https://doi.org/10.22516/25007440.1366

Original article

Association Between Altitude and Gastric Lesions in Patients Treated at a Tertiary-Care Hospital in Pasto, Colombia

Lady Johana Melo-Bastidas,[1] Darlynne Xiomara Alfaro-Benavides,[1]* Melissa Del Rosario Bastidas-Riascos,[2] Karol Daniela Pérez-Pantoja,[3] Karen Milena Lucero-Coral,[4] Yinna Lizbeth Escobar-Flórez.[4]

OPEN ACCESS

Citation:
Melo-Bastidas LJ, Alfaro-Benavides DX, Bastidas-Riascos MR, Pérez-Pantoja KD, Lucero-Coral KM, Escobar-Flórez YL. Association Between Altitude and Gastric Lesions in Patients Treated at a Tertiary-Care Hospital in Pasto, Colombia. Revista. colomb. Gastroenterol. 2025;40(4):401-411.
https://doi.org/10.22516/25007440.1366

[1] Master's Degree in Epidemiology. Professor, Universidad de Nariño. Pasto, Colombia.
[2] Internist, Specialist in Gastroenterology and Digestive Endoscopy. Gastroenterologist at Hospital Universitario Departamental de Nariño, Fundación Hospital San Pedro. Pasto, Colombia.
[3] Universidad de Nariño. Medical Intern, Hospital Universitario Departamental de Nariño. Pasto, Colombia.
[4] Universidad de Nariño. Medical Intern, Fundación Hospital San Pedro. Pasto, Colombia.

***Correspondence:** Darlynne Xiomara Alfaro-Benavides.
xiomibe@hotmail.com

Received: 22/04/2025
Accepted: 05/11/2025

CC BY NC ND

Abstract

Introduction: Gastric cancer (GC) constitutes a major global public health burden, and Nariño remains the Colombian region with the highest prevalence. Although multiple risk factors have been identified, the relationship between chronic hypoxia associated with altitude of residence and the presence of precursor lesions for malignancy remains unclear. **Objective:** To assess the potential association between the Pelayo Correa carcinogenesis model and altitude-of-residence strata in a patient population receiving care at Fundación Hospital San Pedro (FHSP). **Materials and Methods:** An observational, analytical, cross-sectional study was conducted in patients older than 18 years who underwent upper endoscopy and resided in different geographical areas of Nariño categorized by altitude (meters above sea level): low (<1500 m), intermediate (1500–2500 m), and high (>2500 m). Sociodemographic, clinical, and endoscopic variables were recorded. Patients were contacted by telephone to verify or complement missing information. A stratified random sampling strategy was applied according to altitude group. Descriptive analyses were performed, and associations were evaluated using the chi-square test. **Results:** A total of 315 patients were included, 66% of whom were women. Premalignant lesions increased progressively from proximal to distal segments. The prevalence of *Helicobacter pylori* infection was 42.9%. No statistically significant association was identified between altitude strata and premalignant gastric lesions. **Conclusions:** No significant association was observed between altitude and the presence of premalignant lesions. Nonetheless, a tendency was noted in which patients diagnosed with gastric cancer predominantly resided in high-altitude areas.

Keywords

Gastric neoplasms, risk factors, altitude, atrophic gastritis.

INTRODUCTION

Gastric cancer (GC) is a global public health problem and is more frequent in the Pacific basin and high-altitude areas across East Asia and the American continent, particularly along the Central American mountain range, the Andes, and other regions of South America, where the highest incidence rates in the world have been described. In contrast, regions such as North America, West Africa, and Central and South Asia have lower incidence rates[1,2]. In Colombia, we observe a similar pattern. For example, in Cartagena, a Caribbean coastal city with 887,946 inhabitants, the annual incidence is 2 per 100,000 inhabitants. Likewise, in Cali, with 2,227,642 inhabitants and located at 1,018 meters above sea level, the prevalence of GC is three times lower (19%) compared with that found among immigrants from Nariño (58%)[3–7].

Regarding the etiopathogenesis of GC, Pelayo Correa proposed a hypothesis based on the sequential evolution

of histological conditions that precede the onset of invasive cancer: superficial gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia, and finally cancer, all of which are visible on endoscopy[3,8]. Several risk factors have been highlighted, including alcohol consumption, tobacco use, or nonsteroidal anti-inflammatory drugs (NSAIDs); low intake of fruits and vegetables; water sanitation; and *Helicobacter pylori* infection, among others. However, its etiology has not been fully clarified[9–15]. In the Department of Nariño, there appears to be a particular risk factor associated with chronic hypoxia and altitude. Correa and colleagues[16,17] report that, in 2014, the risk of GC among inhabitants of Túquerres, a municipality in Nariño with approximately 40,038 inhabitants located high in the Andes, was 150 cases per 100,000 inhabitants, one of the highest in the continent; whereas only 200 kilometers away, in Tumaco, a coastal municipality with approximately 221,469 inhabitants (the second largest municipality in Nariño), that risk was much lower, at only 6 cases per 100,000 inhabitants[3,16,17].

In their study including the Department of Nariño, Correa and colleagues[3,16] propose that Nariño exhibits a high genetic susceptibility due to the presence of the 511T allele of the gene encoding interleukin-1β, which is highly prevalent in the population, and that *H. pylori* strains in the region possess recognized virulence factors (cagA-positive and vacA s1m1)[16]. Similarly, other authors such as Arias and colleagues[17] report that Colombia shows higher GC prevalence and mortality associated with altitude, with more cases reported in the Andes than in coastal regions. This phenomenon has been documented in the Department of Boyacá, where regional heterogeneity was identified: the northeastern area (Norte and Valderrama provinces) presented high incidence and mortality, the central region showed moderate rates, and municipalities in the west exhibited low disease burden[17,18]. In other countries, such as Peru, Quiñones and colleagues[19,20] conducted several analyses and found a significant association between chronic gastritis and intermediate and high altitude, but not very high altitude. This may be explained by hypobaric hypoxia at altitude (which may induce changes in the gastric wall), physiological adaptation to altitude in the Peruvian population, and other sociodemographic variables. Finally, Amani and colleagues[21] analyzed the relationship between altitude, distance from a volcano in northeastern Iran, and GC incidence. Their results showed that GC rates were significantly higher in rural than urban populations, leading to the conclusion that proximity to the volcano increases GC incidence[20,22].

Another mechanism through which altitude may damage the gastric mucosa is polycythemia[22,23]. Studies in Tibetans living at high altitude with altitude-induced polycythemia have shown pathological changes in the gastric mucosa suggestive of apoptosis. In addition, patients with altitude-induced polycythemia showed higher frequency of *H. pylori* infection. Likewise, it has been described that people living at high altitude produce higher levels of hydrochloric acid due to vagal stimulation triggered by chronic hypoxia[23–26].

For these reasons, multiple hypotheses suggest that living at higher altitude is associated with greater rates of *H. pylori* infection and, consequently, with the development of the gastric carcinogenesis cascade. However, we still need to identify potential early diagnostic markers with impact both nationally and internationally.

OBJECTIVE

We sought to determine whether there is an association between the carcinogenesis model described by Pelayo Correa and the altitudinal zones of residence in a population treated at Fundación Hospital San Pedro (FHSP), Nariño, Colombia, in 2023.

MATERIALS AND METHODS

Study Design and Participant Selection

We conducted an observational, analytical, cross-sectional study including patients older than 18 years residing in the Department of Nariño who underwent upper gastrointestinal endoscopy with biopsy in the gastroenterology department of FHSP between January 1, 2023, and December 31, 2023. We included patients who had resided for a minimum of 10 years in either urban or rural areas of any of the 64 municipalities in the Department of Nariño. We excluded patients whose endoscopic procedures were of poor quality (full stomach, non-compliance with fasting time, or poorly readable endoscopies), as well as those with diagnoses such as foreign bodies, caustic burns, esophageal strictures, fistulas or wall defects, mucosal trauma, and those unable to provide informed consent. The research project was approved by the FHSP Ethics and Research Committee, and we obtained informed consent from all participating patients.

Endoscopy and Data Collection

We obtained the results of upper gastrointestinal endoscopies from a database provided by Fundación Hospital San Pedro. We reviewed patients' medical records to collect sociodemographic and clinical variables, personal and

family history, habits, exposure to biomass, endoscopic reports, and biopsy results. Based on geographic distributions in Nariño[1,12], we classified patients according to their area of residence into: low-altitude zone (<1,500 masl), including El Charco, Tumaco, Barbacoas, and Policarpa; intermediate-altitude zone (1,500–2,500 masl), including La Unión, Samaniego, Sandoná, Buesaco, and Tangua; and high-altitude zone (>2,500 masl), including Pasto, Ipiales, Túquerres, among others[1,12]. We conducted telephone interviews with patients to verify or complete information not available in the medical record, including confirmation of the minimum 10-year residence requirement, which was one of the eligibility criteria.

Study Phases

We conducted the study in two phases. In the first phase, we performed a pilot test with ten patients, applying the data collection instrument to the clinical record and conducting a structured telephone interview to identify and correct shortcomings and refine the final instruments. In the second phase, we applied the final data collection instrument to all clinical records and conducted telephone interviews with patients included in the selected sample.

Statistical Analysis

We systematized the information obtained through the data collection instruments and interviews and constructed the study database in MS Excel. We then performed descriptive univariate and bivariate statistical analyses for all variables of interest. We present qualitative variables as proportions using absolute and relative frequencies. We assessed normality for numerical variables and expressed measures of central tendency and dispersion as mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate. We conducted a bivariate analysis and calculated crude prevalence ratios as measures of association. We assessed statistical significance using the chi-square test with a p-value <0.05. We performed all analyses using SPSS version 23 (licensed to Universidad de Nariño).

Ethical Considerations

In accordance with Resolution 8430 of 1993 of the Ministry of Health and Social Protection, this investigation corresponds to a study with minimal risk (Item A, Article 11, Title II, Chapter I). We collected information using data collection instruments applied to clinical records and through telephone interviews with patients, after obtaining prior authorization and signing of informed consent by the participants.

RESULTS

We included 315 patients treated in the gastroenterology service of a tertiary-care hospital in Nariño, Colombia. Most were women (66.7%; n = 210), while 33.3% (n = 105) were men. The predominant age group consisted of older adults between 60 and 90 years, representing 45.1% (n = 142), followed by those aged 46–60 years (33.3%; n = 105), and, to a lesser extent, patients between 18 and 45 years (21.6%; n = 68).

Regarding blood group, type O was the most frequent, present in 69.2% (n = 218) of participants, followed by type A (18.1%; n = 57), type B (10.5%; n = 33), and type AB (2.2%; n = 7). With respect to Rh factor, 95.9% (n = 302) were Rh-positive and only 4.1% (n = 13) were Rh-negative.

In relation to altitude of residence, 70.8% (n = 223) of patients lived in high-altitude areas (>2,500 masl), 18.4% (n = 58) in intermediate-altitude areas (1,500–2,500 masl), and 10.8% (n = 34) in low-altitude areas (<1,500 masl).

Sociodemographic, clinical, and histopathological characteristics of patients who underwent upper gastrointestinal endoscopy at Fundación Hospital San Pedro in 2023

Regarding clinical variables, we found documentation of the reason for endoscopy in 31.4% of patients, and the most frequent symptom was abdominal pain, reported in 19% (n = 60); followed by hematemesis/melena in 5.4% (n = 17); vomiting in 2.9% (n = 9); pallor/anemia in 1.6% (n = 5); gastroesophageal reflux disease (GERD) in 1.3% (n = 4); weight loss in 1% (n = 3); and, finally, suspected malignant neoplasm in 0.3% (n = 1) (**Tables 1 and 2**).

In the histopathological findings, 42.9% (n = 135) of patients had *H. pylori* infection according to the pathology report. Chronic atrophic gastritis was the most frequent preneoplastic lesion, accounting for 33.3% (n = 105); followed by chronic superficial gastritis at 32.7% (n = 103); intestinal metaplasia at 25.1% (n = 79); advanced gastric cancer at 2.5% (n = 8); and dysplasia at 1.3% (n = 4). The gastric antrum was the most frequent location of preneoplastic lesions, observed in 81.6% (n = 257); followed by the gastric body in 48.3% (n = 152); and, finally, the incisura in 16.2% (n = 51).

Regarding patient habits, 16.5% (n = 52) reported being smokers. Of these, 11.4% (n = 36) had a smoking index lower than 10, and no patient had an index higher than 41. Meanwhile, 24% (n = 78) reported being social drinkers. Among the 81 patients who reported alcohol consumption, 16.8% (n = 53) had consumed alcohol for more than 10 years. Finally, 61% (n = 192) of patients consumed low-nutritional-value foods fewer than three times per week;

however, approximately 66.3% (n = 209) reported consuming fruits and vegetables more than three times per week (**Table 2**).

Endoscopic and histological characteristics and their relationship with altitude of the area of residence (low <1,500 masl; intermediate 1,500–2,500 masl; high >2,500 masl)

When we analyzed the association between altitude of residence and the presence of preneoplastic gastric lesions, we did not find statistically significant differences. Compared with patients from high-altitude areas, those residing in intermediate-altitude zones showed a slightly higher probability of presenting chronic superficial gastritis (prevalence ratio [PR]: 1.052; 95% confidence interval [CI]: 0.976–1.134; $p = 0.182$) and chronic atrophic gastritis (PR: 1.029; 95% CI: 0.950–1.115; $p = 0.478$), while the risk for intestinal metaplasia was practically equivalent (PR: 1.007; 95% CI: 0.943–1.076; $p = 0.830$) (**Table 3**).

Table 1. Sociodemographic characteristics (participants n = 315)

Characteristic	n (%)
Sex	
- Female	210 (66.7)
- Male	105 (33.3)
Age	
- 60 to 90 years	142 (45.1)
- 46 to 60 years	105 (33.3)
- 18 to 45 years	68 (21.6)
Blood group	
- O	218 (69.2)
- A	57 (18.1)
- B	33 (10.5)
- AB	7 (2.2)
Rh factor	
- Positive	302 (95.9)
- Negative	13 (4.1)
Altitude of residence	
- High (>2,500 masl)	223 (70.8)
- Intermediate (1,500–2,500 masl)	58 (18.4)
- Low (<1,500 masl)	34 (10.8)

Author's own research.

Table 2. Clinical characteristics, history, habits, and histological diagnosis of patients (n = 315)

Item	n (%)
Reason for endoscopy	
- Documented in medical record	99 (31.5)
- Abdominal pain	60 (19.0)
- Hematemesis/melena	17 (5.4)
- Vomiting	9 (2.9)
- Pallor/anemia	5 (1.6)
- Gastroesophageal reflux disease	4 (1.3)
- Weight loss	3 (1.0)
- Suspected malignant neoplasm	1 (0.3)
- Family history of gastric cancer*	61 (19.4)
Personal history	
- Smoker	52 (16.5)
Smoking index	
- Less than 10	36 (70.6)
- 10 to 20	8 (15.7)
- 21 to 40	7 (13.7)
- More than 41	0 (0.0)
Alcohol consumption	
- No consumption	233 (74.0)
- Social drinker	78 (24.8)
- Alcohol dependence	4 (1.3)
Years of alcohol consumption	
- Less than 1 year	9 (11.4)
- 1 to 5 years	7 (8.9)
- 5 to 10 years	10 (12.7)
- More than 10 years	53 (67.1)
- Exposure to biomass	127 (40.3)
- Exposure to heavy metals or radiation	23 (7.3)
Frequency of consumption of low-nutritional-value foods (LNVF)**	
- Sometimes	192 (61.0 %)
- Never	99 (31.4)
- Frequently	24 (7.6)
Frequency of consumption of fruits and vegetables	
- Frequent	209 (66.3)
- Sometimes	101 (32.1)
- Never	5 (1.6)
H. pylori infection	
- Yes	135 (42.9)
- No	180 (57.1)
Histological diagnosis	
- Chronic atrophic gastritis	105 (33.3)
- Chronic superficial gastritis	103 (32.7)
- Intestinal metaplasia	79 (25.1)
- Normal	16 (5.1)
- Advanced gastric cancer	8 (2.5)
- Dysplasia	4 (1.3)
Location	
- Body	152 (48.3)
- Antrum	257 (81.6)
- Incisura	51 (16.2)

*Family history of gastric cancer in first- or second-degree relatives. **Low nutritional value foods (LNVF): packaged, processed, or canned products with excess salt, sodium, saturated fats, or added sugars. Author's own research.

Table 3. Association between altitude of residence and gastric lesions

Altitude of Residence	Chronic Superficial Gastritis	*p*-Value	Chronic Atrophic Gastritis	*p*-Value	Intestinal Metaplasia	*p*-Value
	PR (95% CI)		PR (95% CI)		PR (95% CI)	
High	1		1		1	
Intermediate	1.052 (0.976-1.134)	0.182	1.029 (0.950-1.115)	0.478	1.007 (0.943-1.076)	0.830
Low	1.013 (0.916-1.121)	0.800	1.075 (0.983-1.176)	0.112	0.942 (0.853-1.039)	0.233
Altitude of Residence	**Dysplasia**	***p*-Value**	**Advanced Gastric Cancer**	***p*-Value**	**Normal**	***p*-Value**
	PR (95% CI)		PR (95% CI)		PR (95% CI)	
High	1		1		1	
Intermediate	1.005 (0.998-1.011)	0.156	0.983 (0.953-1.013)	0.270	1.001 (0.969-1.035)	0.949
Low	0.975 (0.936-1.016)	0.228	0.979 (0.939-1.021)	0.327	1.028 (1.012-1.043)	0.000

CI: confidence interval; PR: prevalence ratio. Author's own research.

In low-altitude areas, we observed a higher probability of atrophic gastritis (PR: 1.075; 95% CI: 0.983–1.176; p = 0.112) and a slightly lower probability of intestinal metaplasia (PR: 0.942; 95% CI: 0.853–1.039; p = 0.233), although, again, without statistical significance. These findings do not allow us to establish a conclusive relationship between altitude and the development of these preneoplastic lesions, highlighting the need for additional studies with longitudinal designs and greater control of confounding variables.

In contrast, when we evaluated the presence of normal gastric mucosa, we found a statistically significant association among patients residing in low-altitude zones, who showed a higher probability of not presenting gastric lesions (PR: 1.028; 95% CI: 1.012–1.043; p = 0.000), compared with residents of high-altitude areas. This finding suggests a possible difference in the distribution of lesions according to altitude; however, it must be interpreted with caution given the observational design of the study and the lack of statistical significance for most of the other analyzed variables.

Presence of *Helicobacter pylori* and Its Relationship with Premalignant Lesions

We found that patients with *H. pylori* infection had a 13.2% higher probability of presenting chronic superficial gastritis, with a statistically significant difference (prevalence ratio [PR]: 1.132; 95% confidence interval [CI]: 1.067–1.201; p = 0.000). We also found that patients with *H. pylori* infection had a 17.7% lower probability of developing chronic atrophic gastritis (PR: 0.823; 95% CI: 0.771–0.879; p = 0.000).

Patients with *H. pylori* infection showed a 1.9% increase in the probability of presenting advanced gastric cancer (PR: 1.019; 95% CI: 1.002–1.036; p = 0.031), and those with *H. pylori* infection had a 3.7% higher probability of not presenting any type of gastric lesion (PR: 1.037; 95% CI: 1.014–1.059; p = 0.001) (**Table 4**).

Association between Altitude of Residence and *Helicobacter pylori* Infection

Patients living in intermediate-altitude areas had a 6.4% higher probability of *H. pylori* infection compared with those from high-altitude zones (PR: 1.064; 95% CI: 0.977–1.158; p = 0.154), while those living in low-altitude areas had a 1.7% lower probability of *H. pylori* infection compared with those from high-altitude zones, although this association was not statistically significant (PR: 0.983; 95% CI: 0.874–1.105) (**Table 5**).

DISCUSSION

This study was conducted in Colombia, a country with a high prevalence of gastric cancer (GC), particularly in the Department of Nariño, where the disease shows even higher rates. Its relevance lies in the sociodemographic characterization of a population that has been scarcely studied, which has hindered effective control of GC. According to recent data (GLOBOCAN 2022), while the global incidence of GC has been decreasing, in Colombia it continues to rise[4–6].

Table 4. Association between *H. pylori* Infection and Gastric Lesions

	Chronic Superficial Gastritis	*p*-Value	Chronic Atrophic Gastritis	*p*-Value	Intestinal Metaplasia	*p*-Value
	PR (95% CI)		PR (95% CI)		PR (95% CI)	
H. pylori infection	1.132 (1.067-1.201)	0.000	0.823 (0.771-0.879)	0.000	0.999 (0.947-1.053)	0.969
	Dysplasia	***p*-Value**	**Advanced Gastric Cancer**	***p*-Value**	**Normal**	***p*-Value**
	PR (95% CI)		PR (95% CI)		PR (95% CI)	
H. pylori infection	1.005 (0.993-1.017)	0.443	1.019 (1.002-1.036)	0.031	1.037 (1.014-1.059)	0.001

CI: confidence interval; PR: prevalence ratio. Author's own research.

Table 5. Association between Altitude of Residence and *H. pylori* Infection

Altitude of Residence	*H. pylori* Infection PR (95% CI)	*p*-Value
High	1	
Intermediate	1.064 (0.977-1.158)	0.154
Low	0.983 (0.874-1.105)	0.773

CI: confidence interval; PR: prevalence ratio. Author's own research.

The main objective of this study was to explore the association between living in high-altitude areas and the presence of premalignant gastric lesions within the framework of Pelayo Correa's carcinogenesis model. Although we did not find a statistically significant association, we observed a consistent trend toward a higher presence of GC among patients from areas above 2,500 masl. This finding is consistent with previous studies conducted in mountainous regions of Latin America and Asia[2,19,20], particularly the study by Quiñones-Laveriano and colleagues[19], who reported a significant association between the diagnosis of chronic gastritis and living at high altitudes (p <0.001), and the study by Sharma PK and colleagues[27], who indicated that gastric pathology at high altitude shows important differences compared with that observed in populations living at sea level, including a higher prevalence of *H. pylori* infection, a key factor in the development of chronic gastritis[19–35]. We believe that the lack of a statistically significant association in our study between altitude and premalignant lesions may also depend on sample size and difficulties in accurately establishing the demographic zone for some participants. Several patients are born in specific regions but move to other areas during their lifetime due to work or personal reasons; there are also patients who may experience hypoxia induced by other diseases or hypoxia associated with occupational activities. These were confounding variables that we attempted to control in this study. However, experimental or other types of studies are needed to evaluate this association more directly.

Several studies have demonstrated the role of hypoxia as an inducer of gastric cancer, such as the work by Muz B and colleagues[36], which highlights that oxygen levels in hypoxic tumor tissues are lower than in normal tissues, averaging between 1% and 2% oxygen or even less. The central hypothesis of this research proposes that hypobaric hypoxia, a typical condition of high-mountain regions, may act as an environmental cofactor in gastric carcinogenesis. This condition produces a chronic decrease in the partial pressure of oxygen, inducing mechanisms such as oxidative stress, apoptosis, persistent inflammation, and alterations in angiogenesis, mediated by hypoxia-inducible factor 1 alpha (HIF-1α)[23,37]. Histopathological studies conducted in these regions have documented changes in the gastric mucosa compatible with severe atrophic gastritis, metaplasia, and dysplasia[20,30]. Secondary polycythemia due to altitude may further aggravate these processes by generating microvascular congestion and damage to the mucosal barrier[24,37].

In addition, both short- and long-term hypoxia have been shown to increase radioresistance of cancer cells *in vitro*[24] and *in vivo*[30,38]. Prolonged exposure to hypoxia is associated with a high frequency of DNA breaks and accu-

mulation of DNA replication errors, as hypoxia interferes with DNA repair systems, including homologous recombination and mismatch repair, potentially leading to genetic instability and mutagenesis[38]. Hypoxia induces metabolic and molecular changes in endothelial cells, increasing the expression of proangiogenic molecules and blood vessel formation, thereby supplying more oxygen and nutrients to tumor cells.

Cancer has long been described as a "wound that never heals," partly because of inflammation, one of the enabling characteristics of cancer originally described by Hanahan and Weinberg[39,40]. Hypoxia and inflammation are intricately interconnected, as demonstrated by evidence that hypoxia can directly induce inflammatory signaling[41]. In the context of malignancy, multiple cancer-related genes are regulated by both HIF-1α and nuclear factor kappa B (NF-κB), including cyclooxygenase 2 and interleukin 6 (IL-6)[40]. This illustrates the complex crosstalk among signaling pathways and the difficulty in disentangling the net influence of specific factors within this network, described as "an upper gastrointestinal cancer model of inflammatory origin"[42].

Hypoxia has also been shown to influence immune evasion, altering antigen uptake and migration in dendritic cells while simultaneously increasing vascular endothelial growth factor production. This disrupts the bridge between the innate antitumor immune response and the adaptive response, while also enhancing angiogenic signaling. Hypoxia-inducible factor-mediated transcription of IL-6 results in subsequent recruitment of immunosuppressive myeloid-derived cells and, to a greater extent, protumorigenic regulatory T lymphocytes[42].

The primary importance of inflammation in the etiology of gastric cancer is further supported by histological assessment of inflammatory status based on neutrophil recruitment (reflecting acute inflammation) and monocyte infiltration (reflecting chronic inflammation), known as the *Sydney System*. This demonstrated a significant correlation with HIF-1α expression from normal to metaplastic tissue, but no association between other stages or with overall inflammatory status[43].

Several studies have shown that hypoxia appears to drive tumor cell plasticity and, consequently, vasculogenic mimicry, a process that allows malignant cells to replace endothelial cells and form vascular networks, thereby evading true angiogenic activity[42]. In an *in vitro* analysis of oral squamous cell carcinoma (OSCC) cells, RNA interference targeting HIF-1α inhibited both vasculogenic mimicry (in three-dimensional culture) and cell proliferation[44].

In our study, the most frequently identified preneoplastic lesion was chronic atrophic gastritis, followed by chronic superficial gastritis and intestinal metaplasia, findings consistent with Bedoya and colleagues[28]. However, studies such as that by Pinto D.[29] show a different distribution, reporting a higher prevalence of intestinal metaplasia (14.4%), followed by chronic atrophic gastritis (11%) and gastric dysplasia (2.5%). This difference may be explained by the fact that Pinto's study included only patients with *H. pylori* infection, unlike our study, which included all patients regardless of infection status. It is noteworthy that the sequence of lesions found in these studies differs from that described by Pelayo Correa[3–8], suggesting the possible influence of other factors in the progression of gastric carcinogenesis—one of which may be the influence of hypobaric hypoxia or hypoxia induced by patient-related pathologies.

Preneoplastic lesions in our study were predominantly located in the gastric antrum, followed by the body and the angular incisura (**Table 2**). This pattern is consistent with studies by Recavarren-Arce and colleagues and Fabián and colleagues[30,31], who reported more than 90% of preneoplastic lesions in the antrum (p <0.014). This distribution reinforces theories suggesting greater susceptibility of this region to carcinogenic processes[31,32]. Regarding risk factors associated with gastric cancer, we observed an association between high consumption of salt, smoked or canned foods, and low fruit and vegetable intake with increased GC risk. In fact, Yomaira and colleagues[34] demonstrated that consuming more than two daily portions of vegetables significantly reduces the probability of presenting precursor lesions of malignancy (OR: 0.53; 95% CI: 0.27–0.99). Contrary to expectations, in our study most patients were not smokers (83.5%) or alcohol consumers (74%), and did not report a family history of gastric cancer (80.6%), findings consistent with Muñoz and colleagues[33]. This suggests the presence of other relevant factors in the pathogenesis of gastric cancer, such as diet, hypoxia, or altitude.

In our study, *H. pylori* infection was significantly associated with a 13.2% increase in the probability of developing chronic superficial gastritis and a 1.9% increase in the probability of presenting advanced gastric cancer. These findings are consistent with the reports of Seoane and colleagues[45], who found a high prevalence of *H. pylori* in patients with distal gastric adenocarcinoma (73.6% versus 48.6% in proximal tumors; p <0.05). However, we observed a decrease in the prevalence of *H. pylori* in patients with atrophic gastritis, which has also been reported by other studies. In particular, Corso CL and Aponte D.[46] highlight that *H. pylori* tends to disappear in advanced stages of the carcinogenic cascade, such as atrophy and metaplasia. This was confirmed in our study, where *H. pylori* infection was associated with a 17.7% reduction in the probability of presenting atrophic gastritis. This suggests that progression toward malignancy may depend on additional factors beyond bacterial infection.

It has also been proposed that hypoxic conditions alter the dynamics of *H. pylori* infection, favoring its persistence in the early stages of gastritis. However, as noted, its presence tends to decline as the Correa cascade progresses, suggesting that hypoxia may perpetuate epithelial damage even in the absence of the microorganism[45,46]. Hypoxia also regulates inflammatory mediators and growth factors and induces immunoresistance and immunosuppression, allowing tumor cells to evade immune surveillance[47]. Therefore, the hypoxic phenotype of stromal and immune cells within the tumor microenvironment, together with *H. pylori* infection, is gaining increasing importance in the pathogenesis of gastric cancer and plays a fundamental role in tumor progression and dissemination[48,49].

The trend observed in this study, together with the available scientific evidence, indicates that hypobaric hypoxia may play an important role in gastric cancer development, either independently or synergistically with other factors. Although we were unable to establish a causal association, our findings justify the need for further research with molecular and genetic approaches. These should include evaluation of hypoxia biomarkers, analysis of inflammatory responses (such as the IL-1β-511T allele), and characterization of gastric tissue.

In regions such as southern Colombia, where gastric cancer burden is high and heterogeneous, understanding the impact of altitude may have important implications for prevention strategies, screening, and epidemiological surveillance, particularly in populations living in mountainous areas.

LIMITATIONS

One limitation of this study is that we were unable to analyze the relationship between altitudinal zones of residence and gastric biopsy results according to the OLGA and OLGIM classification systems, which allow assessment and determination of the extent of atrophy and the degree of intestinal metaplasia, respectively. This was due to the lack of standardized reporting of biopsies among institutional pathologists.

CONCLUSIONS

We found that the most frequent preneoplastic lesion was chronic superficial gastritis, followed by chronic atrophic gastritis and metaplasia, which is consistent with the carcinogenesis model described by Pelayo Correa. We did not find a significant association between premalignant lesions and altitude; however, we observed a trend indicating that patients with cancer more often resided in high-altitude areas. Patients with *H. pylori* infection had a higher probability of developing chronic superficial gastritis and advanced gastric cancer. However, once patients had entered Correa's cascade (that is, when atrophy or metaplasia was already present), the prevalence of *H. pylori* decreased. More studies are required to better define the etiopathogenesis of gastric cancer, which may influence the development of these precursor lesions of malignancy.

Conflict of Interest

We declare that the authors of this study have no conflicts of interest. This study was conducted with our own resources and did not use any type of artificial intelligence.

Acknowledgments

We thank Universidad de Nariño and Fundación Hospital San Pedro for facilitating the development of this study, and all the patients who participated in this research.

REFERENCES

1. Bedoya Á, Yépez Y, Calvache D, Cifuentes Y, Lucero N, González P, et al. Investigación de la prevalencia de condiciones precursoras de malignidad gástrica y efecto de la erradicación de infección por helicobacter pylori como prevención primaria del cáncer gástrico en el departamento de Nariño. Rev Colomb Gastroenterol. 2018;33(3):218-225. https://doi.org/10.30944/20117582.81
2. Torres J, Correa P, Ferreccio C, Hernandez-Suarez G, Herrero R, Cavazza-Porro M, et al. Gastric cancer incidence and mortality is associated with altitude in the mountainous regions of Pacific Latin America. Cancer Causes Control. 2013;24(2):249-56. https://doi.org/10.1007/s10552-012-0114-8
3. Correa P, Piazuelo MB. Cáncer gástrico: El enigma colombiano. Rev Colomb Gastroenterol. 2010;25(4):393-402.
4. Bravo LE, García LS, Collazos P, Carrascal E, Ardila EKG, Millan E, et al. Cancer epidemiology in Cali, 60 years of experience. Colomb Med. 2022;53(1):e4048035. https://doi.org/10.25100/cm.v53i1.5050
5. Grueso FM. Censo Nacional de Población y Vivienda 2018 [Internet]. Bogotá: DANE; 2018 [consultado el 2 de febrero de 2025]. Disponible en: https://www.dane.gov.co/index.php/estadisticas-por-tema/demografia-y-poblacion/censo-nacional-de-poblacion-y-vivienda-2018
6. International Agency for Research on Cancer. 170 Colombia fact sheets [Internet]. Lyon: Globocan; 2020 [consultado el 23 de marzo de 2025]. Disponible en:

https://gco.iarc.who.int/media/globocan/factsheets/populations/170-colombia-fact-sheet.pdf
7. Bello MN, Biarge FS, Arnal MJD, Sejas AG, González MAG. Actualización en cáncer gástrico. Medicine - Programa de Formación Médica Continuada Acreditado. 2020;13(3):149-158. https://doi.org/10.1016/j.med.2020.01.020
8. Correa P. A Human Model of Gastric Carcinogenesis. Cancer Res. 1986;48(13):3554-60.
9. Lochhead P, El-Omar EM. Helicobacter pylori infection and gastric cancer. Best Pract Res Clin Gastroenterol. 2007;21(2):299-312. https://doi.org/10.1016/j.bpg.2007.02.002
10. Guzmán KA, Pazos A. Helicobacter pylori: microorganismo patógeno o mutualista en poblaciones colombianas. Univ Salud. 2023;25(1):154-165. https://doi.org/10.22267/rus.232501.292
11. Luo W, Fedda F, Lynch P, Tan D. CDH1 Gene and Hereditary Diffuse Gastric Cancer Syndrome: Molecular and Histological Alterations and Implications for Diagnosis And Treatment. Frontiers in Pharmacology. 2018;9:1372. https://doi.org/10.3389/fphar.2018.01421
12. Riihimäki M, Hemminki A, Sundquist K, Sundquist J, Hemminki K. Metastatic spread in patients with gastric cancer. Oncotarget. 2016;7(32):52307-52316. https://doi.org/10.18632/oncotarget.10740
13. Ortego J, Cebrián C. Precursores del cáncer gástrico. Factores de riesgo, condiciones y condiciones premalignas de la mucosa gástrica. GH Continuada. 2001;1(2):77-84.
14. Rugge M, Meggio A, Pennelli G, Piscioli F, Giacomelli L, De Pretis G, et al. Gastritis staging in clinical practice: The OLGA staging system. Gut. 2007;56(5):631-6. https://doi.org/10.1136/gut.2006.106666
15. Carlin Ronquillo A, Ventura León A, Espinoza Ríos JL, Bravo Paredes EA, Gómez Hinojosa P, Alva Solis S, et al. Distribución de estadios de OLGA y OLGIM según edad y estado del Helicobacter pylori en un hospital público nivel III en Lima, Perú. Acta Gastroenterol Latinoam. 2021;51(1):64-71. https://doi.org/10.52787/UCCM2971
16. Haenszel W, Duque E, Garcia FT, Bolanos O. Gastric cancer in colombia. iii. natural history of precursor lesions. J Natl Cancer Inst. 1976;57(5):1021-30. https://doi.org/10.1093/jnci/57.5.1021
17. Arias-Sosa LA, Cuspoca-Orduz AF, Siabato-Barrios JA, Eslava-Roa JS. Incidencia y mortalidad del cáncer gástrico en el departamento de Boyacá-Colombia. Acta Gastroenterol Latinoam. 2018;48(3):181-189.
18. Barreto Norato C, Limas Solano L, Porras A, Rico A. Carga de enfermedad de cáncer gástrico durante los años 2010 y 2019 en Tunja, Boyacá, Colombia. Rev Colomb Gastroenterol. 2022;38(1):31-38. https://doi.org/10.22516/25007440.916
19. Quiñones-Laveriano DM, De La Cruz-Vargas JA, Quintana-Gomez S, Failoc-Rojas VE, Lozano-Gutiérrez J, Mejia CR. Association between the altitude of residential areas and clinical diagnosis of chronic gastritis in ambulatory patients of Peru: A cross-sectional analytic study. Medwave. 2020;20(6):e7972. https://doi.org/10.5867/medwave.2020.06.7972
20. Jovita VP, Douglas LG, Francisco AP, Felipe SM, Vitaliano MV. Cáncer gástrico en los andes peruanos: 170 casos observados en Huaraz. Revista de Gastroenterología del Perú. 2000;20(3):250-256.
21. Arvelo F, Cotte C. Hipoxia en la malignidad del cáncer: Revisión. Invest Clin. 2009;50(4):529-546.
22. Amani F, Ahari SS, Barzegari S, Hassanlouei B, Sadrkabir M, Farzane E. Analysis of relationships between altitude and distance from volcano with Stomach Cancer incidence using a geographic information system. Asian Pac J Cancer Prev. 2015;16(16):7087-7091. https://doi.org/10.7314/APJCP.2015.16.16.6889
23. Muñoz Cedeño RG, Martínez Ballesteros PE, Paullan Sani V, Rodríguez Chica GN. Caracterización clínica, histológica y endoscópica del cáncer gástrico en el Hospital de Especialidades Dr. Abel Gilbert Pontón, Ecuador. Rev Colomb Gastroenterol. 2021;36(2):163-71. https://doi.org/10.22516/25007440.558
24. Romańczyk M, Ostrowski B, Marek T, Romańczyk T, Błaszczyńska M, Budzyń K, et al. Composite detection rate as an upper gastrointestinal endoscopy quality measure correlating with detection of neoplasia. J Gastroenterol. 2021;56(7):651-8. https://doi.org/10.1007/s00535-021-01790-3
25. Bedoya A, Sanson F, Yepez Y, Santacruz C, Cifuentes Y, Calvache D, et al. Prevalencia y severidad de las condiciones precursoras de malignidad en un área de alto riesgo de cáncer gástrico. Rev Colomb Gastroenterol. 2012;27(3):275-281.
26. Pinto D. condiciones preneoplásicas gástricas según nivel de altitud en pacientes positivos para Helicobacter pylori en un centro endoscópico de Lima, Perú 2016 - 2018. Universidad Peruana Cayetano Heredia; 2019.
27. Bouras E, Tsilidis KK, Triggi M, Siargkas A, Chourdakis M, Haidich AB. Diet and Risk of Gastric Cancer: An Umbrella Review. Nutrients. 2022;14(9):1764. https://doi.org/10.3390/nu14091764
28. Recavarren-Arce S, Ramirez-Ramos A, Gilman RH, Chinga-Alayo E, Watanabe-Yamamoto J, Rodriguez-Ulloa C, et al. Severe gastritis in the Peruvian Andes. Histopathology. 2005;46(4):374-9. https://doi.org/10.1111/j.1365-2559.2005.02102.x
29. Tafoya-Ramírez F, Günther J, Mijangos-Cruz R, Velásquez-Paz A. Lesiones premalignas en mucosa gástrica y su relación con Helicobacter pylori en biopsias gástricas. Evid Med Invest Salud. 2011;4(1):7-9.
30. Scheidl E, Benz C, Loeff P, Groneck V, König A, Schulte-Fischedick A, et al. Frequency and types of pathological upper gastrointestinal endoscopy findings in clinically healthy individuals. Drugs in R&D. 2020;20(2):115-24. https://doi.org/10.1007/s40268-020-00303-6

31. Roldán-Delfino LM, León Ramírez SM, Roldán Molina LF, Niño Ramírez SF, Arismendy López de Mesa AF, Bejarano Rengifo EJ, et al. Asociación entre variables de hábitos de alimentación y la presencia de cambios tróficos gástricos en una institución de gastroenterología de Medellín, Colombia. Rev Colomb Gastroenterol. 2023;38(3):304-310. https://doi.org/10.22516/25007440.1024
32. Yepez Caicedo Y, Ricaurte Enriquez PA, Bedoya Urresta A, Berbesi Fernández DY. Condiciones precursoras de malignidad gástrica y su asociación con hábitos alimentarios. Rev Colomb Gastroenterol. 2017;32(3):249-258. https://doi.org/10.22516/25007440.152
33. Sharma PK, Suri TM, Venigalla PM, Garg SK, Mohammad G, Das P, et al. Tropical Gastroenterology. 2008;29(2):100-106.
34. Ramírez Ramos A, Mendoza Requena D, Leey Casella J, Guerra Valencia J. Estudio del Helicobacter pylori en el Perú. Rev Peru Med Exp Salud Publica. 2002;19(4):209-14.
35. Hernández López E del C, Villagrán Blanco CI, Carías Alvarado CC, Hernández B, Barrios Menéndez JC, Pérez-Pérez GI. Identificación y evaluación de condiciones gástricas premalignas asociadas a la infección por Helicobacter pylori. Rev Cubana Med Trop. 2022;74(1): e1370.
36. Muz B, de la Puente P, Azab F, Azab AK. The role of hypoxia in cancer progression, angiogenesis, metastasis, and resistance to therapy. Hypoxia (Auckl). 2015;3:83-92. https://doi.org/10.2147/HP.S93413
37. Seoane A, Bessa X, Balleste B, O'callaghan E, Panadès A, Alameda F, et al. Helicobacter pylori y cáncer gástrico: relación entre el subtipo histológico y la localización del tumor. Gastroenterología Y Hepatología. 2005;28(2):60-4. https://doi.org/10.1157/13070701
38. Casazza A, Di Conza G, Wenes M, Finisguerra V, Deschoemaeker S, Mazzone M. Tumor stroma: a complexity dictated by the hypoxic tumor microenvironment. Oncogene. 2014;33(14):1743-1754. https://doi.org/10.1038/onc.2013.121
39. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144:646-674. https://doi.org/10.1016/j.cell.2011.02.013
40. Dvorak HF. Tumors: wounds that do not heal-redux. Cancer Immunol Res 2015;3:1-11. https://doi.org/10.1158/2326-6066.CIR-14-0209
41. Bartels K, Grenz A, Eltzschig HK. Hypoxia and inflammation are two sides of the same coin. Proc Natl Acad Sci USA. 2013;110:18351-2. https://doi.org/10.1073/pnas.1318345110
42. King R, Hayes C, Donohoe CL, Dunne MR, Davern M, Donlon NE. Hypoxia and its impact on the tumour microenvironment of gastroesophageal cancers. World J Gastrointest Oncol. 2021;13(5):312-331. https://doi.org/10.4251/wjgo.v13.i5.312
43. Ling FC, Khochfar J, Baldus SE, Brabender J, Drebber U, Bollschweiler E, et al. HIF-1alpha protein expression is associated with the environmental inflammatory reaction in Barrett's metaplasia. Dis Esophagus. 2009;22:694-699. https://doi.org/10.1111/j.1442-2050.2009.00957.x
44. Tang NN, Zhu H, Zhang HJ, Zhang WF, Jin HL, Wang L, et al. HIF-1α induces VE-cadherin expression and modulates vasculogenic mimicry in esophageal carcinoma cells. World J Gastroenterol. 2014;20:17894-904. https://doi.org/10.3748/wjg.v20.i47.17894
45. Chacaltana A, Rodríguez C, Urday C, Ramon W, Espinoza J, Velarde H, et al. condiciones gástricas preneoplásicas y helicobacter pylori en despistaje endoscópico para cáncer gástrico en población de nivel socioeconómico medio y alto. Rev Gastroenterol Peru. 2009;29(3):218-25.
46. Martínez Leyva L, Montero González T de J, Piñol Jiménez FN, Palomino Besada A, González-Carbajal Pascual M, Días Morejón D. Helicobacter pylori y cáncer gástrico. Rev Cuba Med Mil. 2020;49(4):e966.
47. Baudry N, Danialou G, Boczkowski J, Vicaut E. In vivo study of the effect of systemic hypoxia on leukocyte-endothelium interactions. Am J Respir Crit Care Med. 1998;158(2):477-483. https://doi.org/10.1164/ajrccm.158.2.9701074
48. Kourembanas S, Bernfield M. Hypoxia and endothelial-smooth muscle cell interactions in the lung. Am J Respir Crit Care Med. 1994;11(4):373-374. https://doi.org/10.1165/ajrcmb.11.4.7917305
49. Michiels C, Arnould T, Remacle J. Endothelial cell responses to hypoxia: initiation of a cascade of cellular interactions. Biochim Biophys Acta. 2000;1497(1):1-10. https://doi.org/10.1016/S0167-4889(00)00041-0