type of anemia shows an OR of 1.3659 (95% CI: 0.9433–1.9779) and 1.2419 (95% CI: 0.7432–2.0752) for hypochromic and microcytic anemia respectively among *H. pylori* infected patients compared with uninfected ones. This relation persists even when adjusted with confounding factors such as age and sex (1.3555 [95% CI: 0.9351–1.9647]) and (1.2420 [95% CI: 0.7423–2.0782]) respectively (Table 4).

Effect of* H. pylori *status on markers of ID (serum iron, TIBC, CST, and ferritin levels). In *H. pylori* positive individuals, rates of 78.05%, 82.44%, 83.86%, and 81.95% were recorded respectively among participants with reduced level of serum iron, increased level of TIBC, reduced level of CST, and reduced level of ferritin compared with 21.95%, 17.56%, 16.14%, and 18.05% recorded in *H. pylori* negative individuals. However, statistical analysis did not reveal any significant difference compared with other corresponding levels for each evaluated iron parameter ($P = 0.14$, 0.35, 0.09, and 0.33, respectively) (Table 6).

A non-significantly lower mean value of serum iron concentration (15.94 ± 0.194 *vs* 16.57 ± 0.4737 µmol/L, $P = 0.17$) and a non-significantly higher level of TIBC (76.19 ± 0.5992 *vs* 74.5 ± 1.347 µmol/L, $P = 0.23$) were detected in the *H. pylori* positive group compared with the *H. pylori* negative group (Table 5). However, a significantly lower mean value of ferritin and CST level was detected in *H. pylori* infected participants compared with uninfected ones. The mean value of ferritin concentration was 55.75 ± 1.334 ng/mL in the *H. pylori* positive group and 62.43 ± 2.959 ng/mL in the *H. pylori* negative group ($t = 2.143$, $P = 0.03$); the mean value of CST $21.32 \pm 0.2498\%$ was obtained in the *H. pylori* infected group *vs* $22.57 \pm 0.5981\%$ in the uninfected ones ($t = 2.099$, $P = 0.03$) (Table 5).

The crude OR of *H. pylori* status on reduced level of serum iron, reduced level of CST, and reduced level of ferritin prevalence were 0.8240 (95% CI: 0.4737–1.4335), 1.4277 (95% CI: 1.0038–2.0305), and 1.0986 (95% CI: 0.7370–1.6375), respectively. Similar trend on age and sex-adjusted OR was observed: 0.8482 (95% CI: 0.4871–1.4768), 1.4188 (95% CI: 0.9967–2.0196), and 1.0513 (95% CI: 0.6881–1.6062), respectively (Table 7).

Effect of* H. pylori *status on ID and IDA. Of 842 patients enrolled, 265 patients had ID, giving a prevalence of ID of 31.47% (265/842) in our sample population. When adjusted with socio-demographic factors, we found a significant relationship between the prevalence of ID and the gender of participants, with a peak of prevalence in men than in women (45.13% in men compared with 20.76% in women, $P < 0.0001$). Regarding age, a slightly higher prevalence of ID (39.53%) was detected among participants in the age group less than 20 years. But the difference was non-significant ($\chi^2 = 8.7669$, $P = 0.11$) (Table 2).

When examining the prevalence of ID with respect to *H. pylori* status, we found that, of the 265 patients with ID, 219 (82.64%) were *H. pylori* positive and 46 (17.36%) were negative, whereas among patients without ID, 80.07% *vs* 19.93% were *H. pylori* infected. This difference was not significant ($P = 0.37$). The OR of *H. pylori* infection on the prevalence of ID was 1.1851 (95% CI: 0.8122–1.7292) and 1.1620 (95% CI: 0.7854–1.7191) after adjusted with confounding factors (Table 7).

Of the overall recruited participants, 216 were diagnosed with IDA, given the IDA prevalence of 25.65% (216/842) in our sample population. Men were significantly more prone to develop IDA than women (39.46% *vs* 14.83%, $P < 0.0001$). Also, participants in the age groups less than 20 years old (30.23%) were more affected by IDA than the other age groups. But the difference was non-significant ($\chi^2 = 5.330$, $P = 0.37$) (Table 2).

Table 2 Distribution of markers of iron deficiency, iron deficiency, and iron deficiency anemia in the study population

Variable	*N* (%)	Sex		Age (years)					
		Women $n = 472$	Men $n = 370$	≤20 $n = 43$	21–30 $n = 164$	31–40 $n = 179$	41–50 $n = 137$	51–60 $n = 158$	≥61 $n = 161$
Serum iron (μmol/L), mean ± SD: 16.28 ± 5.63, range: 6.08–40, median: 5.0									
Low level	82 (9.74)	47 (9.96)	35 (9.46)	1 (2.32)	16 (9.76)	21 (11.73)	15 (10.95)	15 (9.49)	14 (8.69)
Normal level	736 (87.41)	407	329	42	144	154	121	134	141
High level	24(2.85)	18	6	0	4	4	1	9	6
χ^2 (*P* value)		3.720 (0.15)		12.893 (0.22)					
TIBC (μmol/L), mean ± SD: 57.858 ± 15.958, range 31.64–99.9, median: 80.00									
Low level	3 (0.36)	0	3	0	1	1	0	1	0
Normal level	429 (50.95)	239	190	18	90	91	71	80	79
High level	410 (48.69)	233 (49.36)	177 (47.84)	25 (58.14)	73(44.51)	87 (48.60)	66 (48.17)	77 (48.73)	82 (50.93)
χ^2 (*P* value)		3.947 (0.13)		4.936 (0.89)					
CTS (%), mean ± SD: 21.70 ± 7.09, range: 2.00–45.00, median: 20.00									
Low level	378 (44.89)	203 (43.01)	175 (47.30)	21 (48.84)	63 (38.41)	81 (45.25)	62 (45.25)	71 (44.94)	80 (49.69)
Normal level	443(56.61)	256	187	21	95	95	74	81	77
High level	21(2.49)	13	8	1	6	3	1	6	4
χ^2 (*P* value)		1.680 (0.43)		8.489 (0.58)					
Ferritin (ng/mL), mean ± SD: 57.57 ± 37.11, range 10.00–221.00, median: 53.50									
Low level	216 (25.65)	61 (12.92)	155 (41.89)	17 (39.53)	50 (30.49)	46 (25.70)	37 (27.01)	30 (18.99)	36 (22.36)
Normal level	524 (61.04)	355	169	22	96	108	85	113	100
High level	102 (12.11)	56	46	4	18	25	15	15	25
χ^2 (*P* value)		96.977 (***P* < 0.0001**)*		15.301 (0.12)					
Iron deficiency									
Yes	265 (31.47)	98 (20.76)	167 (45.13)	17 (39.53)	59 (35.97)	60 (33.52)	47 (34.31)	39 (24.68)	43 (26.71)
No	577 (68.53)	374 (79.24)	203 (54.86)	26 (60.47)	105 (64.03)	119 (66.48)	90 (65.69)	119 (75.32)	118 (73.29)
χ^2 (*P* value)		57.1257 (***P* < 0.0001**)*		8.7669 (0.11)					
Iron deficiency anemia									
Yes	216 (25.65)	70 (14.83)	146 **(39.46)**	13 **(30.23)**	45 (27.44)	49 (23.37)	39 (28.47)	30 (18.99)	40 (24.84)
No	626 (74.35)	402 (85.17)	224 **(60.54)**	30 **(69.77)**	119 (72.56)	130 (76.63)	98 (71.53)	128 (81.01)	121 (75.16)
χ^2 (*P* value)		(***P* < 0.0001**)*		5.330 (0.37)					

*Bold values are for statistical significant *P* value.

N, n, Number; SD, standard deviation; χ^2, chi-square.

Table 3 Anemia-severity-type distribution according to *H. pylori* status in the study population

Variable	Number	*H. pylori* +ve (%) $n = 681$	*H. pylori* –ve (%) $n = 161$	χ^2 value	*P* value
Sex					
Women	472	380 (80.50)	92 (19.49)		0.75
Men	370	301(81.35)	69 (18.65)		
Age (years)					
≤20	43	39 (90.70)	4 (9.30)	8.381	0.13
21–30	164	141 (85.97)	23 (14.03)		
31–40	179	144 (80.45)	35 (19.55)		
41–50	137	111 (81.02)	26 (19.98)		
51–60	158	122 (77.21)	36 (22.79)		
≥61	161	124 (77.02)	37 (22.98)		
Anemia					
Yes	548	451(82.30)	97(17.70)		0.15
No	294	230 (78.23)	64 (21.77)		
Intensity of anemia					
Mild	377	312 (82.76)	65 (17.24)	6.279	0.09
Moderate	162	134 (82.72)	28 (17.28)		
Severe	9	5 (55.55)	4 (44.45)		
Hypochromic anemia					
Yes	233	180 (77.25)	53 (22.75)		0.07
No	609	501 (82.27)	108 (17.73)		
Microcytic anemia					
Yes	122	102 (83.61)	20 (16.39)		0.40
No	720	579 (80.42)	141 (19.58)		

+ve, positive; −ve, negative; χ^2, Chi-square.

Regarding the prevalence of IDA with respect to *H. pylori* status, we noticed a significant difference in *H. pylori* infection, between patients with and without IDA ($P = 0.04$). In fact, 85.65% *versus* 14.35% of the patients who had IDA were *H. pylori* positive, while 79.23% *versus* 20.77% of patients without IDA were *H. pylori* infected.

The strength of the association of *H. pylori* infection and IDA shows that *H. pylori* infected patients were 1.5636 times more subjected to IDA than uninfected patients (OR: 1.5636, 95% CI: 1.0206–2.3953) with a significant difference ($P = 0.04$). This positive relationship persists even after being adjusted with age and sex (OR = 1.5742, 95% CI: 1.0112–2.4506, $P = 0.04$) (Table 7).

Discussion

In this cross-sectional study, we assessed the association between *H. pylori* infection, anemia, ID, and IDA among dyspeptic patients attending two reference health facilities in the Littoral region of Cameroon, an area with high prevalence of *H. pylori* infection. Our results showed that anemia has the greatest burden in Cameroon in low-income settings. The prevalence of anemia, ID, and IDA was 65.08% (548/842), 31.47% (265/842), and 25.65% (216/842), respectively, in our sample population.

The prevalence of *H. pylori* in the study population was 80.88%: 80.51% among women and 81.35% among men. We did not observe any significant difference in relation to gender ($P = 0.75$). Some authors believe that *H. pylori* infection is more common in male.[9,25] The rate of *H. pylori* infection was relatively constant with increasing age from less than 20 years to less than 61 years ($P = 0.13$). However, the pattern of age-dependent progression was found in other studies.[9,25]

The prevalence of anemia in the current study was 65.08% (548/842), which is higher than that obtained in previous studies done in Cameroon and in some countries within Africa. Few investigations showed that anemia has the greatest burden among adults or special cohort in Cameroon. Anemia was seen in 39.3% of adults dwelling in urban areas in Cameroon,[26] 41.4% in a cohort of diabetic,[27] and 39.8% in pregnant women at an urban tertiary hospital.[28] In Congo-Brazzaville and Tanzania, a prevalence of 42% in the general population[29] and 57% in patients with heart failure[30] has been reported respectively. However, the current prevalence of anemia is close to the 64.6% reported by Mukaya *et al*. in the emergency setting with prevalent symptoms of anemia.[31]

Regarding the severity of anemia, mild, moderate, and severe anemia were detected respectively among 44.77 (377/842), 19.24 (162/842), and 1.07% (9/842) of our sample population. A previous investigation on anemia in Cameroon revealed that anemia was mild in 30.5%, moderate in 8.1%, and severe in 0.8% among a cohort of 236 participants.[26] These findings, coupled with ours, show that the prevalence of anemia decreases with severity in our setting.

Concerning the type of anemia, the prevalence of microcytosis, normocytosis, and macrocytosis was 14.49%, 85.51%, and 0%, respectively, in our sample population. Regarding red blood cell color, hypochromia and normochromia were detected in 27.67% and 73.73% of participants, respectively. The absence of macrocytosis among our anemic population can imply that the anemia might not be caused by vitamin B12 deficiency[32] and the

Table 4 Strength of the association between anemia-severity-type and *H. pylori* infection in the study population using univariate and multivariate logistic regression analysis

Variable	*N*	Present *n* (%)	Absent *n* (%)	Univariate logistic regression		Multivariate logistic regression	
				OR (95% CI)	*P* value	OR (95% CI)	*P* value
Anemia		548	294				
H. pylori status							
Yes	681	451(66.23)	230(33.77)	1.2938 (0.9087–1.8421)	0.15	(1.2907 (0.8912–1.8693)	0.1768
No	161	97(60.25)	64(39.75)				
Age ≤20							
Yes	43	30(69.77)	13 (30.23)	1.2518 (0.6426–2.4386)	0.50	0.7570 (0.3783–1.5148	0.4315
No	799	518 (64.83)	281(35.17)				
Gender							
Female	472	250 (52.97)	222 (47.03)	0.2721 (0.1987–0.3726)	**<0.0001***	0.2709 (0.1977–0.3713	**<0.0001***
Male	370	298 (80.54)	72 (19.46)				
Hypochromia		233 (27.67)	609 (72.33)				
H. pylori status							
Yes	681	180 (26.43)	501 (73.57)	1.3659 (0.9433–1.9779)	0.09	1.3555 (0.9351–1.9647)	0.10
No	161	53 (32.92)	108 (67.08)				
Age ≤20							
Yes	43	9 (20.93)	34 (79.07)	0.6797 (0.3208–1.4399)	0.31	0.7072 (0.3331–1.5014)	0.36
No	799	224 (28.04)	575 (71.96)				
Gender							
Female	472	124 (26.27)	348 (73.73)	1.1720 (0.8654–1.5873)	0.30	1.1724 (0.8651–1.5890)	0.30
Male	370	109 (29.46)	261 (70.54)				
Microcytosis		123 (14.61)	719 (85.39)				
H. pylori status							
Yes	681	103(15.12)	578(84.88)	1.2419 (0.7432–2.0752)	0.40	1.2420 (0.7423–2.0782)	0.40
No	161	20(12.42)	141(87.58)				
Age ≤20							
Yes	43	7 (16.28)	36(83.72)	0.8646 (0.3758–1.9896)	0.73	0.8931 (0.3872–2.0602)	0.79
No	799	116(14.52)	683(85.48)				
Gender							
Female	472	76(16.10)	396(83.90)	1.2983 (0.8763–1.9235)	0.19	1.2995 (0.8769–1.9258)	0.19
Male	370	47(12.70)	323(87.30)				
Mild anemia		377 (44.77)	465 (55.23)				
H. pylori status							
Yes	681	312 (82.76)	369 (79.35)	1.2488 (0.8808–1.7704)	0.21	1.2339 (0.8637–1.7628)	0.24
No	161	65 (17.24)	96 (20.65)				
Age ≤20							
Yes	43	22 (5.84)	21 (4.52)	0.7632 (0.4130–1.4103)	0.38	0.7415 (0.3956–1.3897)	0.35
No	799	355 (94.16)	444 (95.48)				
Gender							
Female	472	170 (45.09)	302 (64.95)	0.4433 (0.3356–0.5855)	**<0.0001***	0.4418 (0.3343–0.5839)	**<0.0001***
Male	370	207(54.91)	163 (35.05)				
Moderate anemia		162 (19.24)	680 (80.76)				
H. pylori status							
Yes	681	134 (82.72)	547 (80.44)	1.1636 (0.7426–1.8234)	0.50	1.1595 (0.7383–1.8211)	0.52
No	161	28 (17.28)	133 (19.56)				
Age ≤20							
Yes	43	8 (4.94)	35 (5.15)	1.0440 (0.4749–2.2954)	0.91	1.0399 (0.4709–2.2965)	0.92
No	799	154 (95.06)	645 (94.85)				
Gender							
Female	472	77 (47.53)	395 (58.09)	0.6536 (0.4634–0.9219)	**0.01***	0.6545 (0.4639–0.9233)	**0.01***
Male	370	85 (52.47)	285 (41.91)				
Severe anemia		9 (1.07)	833 (98.93)				
H. pylori status							
Yes	681	4 (44.44)	676 (81.15)	0.2903 (0.0771–1.0935)	0.06	0.2960 (0.0784–1.1186)	0.07
No	161	4(44.44)	157 (18.85)				

(*Continues*)

Table 4 (Continued)

Variable	*N*	Present *n* (%)	Absent *n* (%)	Univariate logistic regression OR (95% CI)	*P* value	Multivariate logistic regression OR (95% CI)	*P* value
Age ≤20							
Yes	43	0 (0.00)	43 (5.16)	64 216.4479 (0.000 > 1.0E12)	0.97	39 458.1756 (0.000 > 1.0E12)	0.97
No	799	9 (100.00)	790 (94.84)				
Gender							
Female	472	3 (33.33)	469 (56.30)	0.3881 (0.0964–1.5621)	0.18	0.3857 (0.0955–1.5578)	0.18
Male	370	6 (66.67)	364 (43.70)				

*Bold values are for statistical significant *P* value.
Adjusted OR and 95% CI were calculated by adjusting for the potential confounders, including age, sex.
95% CI, 95% confidence intervals; N, n, number; OR, odds ratio.

Table 5 Mean value + SD of erythroid-related indices and iron parameters according to *Helicobacter Pylori* status

Variable ($n = 842$)	Mean ± SD	*H. pylori* +ve $n = 688$	*H. pylori* –ve $n = 159$	*t* value	*P* value
HB (g/dL)	11.630 ± 1.429	11.45 ± 0.0478	11.74 ± 0.125	2.485	**0.01***
HTC (%)	35 983 ± 3379	35.82 ± 0.122	36.68 ± 0.317	2.9	**0.04***
RBC (10^9/L)	4289 ± 0.555	4.273 0.020	4.363 0.520	1.863	0.06
MCHC (pg)	32 670 ± 2.174	32.82 ± 0.084	32.23 ± 0.159	3.121	**0.02***
MCV(fl)	83.088 ± 5293	82.81 ± 0.192	83.49 ± 0.462	1.501	0.13
Serum iron (μmol/L)	16.286 ± 5.63	15.94 ± 0.194	16.57 ± 0.474	1.363	0.17
TIBC (μmol/L)	76.929 ± 15.958	76.19 ± 0.599	74.5 ± 1.347	1.2	0.23
CST (%)	21.702 ± 7.092	21.32 ± 0.249	22.57 ± 0.598	2.099	**0.04***
Ferritin (ng/mL)	57.571 + 37.117	55.75 ± 1.334	62.43 ± 2.959	2.143	**0.03***

*Bold values are for statistical significant *P* value.
+ve, positive; −ve, negative.
CST, coefficient of transferrin saturation; HB, hemoglobin; HTC, hematocrit; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; RBC, red blood cell; SD, standard deviation; TIBC, total iron-binding capacity.

Table 6 Distribution of iron parameters levels according to *Helicobacter pylori* status

Variable	Number	*H. pylori* +ve (%) $n = 681$	*H. pylori* –ve (%) $n = 161$	χ^2	*P* value
Serum iron (μmol/L)					
Low level	82	64 (78.05)	18 (21.95)	3.847	0.14
Normal level	736	601 (81.67)	135 (18.33)		
High level	24	16 (66.67)	8 (33.33)		
TIBC (μmol/L)					
Low level	3	310 (0.00)	0 (0.00)	2.0869	0.35
Normal level	429	340 (79.25)	89 (20.75)		
High level	410	338 (82.44)	72 (17.56)		
CTS (%)					
Low level	378	317 (83.86)	61 (16.14)	4.649	(0.09)
Normal level	443	349 (78.78)	94 (21.22)		
High level	21	15 (71.43)	6 (28.57)		
Ferritin (ng/mL)					
Low level	216	177 (81.94)	39 (18.05)	2.199	(0.33)
Normal level	524	427 (81.49)	97 (18.51)		
High level	102	77 (75.49)	25 (24.51)		

+ve, positive; −ve, negative.
CST, coefficient of transferrin saturation; TIBC, total iron-binding capacity.

presence of microcytosis/hypochromia may reflect the prevalence of ID in this cohort.[33]

Exploration of ID through serum iron, TIBC, CST, and ferritin measurements was also investigated. ID and IDA were found in 31.47% and 25.65% of our sample population. Similarly, high prevalence of ID in children has been described in some African countries: 40% in Tanzania[34] and 41% in Nigeria.[35] In a study conducted in Nigeria, ID was found to be responsible for 57% of the anemia in 1–15-year-old children.[36] However, the current prevalence of IDA is far higher than the

Table 7 Strength of the association between iron parameters—iron deficiency, iron deficiency anemia, and *Helicobacter pylori* infection in the study population using univariate and multivariate logistic regression analysis

				Univariate logistic regression		Multivariate logistic regression	
Variable	*N*	Present *n* (%)	Absent *n* (%)	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Low iron serum level		82 (9.74)	760 (90.26)				
H. pylori status							
Yes	681	64 (78.05)	617 (81.18)	0.8240 (0.4737–1.4335)	0.49	0.8482 (0.4871–1.4768)	0.56
No	161	18 (21.95)	143 (18.82)				
Age ≤20							
Yes	43	1 (1.22)	42 (5.53)	4.7378 (0.6435–34.8801)	0.12	4.6697 (0.6335–34.4186)	0.13
No	799	81 (98.78)	718 (94.47)				
Gender							
Female	472	47 (57.32)	425 (55.92)	1.0583 (0.6678–1.6771)	0.80	1.0660 (0.6721–1.6909)	0.78
Male	370	35 (42.68)	335 (44.08)				
Low CST level		378 (44.89)	464 (55.11)				
H. pylori status							
Yes	681	317 (83.86)	364 (78.45)	1.4277 (1.0038–2.0305)	**0.04***	1.4188 (0.9967–2.0196)	**0.05***
No	161	61 (16.14)	100 (21.55)				
Age ≤20							
Yes	43	21 (5.56)	22 (4.74)	0.8453 (0.4575–1.5620)	0.59	0.8693 (0.4692–1.6104)	0.65
No	799	357 (94.44)	442 (95.26)				
Gender							
Female	472	203 (53.70)	269 (57.97)	0.8409 (0.6396–1.1055)	0.21	0.8416 (0.6396–1.1072)	0.21
Male	370	175 (46.30)	195 (42.03)				
Low ferritin level		216 (25.65)	626 (74.35)				
H. pylori status							
Yes	681	177 (81.94)	504 (80.51)	1.0986 (0.7370–1.6375)	0.64	1.0513 (0.6881–1.6062)	0.81
No	161	39 (18.06)	122 (19.49)				
Age ≤20							
Yes	43	17 (7.87)	26 (4.15)	0.2059 (0.1467–0.2890)	**<0.0001***	0.4251 (0.2143–0.8434)	**0.01***
No	799	199 (92.13)	600 (95.85)				
Gender							
Female	472	61 (28.24)	411 (65.65)	0.5069 (0.2694–0.9536)	**0.03***	0.2013 (0.1430–0.2834)	**<0.0001***
Male	370	155 (71.76)	215 (34.35)				
Iron deficiency		265 (31.47)	577 (68.53)				
H. pylori status							
Yes	681	219 (82.64)	462 (80.07)	1.1851 (0.8122–1.7292)	0.37	1.1620 (0.7854–1.7191)	0.45
No	161	46 (17.36)	115 (19.93)				
Age ≤20							
Yes	43	17 (6.41)	26 (4.51)	0.6883 (0.3668–1.2917)	0.24	0.6414 (0.3326–1.2368)	0.18
No	799	248 (93.59)	551 (95.49)				
Gender							
Female	472	98 (36.98)	374 (64.82)	0.3185 (0.2354–0.4310)	**<0.0001***	0.3164 (0.2337–0.4285)	**<0.0001***
Male	370	167 (63.02)	203 (35.18)				
Iron deficiency anemia		216 (25.65)	626 (74.35)				
H. pylori status							
Yes	681	185 (85.65)	496 (79.23)	1.5636 (1.0206–2.3953)	**0.04***	1.5742 (1.0112–2.4506)	**0.04***
No	161	31 (14.35)	130 (20.77)				
Age ≤20							
Yes	43	13 (6.02)	30 (4.79)	0.7860 (0.4022–1.5360)	0.48	0.7531 (0.3720–1.5248)	0.43
No	799	203(93.98)	596 (95.21)				
Gender							
Female	472	70 (32.41)	402 (64.22)	0.2672 (0.1924–0.3710)	**<0.0001***	0.2652 (0.1907–0.3688)	**<0.0001***
Male	370	146 (67.59)	224 (35.78)				

*Bold values are for statistical significant *P* value.

Adjusted OR and 95% CI were calculated by adjusting for the potential confounders, including age, sex.

95% CI, 95% confidence intervals; N, n, number; OR, odds ratio.

prevalence of 0.37%: 0.17% for male and 0.20% for female reported in Chinese population in 2008.[37]

The specialty of our sample population may explain such a difference. Blood loss from the gastrointestinal tract is the most common cause of anemia in men and postmenopausal women. This later cause could give credit to the highest prevalence of anemia in our population because we enrolled only dyspeptic patients or participants with gastrointestinal related disorders who are thought to be at risk of anemia through gastrointestinal blood loss compared with healthy individuals or general population. Thus, the incidence rate of anemia, ID, or IDA among dyspeptic patients would be higher than that in the healthy or general population. As illustrated, the current prevalence of anemia is comparable to the 64.6% prevalence observed in the emergency setting with prevalent symptoms of anemia.[31] The selection of participants for both sex and the age range difference in this study compared with previous studies may also explain such observation. In fact, in our sampling processes, we included both males and females aged up to 15 years old instead of only women in reproductive age or children who have a relatively high iron requirement to meet the demands of growth and menstrual blood loss. Another plausible justification for variation in the prevalence of anemia and iron deficiencies may be the difference in socioeconomic status, cultural, and dietary patterns across setting or study area.[38]

Regarding the distribution of anemia, ID, and IDA according to gender, men were significantly more affected by anemia than women (80.54% men *vs* 52.97% women, $P < 0.001$), and were also significantly more affected at any severity of anemia compared with women ($P < 0.001$). The present prevalence of anemia in women is close to the prevalence of 59.4% reported among women in the same region of Cameroon in 2004.[39] However, results of the present study showing a higher odd ratio of anemia in men than in women are in disagreement with previous data revealing a prevalence of 27.7% in males compared with 55.6% in females with a female sex associated high OR for anemia of 3.3 ($P < 0.001$) in Cameroon.[26] Our findings are also in contrast with previous reports in Benin showing a prevalence of 50% of anemia in women *versus* 20% in men.[40]

Mild anemia mostly in men and mild to moderate in women had been found in Cameroon ($P < 0.001$),[26] which is not consistent with our results. However, the prevalence of 36.02%, 16.31% and 0.63%, respectively, for mild, moderate, and severe anemia observed among women in this study is near to the prevalence of 21.5%, 17.4%, and 0.8% for mild, moderate, and severe anemia reported among women in the 2018 Cameroon Demographic and Health Survey.[41] As in anemia, men were significantly more affected than women regarding iron deficiencies: 45.13% *versus* 20.76% for ID ($P < 0.001$), 39.46% *versus* 14.83% for IDA ($P < 0.001$). It is known that the burden of anemia is highest in females less than 40 years old (premenopausal women) due to blood loss during menstruation, and gradually declines with increasing age.[26] The present fewer odds of anemia, ID, and IDA among women in this study although unexpected could be due to the fact that women in our population were mainly postmenopausal women than premenopausal women, because approximately 40% (37.9%) of our sample population was above 40 years old and women are the predominant gender. The fact that women commonly have routine follow-up cares, a good opportunity to get key information/message about prevention of anemia from health personals than men who are not used to being frequent in health facilities may also justify such observation.

Examining age and anemia, the peak of anemia (approximately 70%) was found in the age groups less than 20 years and above 61 years old ($P = 0.51$). The present finding on the prevalence of anemia relative to age is in accordance with previous data observed in studies within Africa, reporting that younger ones and seniors are more subjected to anemia. In fact, approximately 80% and 50% of preschool and school children, respectively, in Benin were found to be anemic,[40] and 76% of preschool children in the Littoral region of Kenya.[42] A higher prevalence of anemia in people older than 50 years was reported by Mugisha *et al*.[43]

Younger participants were the most affected by microcytosis ($P = 0.81$) or hypochromia ($P = 0.50$) with an age-dependent decrease tendency. Similar decrease in microcytosis with increasing age was reported in the literature. A previous investigation on anemia among children revealed that the highest prevalence of microcytosis (56%) was recorded in the 12-month age group, which then decreased and reached approximately 20% after 18 months.[44] These authors also recorded only few cases of macrocytosis in their sample population, which is consistent with our result on the rarity of macrocytosis.[44]

No significant relationship was found between age and ID ($P = 0.11$) nor with IDA, although younger participants were mostly affected ($P = 0.37$). The present pattern of anemia, ID, and IDA relative to age could be explained by relatively high iron requirement to meet the demands of growth in children and occult blood loss in aging men because the burden of anemia increases gradually with age in men.[26]

The distribution of anemia according to *H. pylori* status showed that *H. pylori* infected patients were 1.2938 times more subjected to anemia than the uninfected ones ($P = 0.15$), with a similar trend after adjusting for age and sex (OR: 1.2907, 95% CI: 0.8912–1.8693, $P = 0.17$). In addition, we observed a significantly low hemoglobin level ($P = 0.01$), lower hematocrit level ($P = 0.04$), and a marginal low red blood cell count ($P = 0.06$) in *H. pylori* positive group compared with *H. pylori* negative group. Based on the above results, we believe that a positive association between *H. pylori* infection and hemoglobin level exists. In a cross-sectional study on asymptomatic male senior citizens at the General Hospital of Chinese, the crude OR of *H. pylori* status on anemia prevalence was 2.53 (95% CI: 1.05–6.09; $P = 0.033$) compared with the *H. pylori* negative individuals, with similar results after adjusting for age in the logistic regression.[45] Moreover, in the Chinese population, a retrospective study exploring the association between *H. pylori* infection and anemia reported a significantly higher prevalence of anemia in the *H. pylori* positive group than in the *H. pylori* negative group after adjusting for potential confounders (OR = 1.19; 95% CI: 1.03, 1.39; $P = 0.021$).[33] Similarly, a community-based study of Arabs found a significantly low hemoglobin level in children aged 6–9 years who were infected with *H. pylori* compared with their uninfected peers.[46] Also, a meta-analysis of randomized control trials of *H. pylori* eradication has indicated that eradication can increase hemoglobin levels.[14]

Regarding the severity of anemia, OR of 1.2488 (95% CI: 0.8808–1.7704, $P = 0.21$) for mild anemia and 1.1636 (95% CI: 0.7426–1.8234, $P = 0.50$) for moderate anemia were recorded in *H. pylori* positive group compared with *H. pylori* negative ones, with a constant trend even after adjusting with potential confounders (OR: 1.2339, 95% CI: 0.8637–1.7628, $P = 0.24$ and 1.1595, 95% CI: 0.7383–1.8211, $P = 0.52$ respectively), but without significant difference (Table 4).

Analysis of the association between *H. pylori* infection and different types of anemia showed that *H. pylori* infected patients were 1.3659 (95% CI: 0.9433–1.9779, $P = 0.09$) and 1.2419 (95% CI: 0.7432–2.0752, $P = 0.40$) times more affected by hypochromia and microcytosis respectively compared with uninfected patients, even after adjusting for potential confounders (1.3555, 95% CI: 0.9351–1.9647, $P = 0.10$; 1.2420, 95% CI: 0.7423–2.0782, $P = 0.40$). We also observed a significantly high mean value of MCHC ($P = 0.02$) and lower mean value of MCV ($P = 0.13$) between *H. pylori* positive and *H. pylori* negative groups. Similarly, a study assessing the etiological role of *H. pylori* infection in adult Egyptian patients with unexplained or refractory IDA observed a significant correlation of MCV among *H. pylori* positive individuals and *H. pylori* negative ones ($P = 0.046$).[47]

H. pylori infection impairs iron uptake. This mechanism, together with others, may contribute to the depletion of iron in infected patients. In this study, markers of ID within the abnormal range were mainly seen in *H. pylori* infected patients. The OR of *H. pylori* status on reduced level of serum iron, reduced level of CST, and reduced level of ferritin prevalence were 0.8240 (95% CI: 0.4737–1.4335), 1.4277 (95% CI: 1.0038–2.0305), and 1.0986 (95% CI: 0.7370–1.6375), respectively. Similar age and sex-adjusted OR was observed: 0.8482 (95% CI: 0.4871–1.4768), 1.4188 (95% CI: 0.9967–2.0196), and 1.0513 (95% CI: 0.6881–1.6062), respectively. On the other hand, t-test results showed a significant relationship between *H. pylori* infection and low serum CST, and low ferritin level ($P = 0.03$ and 0.03, respectively), in addition to a lower mean value of serum iron level ($P = 0.17$) and higher level of TIBC ($P = 0.23$) in *H. pylori* positive group compared with *H. pylori* negative group, indicating that *H. pylori* infection leads to decreased serum iron level, to decreased serum ferritin level, to increased TIBC levels and decreased CST level. This finding is in accordance with several studies documented. Increased serum level of TIBC and decreased serum ferritin level was found in 55.55% (20/36) of *H. pylori* IgG seropositive patients against 2.78% IgG seropositive patient in control group whose serum TIBC and ferritin levels were normal.[48] Milman *et al*. also found significantly low ferritin levels in patients with immunoglobulin G antibodies to *H. pylori* than in non-infected patients.[49] In Germany, Berg *et al*. observed a 17% decrease in serum ferritin levels associated with *H. pylori* infection.[50] In Alaska, Parkinson *et al*. found significantly low serum ferritin levels related to *H. pylori* infection among children.[51] An American study found that *H. pylori* seropositive healthy individuals had significantly low serum ferritin levels compared with seronegative individuals.[52] However, some studies did not find any correlation between iron parameters and *H. pylori* infection. Collett *et al*. found no tangible differences in serum ferritin levels between *H. pylori* infected and non-infected patients.[53] Similarly, Hou *et al*. found no significant association between *H. pylori* infection and serum iron or ferritin levels.[45]

ID was seen in 82.64% of *H. pylori* positive patients against 17.36% in *H. pylori* negative ones. But this difference was not significant compared with patients without ID ($P = 0.37$). The OR of *H. pylori* infection on the prevalence of ID was 1.1851 (95% CI: 0.8122–1.7292) and 1.1620 (95% CI: 0.7854–1.7191), respectively, before and after adjusting with confounding factors. A significant relationship was found between *H. pylori* infection and IDA, but with a significant difference ($P = 0.04$). *H. pylori* infected patients were 1.5636 times more subjected to IDA than the uninfected patients (OR: 1.5636, 95% CI: 1.0206–2.3953, $P = 0.04$). This positive relationship persists even after adjusted with age and sex (OR = 1.5742, 95% CI: 1.0112–2.4506, $P = 0.04$), indicating that *H. pylori* infected participants are more prone to develop IDA than the uninfected ones.

Some previous studies have reported similar observations. One updated systematic review and meta-analysis study has indicated an association between *H. pylori* infection and an increased likelihood of depleted iron storage.[54] Choe *et al*. also showed that *H. pylori* infection leads to IDA[55]; Milman *et al*. showed that *H. pylori* infection affects iron metabolism in humans,[49] and Seo *et al*. showed that *H. pylori* infection reduced serum ferritin levels in children, which therefore may lead to ID.[56] On the other hand, another study showed there were improvements in hemoglobin levels after the eradication of *H. pylori* infection, with or without iron supplementation, and suggested that treatment of *H. pylori* infection is important to reduce the IDA. In a study carried out by Mozon *et al*., a significant improvement in IDA was observed in patients with *H. pylori* infection and IDA after treating the *H. pylori* infection.[57] Konno *et al*. reported that treatment of *H. pylori* infection can improve IDA in patients with IDA.[58]

Several mechanisms that might explain the correlation between *H. pylori* infection and anemia, ID, or IDA have been suggested. Firstly, *H. pylori*-induced gastritis or duodenitis can lead to gastrointestinal blood loss and eventually to IDA.[4,5] Another possibility is that *H. pylori* sequestrate-free iron, which affects iron transporter molecules, thereby inhibiting free iron absorption.[59] In addition, *H. pylori* for its growth can use the host's iron stores[60] or can compete with the host for the acquisition of alimentary iron.[49,61] Gastric acid is critical for the absorption of iron, *H. pylori* infection can decrease iron absorption through chronic atrophic gastritis, which is associated with hypochlorhydria or achlorhydria[13] or by inhibiting the secretion of ascorbic acid into the gastric juice, which alter iron absorption.[47]

Although many studies have shown the relationship between *H. pylori* infection and ID or IDA, other studies have not shown reliable evidence for a cause–effect relationship between *H. pylori* infection and ID, nor did they reveal clear improvements in the markers of ID after *H. pylori* eradication. Saler *et al*. in their study concluded that *H. pylori* infection was not associated with ID.[62] In Latin America, Santos *et al*. did not find any significant association between *H. pylori* infection and IDA.[63] The serum anti-*H. pylori* IgG and IgA levels regarding IDA did not show any correlation among patients, mostly with gastrointestinal complaints in Iran.[64] Also, no association was found between ID/IDA and *H. pylori* infection in a retrospective study among an older adult population without significant upper gastrointestinal source of blood loss.[47] A study in Australia on seniors also supports a negative effect of *H. pylori* on iron status.[65] This variability in studies could be due to differences in

the geographical and ethnical distribution of patients, age, inclusion criteria, sample size, sampling procedures, and methods of detecting anemia, iron markers, and *H. pylori* infection.

Conclusion

Our findings showed that there is an association between anemia, IDA, and *H. pylori* infection in our sample population. Hence, *H. pylori* infection should always be considered as a possible cause of IDA in our milieu. Taking into account the high prevalence of *H. pylori* infection in our milieu, careful consideration and appropriate interventions for *H. pylori* eradication are crucial not only for the possibility to improve anemia and iron status but also for avoiding hematological complications.

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Ethics Approval Statement

The study was approved by the national institutional Review Board, the National Ethical Committee on human health research in Cameroon (Ethical Clearance N^0 2016/11/837/EC/CNERSH/SP), and all methods and protocols were carried out in accordance with the approved guidelines and regulations.

Patient Consent Statement

Participation was voluntary and each subject involved in the study gave a written consent. The children were enrolled after their parents or legal guardians received an information notice and an oral explanation of the study and provided a written consent.

Data Availability Statement. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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