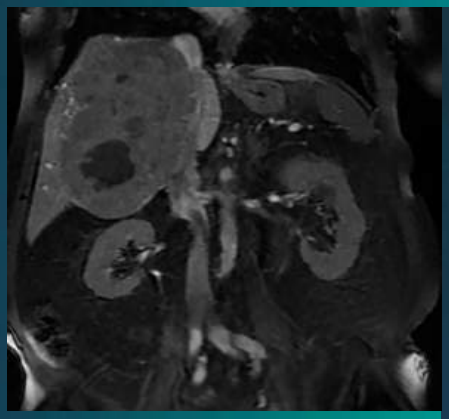
ISSN 0120-9957
ISSN 2500-7440 (Online)
DOI: https://doi.org/10.22516/issn.2500-7440

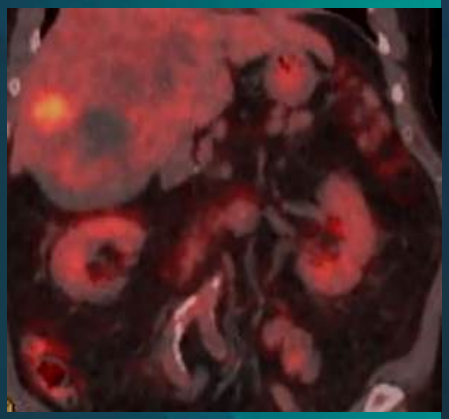
40 YEARS

RCG Revista Colombiana de Gastroenterología

Volume 40 - Number 4
October - December 2025

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Courtesy of the authors: Erick Andrés Cantor-Rizo, Andrés Felipe Bejarano-Ramírez, Zamira Fernanda Gómez-Giraldo, John Alejandro Murillo-Silva, Henry Alexander Vargas-Díaz, Mónica Lorena Tapias-Mantilla.

https://doi.org/10.22516/25007440.1497

Editorial

40 years of the Revista Colombiana de Gastroenterología: challenges and opportunities

David B. Páramo-Hernández.[1*]

OPEN ACCESS

Citation:
Páramo-Hernández D. 40 years of the Revista Colombiana de Gastroenterología: challenges and opportunities. Revista. colomb. Gastroenterol. 2025;40(4):399-400.
https://doi.org/10.22516/25007440.1497

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Received: 26/11/2025
Accepted: 27/11/2025

With this volume, Revista Colombiana de Gastroenterología (RCG) marks 40 years since its founding, having demonstrated steady progress and upward development throughout its editorial life. At present, however, it must confront challenges and obstacles to continue its growth. First, it faces a highly competitive and global publishing market, dominated by oligopolies and characterized by paywalled models that impose very high costs for access to scientific information, yielding high profitability for publishers while providing little or no benefit to authors, reviewers, and editors. In addition, this market has established its own bibliometric indices to assess the quality of scientific articles and research output[(1)].

In contrast to this model stands so-called open science (open access), which has emerged as a growing necessity to democratize access to scientific knowledge so that it is free and unrestricted, given that it is, in fact, a public good. Scientific societies and the academic community must promote a system that values open access, ensures fair compensation for authors and peer review, and fosters more sustainable editorial practices[(2)]. The future of academic publishing should not only be profitable for publishers; it must also ensure that the benefits of research are shared broadly and equitably. We must advocate for change by promoting models that prioritize accessibility, equity, and the free dissemination of knowledge[(1,2)].

Given that the very nature of our journal is open access—and in keeping with its current motto, "A living journal of all for all"—one of the main achievements of this editorial administration has been its inclusion in the Directory of Open Access Journals (DOAJ), which brings together high-quality journals operating under this model.

Another challenge that the academic and medical community must recognize and guard against is the growing threat posed by so-called "predatory" or questionable journals. These are fraudulent scientific publications that charge for article publication without providing a rigorous peer-review process, prioritizing profit over research integrity. They are characterized by deceptive practices such as aggressive solicitation of manuscripts, falsification of metrics (such as impact factor), and the absence or inadequacy of quality control[(3)].

A third challenge that our journal will need to address is the incorporation of technological advances, such as the adoption of artificial intelligence (AI) and machine learning technologies to support peer review, detect plagiarism and scientific misconduct, and facilitate data analysis. Achieving this will require an investment budget for personnel, technology, and training.

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This Volume 40, No. 4 is accompanied by three valuable supplements. Together with the Board of Directors of the Colombian Association of Gastroenterology, chaired by Dr. Diego Aponte Martín, we have decided, in celebration of the 40th anniversary, to publish the updated Clinical Practice Guidelines[4–6]. These three documents were developed with strict methodological and epidemiological rigor and underwent an updated evaluation by subject-matter experts. Undoubtedly, they represent a major contribution for health professionals, institutions, and health policy decision-makers, ultimately aiming to positively impact the health of our population. This issue also includes a diverse and engaging collection of original articles, reviews, and case reports. Among them, we invite readers to consult the Consensus for the Diagnosis and Treatment of Eosinophilic Esophagitis in the Pediatric Population: Diagnosis. Part 1[7]. We also recommend the excellent narrative review Gastric Cancer: Detection and Prevention by Dr. Oliveros and colleagues[8]. Finally, in the Research and Publishing section, it is also essential to read Essential Bioethical Considerations in Biomedical Research: Foundations, Standards, and Indispensable Practices by Dr. Granada[9].

REFERENCES

1. Larivière V, Haustein S, Mongeon P. The Oligopoly of Academic Publishers in the Digital Era. PLoS One. 2015;10(6):e0127502. https://doi.org/10.1371/journal.pone.0127502
2. Arita M, Pulverer B, Uemura T, Sakuma C, Hayashi S. Publishing in the Open Access and Open Science era. Genes Cells. 2024;29(4):275-281. https://doi.org/10.1111/gtc.13100
3. Laine C, Babski D, Bachelet VC, Bärnighausen TW, Baethge C, Bibbins-Domingo K, et al. Predatory journals: What can we do to protect their prey? PLoS Med. 2025;22(4):e1004542. https://doi.org/10.1371/journal.pmed.1004542
4. Aponte Martín DM, Gil Parada FL, Castaño LLano R de J, Bareño Silva J, Ortíz Chamorro AX, Ibarra Burgos JA, et al. Guía colombiana de práctica clínica para el tamizaje de cáncer colorrectal adultos: actualización 2025. Rev. colomb. Gastroenterol. 2025;40(Supl. 2):3-24. https://doi.org/10.22516/25007440.1451
5. Hani de Ardila AC, Cañadas Garrido RA, Aponte Martín DM, Ortiz Chamorro AX, Bareño Silva J, Ibarra Burgos JA, et al. Guía de práctica clínica para el diagnóstico y tratamiento de la enfermedad por reflujo gastroesofágico (ERGE) en adultos: actualización 2025. Rev Colomb Gastroenterol. 2025;40(Supl. 3):3-31. https://doi.org/10.22516/25007440.1450
6. Otero Regino WA, Trespalacios Rangel AA, Marulanda Fernandez H, Rojas Gualdrón DF, Aponte Martín DM, Cañadas Garrido RA, et al. Guía de práctica clínica para el diagnóstico y tratamiento de la infección por helicobacter pylori en adultos: actualización 2025. Rev Colomb Gastroenterol. 2025;40(Supl. 4):3-32. https://doi.org/10.22516/25007440.1458
7. Vera-Chamorro JF, Zambrano-Pérez CA, Carias-Domínguez AM, Higuera-Carrillo M, Riveros-López JP, García-Paba MB, et al. Consenso para el diagnóstico y tratamiento de la esofagitis eosinofílica en población pediátrica: el diagnóstico. Parte 1. Revista. colomb. Gastroenterol. 2025;40(4):450-462. https://doi.org/10.22516/25007440.1371
8. Oliveros-Wilches R, Facundo-Navia H, Pinilla-Morales R, Bonilla A, Aguirre G. Cáncer gástrico: detección y prevención. Revista. colomb. Gastroenterol. 2025;40(4):463-471. https://doi.org/10.22516/25007440.1399
9. Granada-Copete AM. Principios éticos básicos en investigación clínica. Puntos bioéticos esenciales en la investigación biomédica: fundamentos, normas y prácticas indispensable. Revista. colomb. Gastroenterol. 2025;40(4):472-476. https://doi.org/10.22516/25007440.1140

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

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

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

https://doi.org/10.22516/25007440.1369

Original article

Factors Associated With Health Literacy in Patients Diagnosed With Liver Cirrhosis

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Citation:
Martelo-Herazo C, Chamorro-Guzmán N, Yepes-Barreto I. Factors Associated With Health Literacy in Patients Diagnosed With Liver Cirrhosis. Revista. colomb. Gastroenterol. 2025;40(4):412-422. https://doi.org/10.22516/25007440.1369

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Received: 26/04/2025
Accepted: 04/11/2025

Abstract

Introduction: Health literacy (HL) is defined as an individual's ability to obtain, process, and understand medical information required to make appropriate health-related decisions. Low HL has been linked to increased healthcare costs, higher rates of hospitalization, reduced likelihood of liver transplantation, and increased mortality, leading to adverse clinical outcomes, particularly among vulnerable populations. **Objective:** To identify clinical and sociodemographic factors associated with HL levels in a cohort of patients with liver cirrhosis in Cartagena, Colombia. **Methods:** A cross-sectional, observational, and analytical study was conducted in patients diagnosed with cirrhosis and evaluated between September and December 2024. The Spanish version of the Short Assessment of Health Literacy (SAHL-S) was administered, with scores ≤14 classified as inadequate. Additionally, a validated questionnaire from Brazil was used to assess disease knowledge in four domains: signs and symptoms, diagnosis, treatment, and medications. Descriptive statistics and univariate and multivariate logistic regression models were used to identify predictors of HL. **Results:** Ninety-three patients participated (mean age: 63.9 ± 11.7 years; 61.2% women). Adequate HL was observed in 79.6% of participants. Mean knowledge scores were: signs and symptoms, 6.5; diagnosis, 7.2; treatment, 7.7; and medication, 4.1. In univariate analyses, education level, number of dependents, and active employment were associated with adequate HL, whereas older age and a history of hypertension were associated with inadequate HL. In multivariate analyses, education level (OR 1.64; 95% CI: 1.11–2.43) and number of dependents (OR 1.77; 95% CI: 1.06–2.96) remained independent predictors. **Conclusion:** Participants demonstrated overall adequate HL and solid knowledge regarding diagnosis and treatment, although understanding of symptoms and medication use remained limited. Targeted interventions are needed to strengthen HL among individuals living with chronic conditions such as cirrhosis.

Keywords

Health literacy, liver cirrhosis, healthcare.

INTRODUCTION

Health literacy (HL) has gained increasing relevance in the medical sciences. It is defined as individuals' capacity to obtain, process, and understand health-related information in order to make informed decisions about their care[(1)]. This concept encompasses both disease-specific knowledge (including etiology, prognosis, and complications) and the functional skills required to interact effectively with the health care system, such as completing forms, understanding medical recommendations, and managing medical appointments[(2)].

Low health literacy has been associated with multiple adverse outcomes, including increased health care costs (ranging from an additional USD 143 to USD 7,798 per patient), a higher number of hospitalizations, reduced access to organ transplantation, and increased mortality[(3,4)]. These associations can be explained by poorer the-

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rapeutic adherence, missed follow-up visits, inappropriate medication use, and difficulties recognizing symptoms or communicating effectively with health care personnel in this population[5,6]. In Latin America, these effects are even more pronounced due to structural limitations—such as poverty and low educational attainment—that constitute barriers to achieving adequate HL, particularly among the most vulnerable groups[7]. These challenges are amplified in the context of chronic diseases, whose management requires active and sustained patient participation, both in understanding complex instructions regarding medication, diet, and exercise and in ongoing interaction with an increasingly fragmented health care system[8,9].

Liver cirrhosis (LC) represents the terminal stage of chronic liver disease and is characterized by progressive dysfunction of the hepatic parenchyma. Its main etiologies include chronic alcohol consumption, hepatitis C virus infection, fatty liver disease, and autoimmune liver diseases[10]. Potentially life-threatening complications include ascites, esophageal varices, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome, and hepatocellular carcinoma[11,12].

Globally, LC was estimated to account for 2.4% of all deaths in 2019, and more than 122 million cases were reported in 2020[13]. In Colombia, LC is recognized as a public health problem. A recent analysis estimated that, between 2009 and 2016, premature mortality due to this condition resulted in a loss of 687,861 years of life and an economic cost ranging from USD 19.6 to USD 37.8 million[14].

Several international studies have identified clinical and sociodemographic factors associated with low HL in patients with LC, including male sex, low educational level, living alone, being retired, alcoholic etiology of disease, and active smoking. These patients also more frequently exhibit functional impairment, poorer quality of life, a higher number of hospitalizations, multiple comorbidities, more advanced stages of liver disease (according to Child–Pugh and MELD scores), minimal hepatic encephalopathy (according to the West Haven scale), a history of ascites, and depressive symptoms[15–18].

In Colombia, research on HL remains limited. Two studies conducted in the general population found that higher educational level, younger age, and affiliation with the contributory health insurance regime were associated with better HL[19,20]. Additionally, a study carried out at a specialized gastroenterology and hepatology center in Cartagena identified that the main information needs among patients with cirrhosis were related to complications, prognosis, pharmacotherapy, liver cancer, and transplantation[21]. Despite these findings, the literature on HL in patients with LC remains scarce compared with other conditions[17,19,22,23], and inadequate health literacy constitutes a critical barrier to achieving equity in health care.

Various tools have been developed for the objective assessment of HL, most of them in English-speaking countries. Some have been adapted and validated for Spanish-speaking populations, such as eHEALS in Spain[24], SAHLSA-50 in Chile[25], the HLS-EU-Q in patients with hypertension in Mexico[26], and a pilot version of the TOFHLA in Colombia, which achieved translation and cultural adaptation but did not reach formal validation[19]. Among these instruments, the Short Assessment of Health Literacy—Spanish and English (SAHL-S&E) has been validated in both English- and Spanish-speaking populations in the United States. Its Spanish version (SAHL-S) consists of 18 items and allows classification of low HL with a score ≤14, demonstrating good reliability and ease of administration across diverse clinical settings[27].

Currently, no scale has been specifically designed to measure HL in patients with liver cirrhosis[16]. However, a validated instrument is available to assess disease-specific knowledge across four domains: signs and symptoms, diagnosis, treatment, and medication[28]. Such tools allow us to identify, with greater precision, the areas of knowledge with the greatest opportunities for improvement.

Identifying the factors associated with HL in the Colombian population with cirrhosis is a priority. Cultural and social differences relative to high-income countries—where most of the available evidence has been generated—limit the generalizability of those findings to our population. Understanding these determinants allows us to implement more relevant interventions to improve the comprehensive management of patients with chronic liver disease in Colombia. The objective of this study is to identify the factors associated with health literacy in a population of patients with liver cirrhosis treated at a first-level outpatient center in Cartagena, Colombia.

METHODOLOGY

Study Design and Population

We conducted an observational, cross-sectional, analytical study. We included patients with a clinically or histologically confirmed diagnosis of liver cirrhosis who attended a first-level outpatient hepatology care center in Cartagena, Colombia, between September and December 2024.

After obtaining written informed consent, we administered the Spanish version of the Short Assessment of Health Literacy in Spanish (SAHL-S) to all participants, a validated tool for measuring health literacy. This scale consists of 18 items and classifies a score ≤14 as insufficient health literacy.

Additionally, we used a questionnaire originally validated in Brazil and designed to assess disease-specific knowledge about liver cirrhosis. This instrument includes 36 ques-

tions developed from information considered essential for patients to make informed decisions and to promote a better understanding of their disease. The questionnaire covers four domains: signs and symptoms, diagnosis, treatment, and medication. Each of the first three domains has a maximum score of 10 points, whereas the medication domain has a maximum score of 6 points.

Inclusion Criteria

- Patients aged 18 years or older.
- Confirmed diagnosis of liver cirrhosis of any etiology.

Exclusion Criteria

- Presence of physical or cognitive limitations that prevented adequate responses to the researcher's questions.
- Clinical diagnosis of overt hepatic encephalopathy at the time of assessment.

Instruments

During the encounter with each participant, we collected sociodemographic and clinical data through a direct interview. Subsequently, we administered two validated instruments: the Spanish version of the Short Assessment of Health Literacy in Spanish (SAHL-S), used to assess general health literacy, and the structured questionnaire on liver cirrhosis–specific knowledge, which explores key areas such as signs and symptoms, diagnosis, treatment, and medication.

Short Assessment of Health Literacy in Spanish (SAHL-S)

The SAHL-S is a shortened version of the SAHLSA, which in turn is derived from the Rapid Estimate of Adult Health Literacy in Medicine (REALM). This tool, validated in Spanish-speaking populations, consists of 18 items and is easy to administer. For each item, participants are asked to read a medical term aloud and select, from two options, the word with the closest semantic relationship. This procedure allows us to assess both decoding ability and conceptual understanding of the term. A score between 0 and 14 is considered indicative of insufficient health literacy (see **Appendix**).

Liver Cirrhosis Knowledge Questionnaire

This instrument was developed and validated by Stelmach and colleagues[8] in Brazil and was subsequently translated into Spanish for use in this study. The questionnaire includes 36 true/false items organized into three main categories—signs and symptoms, diagnosis, and treatment—as well as a subcategory corresponding to medication. Each main category contains 10 questions, while the medication subcategory includes 6 items. The level of disease-specific knowledge is quantified as the percentage of correct responses in each category, based on information considered essential for informed patient decision-making and comprehensive understanding of the disease.

Statistical Analysis

We described quantitative variables using measures of central tendency and dispersion, depending on whether their distribution was parametric or nonparametric. We expressed qualitative variables as absolute and relative frequencies. To identify factors associated with health literacy (HL), we initially performed a univariate logistic regression analysis. Variables that reached statistical significance (p <0.05) were included in a multivariate logistic regression model, in which the dependent variable was the presence of an adequate level of HL, defined as a score of 15 points or higher on the SAHL-S scale.

Ethical Considerations

We conducted this research in accordance with the ethical principles governing biomedical research involving human subjects, respecting the fundamental rights established in Article 11 (right to life) of the Political Constitution of Colombia, the guidelines of the World Medical Association set forth in the Declaration of Helsinki, Law 23 of 1981, and Resolution 8430 of 1993 of the Ministry of Health. The study protocol was approved by the Scientific Committee and the Bioethics Committee of Universidad de Cartagena and Centro Médico Gastropack.

RESULTS

We included 93 patients in the study. Of these, 61.2% (n = 57) were female, and the mean age was 63.9 years (SD ± 11.7). Most participants (74.2%) reported being in a stable relationship. Regarding educational attainment, 35.5% had completed secondary education and 33.3% had higher education. Most participants (86.0%) resided in urban areas, primarily belonging to socioeconomic strata 2 (38.7%) and 3 (35.5%). More than 60% were unemployed, retired, or pensioners; 77.4% were affiliated with the contributory health insurance regime, and 61.3% had dependents.

With respect to personal history, 11.8% (n = 11) were active smokers. The most frequent comorbidities were arterial hypertension (46.2%), diabetes *mellitus* or prediabetes (44.1%), and obesity (32.3%), with a mean body mass index (BMI) of 27.6 kg/m² (SD ± 4.81). Regarding the etiology of liver cirrhosis, metabolic dysfunction-associated steatotic liver disease (MASLD) and cryptogenic cirrhosis predominated, each with a frequency of 30%. Most

patients (80.0%) were classified as Child–Pugh stage A, with a mean MELD score of 9 (SD ± 2.74). The mean time since cirrhosis diagnosis was 45.5 months (SD ± 43.83).

Regarding hepatic complications, 50% of patients had a history of esophageal varices, 18% had been hospitalized for ascites, and only 6% had experienced episodes of hepatic encephalopathy. None of the participants had undergone transjugular intrahepatic portosystemic shunt (TIPS). The mean SAHL-S score was 15.33, and 79.6% of patients achieved an adequate level of health literacy (defined as a score ≥15) (**Table 1**).

Regarding the liver cirrhosis-specific knowledge questionnaire, the mean scores by domain were as follows: signs and symptoms, 6.5 (SD ± 1.9); diagnosis, 7.2 (SD ± 1.9); treatment, 7.7 (SD ± 1.8); and medication, 4.1 (SD ± 1.1). When we expressed these scores as a proportion of the maximum possible score for each domain, we observed a level of knowledge of 77% for treatment, 72% for diagnosis, 69% for medication, and 65% for signs and symptoms.

Univariate analysis showed that a higher educational level (OR: 1.81; 95% CI: 1.24–2.61; p <0.001), having dependents (OR: 2.03; 95% CI: 1.23–3.33; p = 0.01), and being employed or economically active (OR: 2.20; 95% CI: 1.09–4.51; p = 0.03) were associated with higher levels of health literacy (HL). In contrast, older age (OR: 0.95; 95% CI: 0.90–0.99; p = 0.02) and a history of arterial hypertension (OR: 0.32; 95% CI: 0.12–0.85; p = 0.02) were associated with lower HL levels (**Table 2**).

In the multivariate analysis, educational level (OR: 1.65; 95% CI: 1.12–2.44; p = 0.013) and having dependents (OR: 1.77; 95% CI: 1.06–2.96; p = 0.028) remained independent predictors of adequate health literacy (**Table 3**).

DISCUSSION

People with chronic diseases often have limited access to health information, and factors such as educational level can restrict their ability to understand and process this information. Although they generally seek medical support, this support is not always available, which leads them to develop individual and subjective interpretations influenced by cognitive, social, psychosocial, and cultural processes. These interpretations may be inadequate and contribute to increased health care costs, constituting a public health problem that requires intervention[19].

In our study, we observed an overall high level of health literacy (HL), as only 20.4% of participants scored below 14 points on the SAHL-S. In the liver cirrhosis-specific knowledge questionnaire, we found that patients experienced greater difficulties in recognizing signs and symptoms and in understanding medication-related information. Among social determinants, educational level and the number of dependents emerged as the only independent predictors of adequate HL in the multivariate analysis.

Numerous studies have demonstrated an association between educational level and HL in patients with liver cirrhosis (LC). A prospective study conducted in Germany involving 89 patients showed that fewer years of education were associated with poorer comprehension of health information (β = −0.221; p = 0.041), using the Health Literacy Questionnaire (HLQ) as the assessment tool[17]. Similarly, at Aarhus University Hospital in Denmark, a study of 105 outpatients found that an educational level of fewer than 12 years was associated with lower HL (HR = 0.43; 95% CI: 0.84–0.01; p = 0.05), particularly in the social support for health dimension[15]. Comparable findings have been reported in patients with other chronic conditions, such as heart failure, assessed using instruments like the TOFHLA[4,5].

A prospective cohort study in the United States including 276 liver transplant candidates demonstrated lower HL levels among those with secondary education or less compared with those with higher education (56.4% vs. 36.7%; p = 0.005). After adjusting for educational level and socioeconomic factors, low HL remained independently associated with greater physical frailty and a lower likelihood of being listed for transplantation[29]. Consistent with these findings, our study identified educational level as an independent predictor of adequate HL, likely reflecting a greater ability to understand medical instructions and navigate the health care system, even in highly complex contexts.

In our study, having dependents was positively associated with adequate HL. Patients responsible for the care of others may require stronger cognitive and organizational skills, which could facilitate their interaction with the health care system and the acquisition of knowledge about their own disease and that of those they care for. Similarly, a study of outpatients with LC found that cohabitation was associated with higher HL levels, although this association did not reach statistical significance across HLQ domains[15]. In contrast, a recent systematic review reported that informal caregivers with multiple dependents had lower HL levels than those caring for a single patient[30].

Employment status also showed a direct relationship with HL. In Denmark, a cross-sectional study published in 2021 involving 8,767 participants found that unemployed individuals and those receiving social assistance or sickness benefits had lower HL levels, with the effect being more pronounced among unemployment benefit recipients (OR: 1.78; 95% CI: 1.23–2.56)[31]. Likewise, a 2022 Spanish study of 166 adult patients reported lower HL scores among unemployed individuals, those older than 65 years, and those with incomplete secondary educa-

Table 1. Clinical and Sociodemographic Characteristics of the Study Population*

Variable	n = 93
Female sex	61.3 (57)
Age (years)	63.9 (11.7)
Education level	
- No formal education	1.1 (1)
- Incomplete primary education	5.4 (5)
- Complete primary education	17.2 (16)
- Incomplete secondary education	7.5 (7)
- Complete secondary education	35.5 (33)
- Higher education	33.3 (31)
In a relationship	74.2 (69)
Dependents	
- 0	38.7 (36)
- 1	18.3 (17)
- 2	26.9 (25)
- 3	12.9 (12)
- 4	3.2 (3)
Urban residence	86 (80)
Socioeconomic stratum	
- 1	8.6 (8)
- 2	38.7 (36)
- 3	35.5 (33)
- 4	8.6 (8)
- 5	7.5 (7)
Contribution-based health insurance regime	77.4 (72)
Employment status	
- Unemployed/retired/pensioner	60.2 (56)
- Informal employment	16.1 (15)
- Formal employment	23.7 (22)
Weight (kg)	71.91 (14.76)
Height (m)	1.61 (0.09)
Body mass index	27.61 (4.81)
Active smoking	11.8 (11)
Arterial hypertension	46.2 (43)
Diabetes *mellitus*	44.1 (41)

Variable	n = 93
Heart failure	3.2 (3)
Chronic kidney disease	8.6 (8)
Obesity	32.3 (30)
Thyroid disorders	19.4 (18)
Psychiatric disorders	3.2 (3)
Etiology	
- Chronic alcohol consumption	6.5 (6)
- HBV	7.5 (7)
- HCV	9.7 (9)
- AIH	12.9 (12)
- PBC/AIH	3.2 (3)
- MASLD	30.1 (28)
- Cryptogenic	30.1 (28)
Time since diagnosis (months)	45.49 (43.83)
Child-Pugh classification	
- A	79.6 (74)
- B	18.3 (17)
- C	1.1 (1)
MELD	9 (2.74)
History of ascites	18.3 (17)
History of hepatic encephalopathy	6.5 (6)
History of esophageal varices	49.5 (46)
Elastography (kPa)	28.32 (17.72)
Sodium (mEq/L)	140.23 (3.27)
Creatinine (mg/dL)	0.89 (0.83)
Total bilirubin, (mg/dL)	1.21 (1.04)
Albumin (g/dL)	3.94 (0.56)
INR	1.13 (0.14)
Leukocytes (cells/mm³)	4742.06 (2009.48)
Platelets (cells/mm³)	137578.26 (68081.12)
Ferritin (ng/dL)	35.82 (18.49)
Transferrin saturation (%)	156.94 (185.95)
SAHL-S score	15.33 (3.14)
Adequate health literacy	79.6 (74)

*Numeric variables are expressed as mean (SD), and categorical variables as % (n). PBC: primary biliary cirrhosis; AIH: autoimmune hepatitis; HBV: hepatitis B virus; HCV: hepatitis C virus; INR: international normalized ratio; MASLD: metabolic dysfunction-associated steatotic liver disease; MELD: Model for End-Stage Liver Disease; SAHL-S: Short Assessment of Health Literacy–Spanish. Author's own research.

Table 2. Factors Associated with Health Literacy: Univariate Logistic Regression Analysis*

Variable	OR	95% CI	*p*-Value
Age	0.95	0.90-0.99	0.02
Sex	1.76	0.64-4.79	0.27
Education level	1.81	1.24-2.61	0.002
Relationship status	1.26	0.44-3.55	0.66
Dependents	2.03	1.23-3.33	0.01
Place of residence	0.84	0.21-3.36	0.81
Socioeconomic stratum	1.52	0.92-2.49	0.10
Health insurance regime	1.62	0.56-4.65	0.37
Employment status	2.22	1.09-4.51	0.03
BMI	1.02	0.92-1.12	0.73
Smoking	1.65	0.33-8.23	0.54
History of hypertension	0.32	0.12-0.85	0.02
History of diabetes *mellitus*	1.44	0.55-3.73	0.45
History of CKD	1.05	0.19-5.57	0.96
History of obesity	1.60	0.56-4.56	0.38
History of thyroid disease	1.27	0.37-4.32	0.70
Time since diagnosis	1.01	0.99-1.02	0.20
Child-Pugh classification	2.00	0.55-7.26	0.29
History of ascites	0.57	0.18-1.75	0.33
History of encephalopathy	0.68	0.11-3.95	0.66
History of esophageal varices	0.38	0.14-1.01	0.05
Elastography	1.00	0.96-1.03	0.93
Platelets	1.00	0.99-1.00	0.91
Albumin	2.19	0.77-6.16	0.14
Creatinine	1.09	0.53-2.19	0.81

*The dependent variable was adequate health literacy (score ≥15 points on the SAHL-S scale). DM: diabetes *mellitus*; CKD: chronic kidney disease; HTN: arterial hypertension; 95% CI: 95% confidence interval; BMI: body mass index; OR: odds ratio; SAHL-S: Short Assessment of Health Literacy–Spanish. Author's own research.

Tabla 3. Factors associated with health literacy: multivariate logistic regression analysis

Factor	OR	95% CI	*p*-Value
Education level	1.646	1.112-2.436	0.013
Dependents	1.774	1.063-2.960	0.028

95% CI: 95% confidence interval; OR: odds ratio. Author's own research.

tion, according to the HLQ scale ($\beta = 0.323$; $p = 0.002$; $\beta = 0.413$; $p = 0.009$; and $\beta = 0.176$; $p = 0.03$, respectively)[32]. These results are consistent with our findings, as patients who were actively employed showed higher HL levels. This phenomenon may relate to the need to resolve practical situations and to interact autonomously with the health care system—abilities that may be diminished in older adults or in those who are retired, who often require caregivers, potentially compromising their HL.

Regarding comorbid conditions, previous studies have consistently documented an association between arterial hypertension (HTN) and low HL levels. A systematic review published in 2021 found that patients with higher HL demonstrated better knowledge of hypertension and its management[33]. A cross-sectional study conducted in Brazil with 357 patients with HTN showed that low HL levels, assessed using the TOFHLA, were associated with older age and lower educational attainment[34]. In Iran, a study of 700 hypertensive patients reported that 75.5% had inadequate or partially adequate HL, and a positive correlation was observed between disease-related knowledge and HL level[35]. In line with these findings, our univariate analysis identified HTN as the only clinical history associated with low HL, possibly because these patients tend to be older, have multiple comorbidities, and experience cognitive decline, which limits their ability to acquire, understand, and apply health information.

Given the relevance of HL to clinical outcomes and health care costs, substantial efforts have focused on identifying its sociodemographic and clinical determinants. Disease-specific knowledge is also essential, particularly in chronic conditions such as LC, where social stigma can exacerbate information gaps[30]. In our population, we observed a good level of HL and satisfactory knowledge of LC, especially in the areas of diagnosis and treatment. This finding may be explained by the relatively high educational level observed (approximately 70% had completed secondary education or attained higher education), as well as by the fact that patients with cirrhosis typically receive more medical information than the general population.

In conclusion, low HL represents a critical challenge that must be addressed as an essential component of the comprehensive management of liver cirrhosis. Accessible, high-quality educational materials are needed for patients, family members, and health care personnel to improve knowledge and promote adequate HL[36,37].

CONCLUSION

Educational level and the number of dependents were identified as independent predictors of health literacy (HL) in our population. It is necessary to implement strate-

gies and public policies aimed at strengthening knowledge about chronic diseases and promoting HL as a key tool to improve clinical outcomes and reduce the economic burden on health care systems.

LIMITATIONS

The main limitation of this study is that it was conducted at a single center located in the Colombian Caribbean region. This region has particular cultural, social, and educational characteristics, which may limit the generalizability of our findings to other populations in the country with different contexts. Additionally, the questionnaire used to estimate the level of disease-specific knowledge about liver cirrhosis was developed in Brazil and has not yet been validated in Colombia, which may affect the validity of the estimated knowledge level among participants. Validation of this type of instrument would allow multicenter studies with more robust results at the national level. Nevertheless, the primary objective of this study was not to estimate the level of knowledge about cirrhosis, but rather to identify factors associated with HL using a tool validated for this purpose. In this regard, our findings are consistent with previous studies conducted in diverse geographic regions and sociocultural contexts worldwide, suggesting that certain factors—such as educational level—may play a determining role in HL across a wide spectrum of populations with significant social and cultural differences.

STRENGTHS

Assessing health literacy is a simple method that does not require substantial additional time during routine medical visits, yet it can have short-, medium-, and long-term impacts on the quality of life of patients living with cirrhosis.

RECOMMENDATIONS

Designing a multicenter study with a longer follow-up period could help better elucidate the factors involved in low health literacy levels and enable the implementation of public health strategies to optimize outpatient management and reduce complications and health care costs associated with cirrhosis within local and regional health systems.

Conflict of Interest

None declared.

Funding Sources

The authors' own resources.

APPENDIX

SAHL-S Scale

Stem	Key or Distractor		
1. employment	__work	__education	__I don't know
2. seizures	__dizzy	__calm	__I don't know
3. infection	__kills	__virus	__I don't know
4. medication	__instrument	__treatment	__I don't know
5. alcoholism	__addiction	__recreation	__I don't know
6. kidney	__urine	__fever	__I don't know
7. dose	__sleep	__quantity	__I don't know
8. miscarriage	__loss	__marriage	__I don't know
9. constipation	__blocked	__loose	__I don't know
10. pregnancy	__childbirth	__childhood	__I don't know
11. nerves	__bored	__anxiety	__I don't know
12. nutrition	__healthy	__soda	__I don't know
13. indicated	__instruction	__decision	__I don't know
14. hormones	__growth	__harmony	__I don't know
15. abnormal	__different	__similar	__I don't know
16. diagnosis	__evaluation	__recovery	__I don't know
17. hemorrhoids	__veins	__heart	__I don't know
18. syphilis	__contraceptive	__condom	__I don't know

Liver Cirrhosis Knowledge Questionnaire[8]

Signs and Symptoms

1. Malnutrition is responsible for patient weakness.
2. Itchy skin, yellow discoloration of the skin, ascites, mental confusion (hepatic encephalopathy), and esophageal varices are some of the signs and symptoms of liver cirrhosis.
3. The absence of symptoms indicates that liver cirrhosis is in the early stages of the disease.
4. The accumulation of fluid in the abdomen (ascites) is a common complication of liver cirrhosis.
5. Esophageal varices (dilation of the veins of the esophagus) are rare complications of liver cirrhosis.
6. In some cases, liver cirrhosis presents complications (esophageal varices, mental confusion, ascites) that must be treated and monitored by a physician to prevent worsening of the patient's health status.
7. Fatigue is not a complication of liver cirrhosis; fatigue is caused by major depression.
8. Hepatic encephalopathy presents with mental confusion, disorientation, hand tremors, slurred speech, slow movements, memory loss, and, in more severe cases, can lead to coma.
9. A cirrhotic liver releases toxic substances that can attack the heart and cause heart attacks.
10. Patients who experience episodes of hepatic encephalopathy with signs of mental confusion, disorientation, slow movements, among others, should always be accompanied when leaving home.

Diagnosis

1. Cirrhosis is characterized by liver damage that causes the organ to lose its functions.
2. The only cause of liver cirrhosis is alcohol consumption.
3. It is possible to have liver cirrhosis and hepatocellular carcinoma (liver cancer) at the same time.
4. Liver cirrhosis requires continuous medical supervision to assess disease progression.
5. Liver cirrhosis can be caused by different factors, such as hepatitis B or C, alcohol use, fatty liver disease, and autoimmune diseases.
6. Liver cirrhosis is a contagious disease transmitted by mosquito bites.
7. The disease is often diagnosed when the patient presents complications such as ascites, mental confusion (encephalopathy), esophageal varices, and yellow discoloration of the skin.
8. Liver cirrhosis allows moderate alcohol consumption; that is, it is possible to drink one can of beer, one glass of wine, or one measure of spirits per day.
9. Liver cirrhosis is considered a chronic disease; that is, it will accompany the individual for life.
10. A higher MELD score indicates greater disease severity.

Treatment

1. Treatment of liver cirrhosis requires only medical supervision.
2. When transplantation is indicated as treatment for liver cirrhosis, professional medical follow-up is required (physicians, nurses, psychologists, nutritionists, social workers), both in the preoperative and postoperative stages.
3. Dietary guidance from nutritionists is not indicated in the treatment of liver cirrhosis, as there are no foods that can worsen symptoms or the disease.
4. Liver transplantation is a surgical procedure in which the diseased liver (with cirrhosis) is replaced by a healthy liver.
5. When a patient is placed on the waiting list for liver transplantation, they must undergo evaluations and maintain regular follow-up with several professionals such as nurses, nutritionists, psychologists, social workers, among others.
6. Treatment of liver cirrhosis requires a social support network; that is, assistance from friends or family with hospital visits, medication use, and daily activities.
7. After being placed on the waiting list for liver transplantation, waiting for an organ can be stressful. During this period, symptoms of anxiety and depression may arise and require treatment by psychologists and psychiatrists.
8. To receive appropriate care after transplant surgery, the patient remains hospitalized for a period of time, and in severe cases or in the presence of complications may be admitted to the intensive care unit.
9. After recovery from transplant surgery, it is no longer necessary to continue medical follow-up, considering that the disease has been cured.
10. Patients may experience different emotional reactions (fear, anxiety, sadness, concern) during the treatment of liver cirrhosis, in the pre- and post-transplant stages; therefore, psychological treatment is important.

Medication

1. Medications used to treat liver cirrhosis cause sexual impotence.

2. Medications are not intended to cure liver cirrhosis, but rather to control disease symptoms.
3. It is important that medications are taken according to medical advice, following the prescribed doses and schedules.
4. Transplantation aims to cure liver cirrhosis, which means that after the procedure it is no longer necessary to take any medications.
5. Adherence to medication treatment can be supported by family involvement, which can help, for example, with timing and correct use of medications.
6. After transplantation, the patient must take medications to prevent rejection (immunosuppressive drugs) for the rest of their life.

https://doi.org/10.22516/25007440.1445

Original article

Characterization of Patients With Acute Liver Failure in a Quaternary-Care Hospital in Colombia

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Citation:
Escalante-Pérez S, Muñoz-Maya O, Santos-Sánchez O, Marín-Zuluaga JI, Restrepo-Gutiérrez JC, Donado-Gómez JH. Characterization of Patients With Acute Liver Failure in a Quaternary-Care Hospital in Colombia. Revista. colomb. Gastroenterol. 2025;40(4):423-429. https://doi.org/10.22516/25007440.1445

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Received: 03/09/2025
Accepted: 05/11/2025

Abstract

Objective: To describe the etiology, management, and clinical course of patients diagnosed with acute liver failure (ALF) admitted to Hospital Pablo Tobón Uribe between January 2004 and December 2023. **Patients and Methods:** A retrospective observational study was conducted including all patients with ALF treated at a quaternary-care hospital in Medellín, Colombia. Demographic characteristics, etiologies, clinical evolution, therapeutic interventions—including liver transplantation—and survival outcomes were analyzed. **Results:** Eighty patients were included. The median age was 40 years, and 58% were women. The most frequent etiologies were viral hepatitis (20%), cryptogenic causes (18.8%), and autoimmune hepatitis (16.3%). Acetaminophen-induced toxicity was uncommon (5%). The clinical course was severe: 62.5% developed respiratory failure, and 57% required vasopressor support. Overall, 67.5% met criteria for urgent liver transplantation, of whom 57% ultimately underwent the procedure. Thirty-day overall survival was 55%, with significantly higher survival among transplanted patients (91%) compared with those not transplanted (49%). Leading causes of death included sepsis, intracranial hypertension, and multiorgan failure. **Conclusions**: This cohort, the largest reported in Colombia to date, underscores the critical importance of specialized management and timely access to liver transplantation to improve outcomes in patients with ALF.

Keywords

Acute liver failure, fulminant hepatic failure, liver transplantation, intensive care unit.

INTRODUCTION

Acute liver failure (ALF) is an infrequent but highly lethal clinical entity, characterized by rapid and severe liver dysfunction in patients without prior liver disease. Its classic definition includes the presence of coagulopathy (international normalized ratio [INR] >1.5), hepatic encephalopathy, and symptom onset within a period of less than 26 weeks. This condition may rapidly progress to multiorgan failure, intracranial hypertension, and death if timely access to liver transplantation is not achieved[1,2]. The term ALF encompasses different subtypes according to the timing of clinical presentation: hyperacute (<7 days), acute (8–28 days), and subacute (4–26 weeks), which has implications for both prognosis and transplant indication[3]. Global incidence is estimated at between 2,000 and 3,000 cases

annually and accounts for approximately 4%–6% of indications for adult liver transplantation[4,5].

The causes of ALF vary significantly by geographic region. In developed countries, acetaminophen toxicity is the predominant etiology, accounting for up to 65% of cases in the United Kingdom and the United States[6]. In contrast, in middle- and low-income regions such as Latin America and Asia, acute viral hepatitis—particularly hepatitis A and B—is the leading cause[7,8]. This variability reflects not only differences in exposure to risk factors but also inequalities in access to early diagnosis, specialized management, and liver transplantation.

Multiple studies have shown that prognosis in patients with ALF depends on etiology, the availability of specific treatments, intensive management in specialized units, and, most importantly, timely access to liver transplantation[1,9,10]. In the absence of transplantation, mortality may exceed 80% in patients with poor prognosis according to criteria such as those of King's College; by contrast, post-transplant survival may reach up to 90% in some series[5,11].

In Latin America, information on ALF remains limited. Reported cohorts are scarce, with small sample sizes and high heterogeneity in etiology and outcomes. In Colombia in particular, there are no large studies that comprehensively describe the clinical characteristics, etiologies, and outcomes of patients with ALF. Therefore, the objective of this study is to characterize patients with ALF treated at a quaternary-care university hospital in Medellín, Colombia, over a 20-year period.

METHODOLOGY

We present an observational follow-up study of a cohort of patients with ALF hospitalized at a referral center. A search was conducted in the electronic medical records system to identify patients diagnosed with codes for acute or subacute liver failure (K720) or unspecified liver failure (K729), according to the International Classification of Diseases (ICD-10).

All patients older than 16 years hospitalized between January 1, 2004, and December 31, 2023, were included. Patients were required to meet diagnostic criteria for ALF, defined by the presence of jaundice, INR >1.5, hepatic encephalopathy, and a disease course of <26 weeks. Patients with a history of cirrhosis or other chronic liver diseases were excluded, except for cases of autoimmune hepatitis, Budd-Chiari syndrome, and Wilson disease.

Etiology was defined based on medical history and paraclinical test results obtained during hospitalization. ALF was classified by timing as hyperacute (less than 7 days), acute (8–28 days), and subacute (4–26 weeks). Prognostic assessment was performed using the King's College criteria. Hepatic encephalopathy was graded according to the West Haven scale.

Data were collected through review of medical records in the hospital's electronic registry using a previously designed data collection instrument. Categorical variables were analyzed using absolute and relative frequencies. Continuous variables were described using means and standard deviations or medians and interquartile ranges, according to data distribution assessed with the Shapiro-Wilk test. For survival analysis and outcomes, time to event was estimated using the Kaplan-Meier curve.

Sample size was not estimated *a priori*, as all patients diagnosed with ALF and treated during the study period were included. The study followed the guidelines of the 2024 Declaration of Helsinki, as well as Resolution 008430 of 1993 on clinical research in Colombia, and was approved by the hospital's Ethics Committee.

RESULTS

A total of 80 patients older than 16 years were included in this study. Of these, 58% were women and 41% were men, with an age range of 16 to 71 years. Demographic, clinical, and paraclinical characteristics are shown in **Table 1**. Regarding the diagnostic criteria for ALF, the median prothrombin time (PT) at admission was 37 seconds; median total bilirubin was 37 mg/dL, and 63% of patients had grade I–II hepatic encephalopathy. Overall, 38.8% of patients were classified as having hyperacute ALF.

The main causes were viral hepatitis (20%), with hepatitis B being the most frequent; cryptogenic etiologies (18.8%); and autoimmune hepatitis (16.3%). Only 5% of patients had ALF due to acetaminophen. Ten percent of cases were attributed to other medications, including anticonvulsants (valproic acid, lamotrigine), antituberculous drugs, losartan in combination with captopril, antiretrovirals (efavirenz), antibiotics (levofloxacin combined with amoxicillin), amphetamine use, and the ABVD chemotherapy regimen. In 6.3% of cases, other causes were identified, including thyroid storm or combined etiologies (hepatitis A plus acetaminophen, herbal products plus hepatitis A). Of the four patients with acetaminophen-related ALF, all met King's College criteria; among the 76 patients with other etiologies, 50 patients (65.7%) met King's College criteria. All etiologies are shown in **Table 2**.

Table 3 presents the clinical outcomes during hospitalization. The median length of hospital stay was 13.5 days, with a maximum of 67 days. Sepsis occurred in 47.5% of patients, with the urinary tract being the most frequent source. Overall, 84% of patients received at least one anti-

Table 1. Demographic and Clinical Characteristics at the Time of Diagnosis

Characteristic	(n = 80)
Age in years, median (IQR)	40 (27.25-51)
Sex, n (%)	
- Female	47 (58.8)
- Male	33 (41.3)
Comorbidities, n (%)	
- Neoplasms	3 (3.8)
- Arterial hypertension	9 (11.3)
- Dyslipidemia	4 (5)
- Diabetes	4 (5)
- Obesity	1 (1.3)
- Chronic kidney disease	1 (1.3)
Total bilirubin, mg/dL, median (IQR)	18 (8.8-26.7)
PT, seconds, median (IQR)	37 (25-56.5)
ALT, U/L, median (IQR)	741 (228-2345)
AST, U/L, median (IQR)	746 (211-2596)
Alkaline phosphatase, IU/L, median (IQR)	152.5 (106.7-197)
Sodium, mEq/L, median (IQR)	137 (133-140)
pH, median (IQR)	7.45 (7.28-7.5)
Lactate, mmol/L, median (IQR)	4.45 (2.7-9.6)
Ammonia, median (IQR)	201 (131-355.5)
Serum creatinine, mg/dL, median (IQR)	0.9 (0.7-2.1)
Encephalopathy grade, n (%)	
- Grade I	35
- Grade II	28.7
- Grade III	23.8
- Grade IV	11.3
Acute liver failure classification, n (%)	
- Hyperacute	31 (38.8)
- Acute	24 (30)
- Subacute	25 (31.3)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; IQR: interquartile range (P_{25-75}); PT: prothrombin time. Author's own research.

Table 2. Etiology of Acute Liver Failure

Etiology	(n = 80) n.° (%)
Cryptogenic	15 (18.8)
Hepatitis B	13 (16.3)
Autoimmune hepatitis	13 (16.3)
DILI	8 (10)
Hypoxic-ischemic	7 (8.8)
Acetaminophen	4 (5.0)
Hepatitis A	3 (3.8)
Herbal products	3 (3.8)
Wilson's disease	2 (2.5)
Acute fatty liver of pregnancy	2 (2.5)
White phosphorus	2 (2.5)
Cytomegalovirus	1 (1.3)
Budd-Chiari syndrome	1 (1.3)
Lymphoma	1 (1.3)
Other causes	5 (6.3)

DILI: drug-induced liver injury. Author's own research.

Table 3. Clinical Outcomes

Clinical Outcomes	(n = 80) n.° (%)
Sepsis	38 (47.5)
Progression of encephalopathy	53 (66.3)
Use of at least one antimicrobial agent	70 (87.5)
Use of anticonvulsant prophylaxis	1 (1.3)
Intracranial pressure (ICP) monitoring	27 (33.8)
ICP value, median (IQR)	18 (14- 27)
Use of at least one anti-cerebral edema measure	45 (56.2)
Need for dialysis	30 (37.5)
Respiratory failure	50 (62.5)
Hemodynamic instability	46 (57.5)
Transplantation	31 (38.8)
Death during initial hospitalization	42 (52.5)
Death after discharge	4 (5)

ICP: intracranial pressure. Author's own research.

microbial agent during hospitalization. Respiratory failure developed in 62% of patients, and 57% required vasopressor support. Although median creatinine at admission was within the normal range, 37.5% of patients required renal replacement therapy. At least one anti-cerebral edema measure—hypertonic saline, mannitol, or deep sedation—was administered to 56.2% of patients.

Among the 54 patients who met King's College criteria, 31 patients (57%) underwent transplantation—one due to acetaminophen and the remainder due to other etiologies. Of the remaining patients, six died while on the waiting list, six died before they could be listed, seven had at least one contraindication, and four experienced spontaneous recovery (none in the acetaminophen group).

Outcomes among transplanted patients are shown in **Table 4**. The median waiting time on the transplant list was 2 days, with a maximum of 16 days. Three patients underwent retransplantation: one during the initial hospitalization due to severe ischemic cholangiopathy from hepatic artery thrombosis; another 10 years after the initial transplant due to graft cirrhosis secondary to ductopenia from chronic rejection; and in the third case, the cause was not specified.

Overall survival was 55% at 30 days (**Figure 1A**). Survival among transplanted versus non-transplanted patients at 30, 60, and 365 days was 91% versus 49%, 88% versus 48%, and 86% versus 28%, respectively (**Figure 1B**). The main causes of death across all patients were multiorgan failure, sepsis, and intracranial hypertension; among transplanted patients, mortality due to postreperfusion syndrome and primary graft dysfunction was also noted.

Table 4. Outcomes in Transplanted Patients

Clinical Outcomes	(n = 31) n.° (%)
Transplant-related complications	21 (68)
- Primary graft dysfunction	2 (10)
- Acute cellular rejection	14 (67)
- Chronic cellular rejection	2 (10)
- Anastomotic stricture	3 (14)
- Biliary leak	1 (5)
- Non-anastomotic stricture	1 (5)
- Thrombosis	2 (10)
- Extrinsic obstruction of the hepatic artery	1 (5)
- Arterial vasospasm	1 (5)
- Ischemic necrosis of the hepatic parenchyma	1 (5)
- Portal vein stenosis	1 (5)
- Other	11 (52)
Infections	18 (51)
- CMV	12 (67)
- Fungal	2 (11)
- Bacterial	11 (61)
- Tuberculosis	1 (6)
Liver graft loss	4 (13)
Liver retransplantation	3 (10)

CMV: cytomegalovirus. Author's own research.

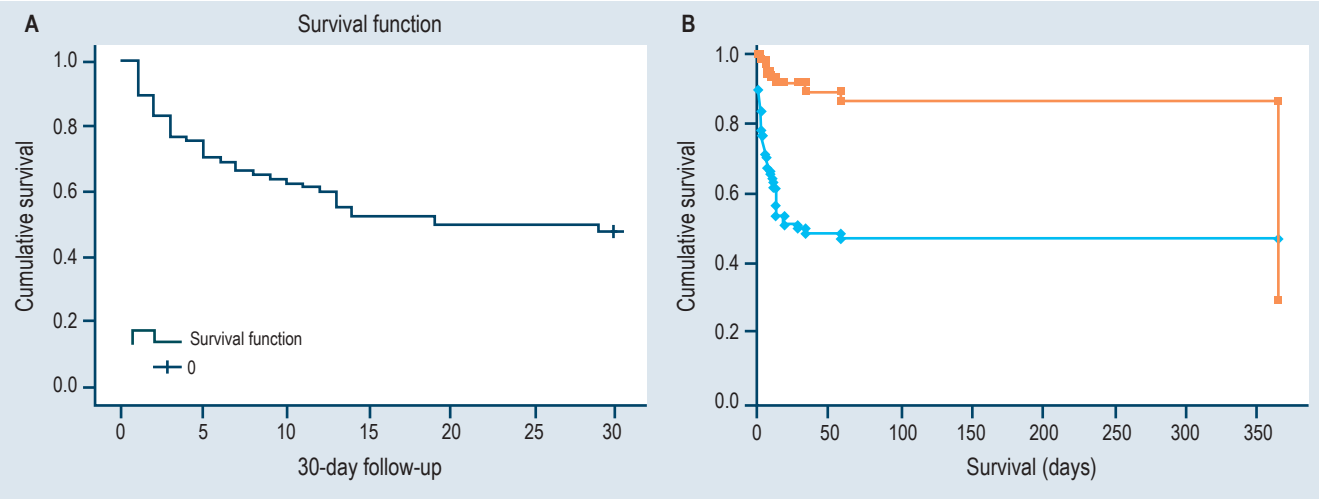


Figure 1. Kaplan-Meier Survival Curves. **A.** Overall 30-day survival. **B.** Cumulative survival according to whether transplantation was performed (orange) or not (blue). Author's own research.

DISCUSSION

Acute liver failure (ALF) remains a severe disease, characterized by abrupt onset, rapid progression, and high mortality[5]. Despite its low incidence, its clinical relevance lies in the need for immediate specialized care and the potential requirement for urgent liver transplantation. Regarding demographic characteristics, it is noteworthy that, consistently in this and other series, ALF predominantly affects young adults and women[9–11]. In this cohort, a median age of 40 years was observed, with 58% of patients being female.

Bilirubin, transaminase, and creatinine levels were similar to those reported in other cohorts, with mean creatinine levels close to 2 mg/dL in a study of the Nordic population[10,12]. These biochemical similarities reinforce clinical comparability across populations, despite etiological differences and structural variations among health care systems.

With respect to etiology, marked differences are evident between developed countries and those in the developing world. In the former, acetaminophen is the most common cause of ALF, with frequencies of 65% in the United Kingdom and 46% in the United States, as consistently described in multiple series[9,11,12]. In contrast, in the present Colombian cohort, acetaminophen accounted for only 5% of cases, being surpassed by viral hepatitis (20%), cryptogenic etiology (18.8%), and autoimmune hepatitis (16.3%). These findings are similar to those reported by Mendizábal and colleagues in Argentina, where the main causes were viral hepatitis (32%), autoimmune hepatitis (26%), and indeterminate etiologies (26%)[10]. Differences in etiology may have important prognostic implications. Acetaminophen toxicity is associated with a better prognosis and higher rates of spontaneous recovery, with transplant-free survival reaching up to 89% at two years in some series[6,12,13]. In contrast, other etiologies, such as autoimmune hepatitis, tend to follow a more protracted and severe course. In this cohort and in the Argentine series, a significant prevalence of autoimmune hepatitis was observed. It is now recognized that this condition may initially present as acute hepatitis and progress to severe forms (INR >1.5), and even to ALF[14]. Although this disease is potentially treatable with corticosteroids, most patients progress and require liver transplantation or die. This suggests that autoimmune hepatitis is a frequent etiology of ALF in Latin America, with severe and late presentations that require transplantation and with a low likelihood of recovery with specific therapy.

Clinical course was severe in this cohort. Sepsis occurred in 47.5% of patients, 62.5% developed respiratory failure, 57% required vasopressor support, and 37.5% required renal replacement therapy (RRT). These figures reflect greater severity compared with other series, such as the Argentine cohort (25% RRT, 24% ventilatory support, and 14% vasopressor use at admission) or the Nordic cohort (21% RRT and 41% mechanical ventilation)[10,12].

Infections were among the leading causes of death in this and other cohorts. Despite antimicrobial use in 84% of patients, sepsis persisted as a major cause of fatal outcomes, consistent with findings reported by Mendizábal and colleagues[10]. Multiple studies have shown that infections negatively impact the natural history of ALF by promoting worsening hepatic encephalopathy, renal failure, and mortality[15]. Across reviewed cohorts, the main causes of death were sepsis, intracranial hypertension, and multiorgan failure[10]. Although universal antimicrobial prophylaxis remains controversial, some centers use it in patients on the transplant waiting list or with multiorgan dysfunction[5,7]. Our findings support the need for studies evaluating the systematic use of broad-spectrum antibacterial and antifungal prophylaxis to reduce the incidence of sepsis and preserve transplant eligibility in suitable candidates.

The use of intracranial pressure (ICP) monitoring was another relevant aspect. In this series, 35.1% of patients had grade III–IV encephalopathy, a figure comparable to other cohorts reporting rates between 38% and 47%[10,11]. ICP monitoring was implemented in 33.8% of cases, and 56.2% received at least one measure for cerebral edema. ICP monitoring remains controversial due to bleeding and infection risks and the lack of conclusive evidence regarding its impact on survival[5,16]. Its use varies widely among studies, ranging from 14% to 65%[11,17]. Current guidelines recommend noninvasive prophylactic measures such as head-of-bed elevation to 30°, deep sedation, normovolemia, adequate mean arterial pressure, and correction of hyponatremia[5]. However, patients with advanced encephalopathy, ammonia levels >150 μmol/L, hyperacute ALF, hemodynamic instability, or need for RRT may benefit from ICP monitoring to optimize management.

Regarding liver transplantation, 57% of patients meeting King's College criteria underwent transplantation, a proportion comparable to the Argentine (54%) and U.S. (59%) series, but lower than that reported in Nordic countries (73%)[10–12]. Twelve patients died while on the waiting list or before listing, reflecting limitations in timely access to transplantation, a phenomenon also described in other series[10,11]. Median waiting time was two days, shorter than that reported in Argentina (3.8 days)[10].

Overall, 30-day survival was 55%, lower than that reported in the United Kingdom (62%), the United States (75%), and Argentina (73%)[9–11]. This difference may be related to prevailing etiology, access to transplantation, and sample size; notably, the British and U.S. cohorts included more than 2,000 patients. Post-transplant survival was 91%, compared with 49% in non-transplanted patients, similar

to other series such as that from the United States (96% vs. 56%), with two-year survival rates of up to 92% among transplanted patients[11,13]. Better transplant-free survival has been documented in acetaminophen-related cases, an etiology that was infrequent in this cohort[12,18].

LIMITATIONS

Among the main limitations of this study are its retrospective, single-center design and relatively small sample size, which limit subgroup analyses and the generalizability of the results. However, this represents one of the largest single-center series reported in Latin America and the most extensive in Colombia. The findings provide valuable data on the clinical, etiological, and outcome characteristics of ALF in a context where causes differ from those observed in developed countries and where barriers to timely access to liver transplantation persist.

CONCLUSION

ALF is an infrequent but highly lethal disease. In recent years, improvements in overall survival have been observed, attributable to specialized intensive care, specific therapies, and the availability of liver transplantation. However, these benefits are not evenly distributed across all settings. In this Colombian cohort, outcomes were consistent with the international literature regarding clinical course and transplant results, while also highlighting specific challenges related to etiology and timely access to treatment.

Early diagnosis, rapid referral to high-complexity centers, and specialized interdisciplinary management are required. In addition, prospective regional studies are needed to evaluate the validity of prognostic models, the role of intracranial pressure monitoring, and the utility of antimicrobial prophylaxis strategies to improve outcomes in this highly complex condition.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

Conflict of Interest

The authors report no conflicts of interest in relation to this article.

REFERENCES

1. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu, Clinical practice guidelines panel, Wendon J, Panel members, Cordoba J, Dhawan A, et al. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. J Hepatol. 2017;66(5):1047-81. https://doi.org/10.1016/j.jhep.2016.12.003
2. Bernal W, Wendon J. Acute Liver Failure. N Engl J Med. 2013;369(26):2525-34. https://doi.org/10.1056/NEJMra1208937
3. Martínez-Martínez LM, Rosales-Sotomayor G, Jasso-Baltazar EA, Torres-Díaz JA, Aguirre-Villarreal D, Hurtado-Díaz de León I, et al. Acute liver failure: Management update and prognosis. Rev Gastroenterol Mex Engl. 2024;89(3):404-17. https://doi.org/10.1016/j.rgmxen.2024.05.002
4. Mercado Díaz MA. Falla hepática aguda en la Unidad de Cuidado Intensivo. Acta Colomb Cuid Intensivo. 2019;19(2):87-96. https://doi.org/10.1016/j.acci.2018.11.004
5. Maiwall R, Kulkarni AV, Arab JP, Piano S. Acute liver failure. Lancet Lond Engl. 2024;404(10454):789-802. https://doi.org/10.1016/S0140-6736(24)00693-7
6. Stravitz RT, Lee WM. Acute liver failure. Lancet Lond Engl. 2019;394(10201):869-81. https://doi.org/10.1016/S0140-6736(19)31894-X
7. Trovato FM, Rabinowich L, McPhail MJW. Update on the management of acute liver failure. Curr Opin Crit Care. 2019;25(2):157-64. https://doi.org/10.1097/MCC.0000000000000583
8. Bernal W, Auzinger G, Dhawan A, Wendon J. Acute liver failure. The Lancet. 2010;376(9736):190-201. https://doi.org/10.1016/S0140-6736(10)60274-7
9. Bernal W, Hyyrylainen A, Gera A, Audimoolam VK, McPhail MJW, Auzinger G, et al. Lessons from look-back in acute liver failure? A single centre experience of 3300 patients. J Hepatol. 2013;59(1):74-80. https://doi.org/10.1016/j.jhep.2013.02.010
10. Mendizabal M, Marciano S, Videla MG, Anders M, Zerega A, Balderramo DC, et al. Changing etiologies and outcomes of acute liver failure: perspectives from 6 transplant centers in Argentina. Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. 2014;20(4):483-9. https://doi.org/10.1002/lt.23823
11. Reuben A, Tillman H, Fontana RJ, Davern T, McGuire B, Stravitz RT, et al. Outcomes in Adults With Acute Liver Failure Between 1998 and 2013: An Observational Cohort Study. Ann Intern Med. 2016;164(11):724-32. https://doi.org/10.7326/M15-2211
12. Brandsaeter B, Höckerstedt K, Friman S, Ericzon BG, Kirkegaard P, Isoniemi H, et al. Fulminant hepatic failure: outcome after listing for highly urgent liver transplanta-

tion-12 years experience in the nordic countries. Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. 2002;8(11):1055-62. https://doi.org/10.1053/jlts.2002.35556
13. Fontana RJ, Ellerbe C, Durkalski VE, Rangnekar A, Reddy RK, Stravitz T, et al. Two-year outcomes in initial survivors with acute liver failure: results from a prospective, multicentre study. Liver Int. 2015;35(2):370-80. https://doi.org/10.1111/liv.12632
14. Muratori L, Lohse AW, Lenzi M. Diagnosis and management of autoimmune hepatitis. BMJ. 2023;380:e070201. https://doi.org/10.1136/bmj-2022-070201
15. Vaquero J, Polson J, Chung C, Helenowski I, Schiodt FV, Reisch J, et al. Infection and the progression of hepatic encephalopathy in acute liver failure. Gastroenterology. 2003;125(3):755-64. https://doi.org/10.1016/S0016-5085(03)01051-5
16. Vaquero J, Fontana RJ, Larson AM, Bass NMT, Davern TJ, Shakil AO, et al. Complications and use of intracranial pressure monitoring in patients with acute liver failure and severe encephalopathy. Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. 2005;11(12):1581-9. https://doi.org/10.1002/lt.20625
17. Rajajee V, Fontana RJ, Courey AJ, Patil PG. Protocol based invasive intracranial pressure monitoring in acute liver failure: feasibility, safety and impact on management. Crit Care Lond Engl. 2017;21(1):178. https://doi.org/10.1186/s13054-017-1762-6
18. Larson AM, Polson J, Fontana RJ, Davern TJ, Lalani E, Hynan LS, et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. Hepatol Baltim Md. 2005;42(6):1364-72. https://doi.org/10.1002/hep.20948

https://doi.org/10.22516/25007440.1455

Original article

Prospective Analysis of Malignant Biliary Stricture Diagnosis: Experience from a Tertiary-Care Hospital

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OPEN ACCESS

Citation:
Zúñiga-Cisneros J, Duarte-Chang C, Mc-Kenzie A, Quirós O, Tuñón C. Prospective Analysis of Malignant Biliary Stricture Diagnosis: Experience from a Tertiary-Care Hospital. Revista. colomb. Gastroenterol. 2025;40(4):430-440.
https://doi.org/10.22516/25007440.1455

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Received: 21/09/2025
Accepted: 30/10/2025

Abstract

Introduction: Malignant biliary strictures represent a persistent diagnostic challenge that requires a coordinated multidisciplinary approach to achieve histopathological confirmation. The limited sensitivity of commonly used diagnostic modalities may delay definitive diagnosis and increase healthcare expenditures. **Methods:** A prospective study was conducted at a tertiary-care hospital in Panama involving patients with malignant biliary strictures (MBS) who underwent drainage via endoscopic retrograde cholangiopancreatography (ERCP). Patients were followed for 12 months, during which all therapeutic and diagnostic procedures, time to histological confirmation, and associated costs were documented. A ROC-curve analysis was performed to determine optimal cutoff values for predictive variables associated with MBS. **Results: A** total of 147 patients with MBS were included, with distal strictures being the most frequent presentation (74%). Pancreatic cancer was the leading underlying malignancy (46.2%), followed by cholangiocarcinoma (36.7%). Cholangiocarcinoma exhibited a notably high proportion of unconfirmed histopathological diagnoses (39%) and incurred the greatest diagnostic costs, with an estimated mean expenditure of USD 12,000. In ROC analyses, the cutoffs associated with malignancy were total bilirubin >8.9 mg/dL, stricture length >1.5 cm, and CA 19-9 >35 U/mL. **Conclusion:** Elevated total bilirubin levels, longer stricture length, and higher CA 19-9 concentrations emerged as predictive factors for MBS. Conventional ERCP-based diagnostic techniques, including brush cytology and biopsy, demonstrated limited diagnostic accuracy, necessitating the use of alternative methods, repeated procedures, and consequently higher costs. Standardizing diagnostic protocols that prioritize more sensitive and specific modalities is essential to enhance diagnostic efficiency and improve care for patients with suspected MBS.

Keywords

Bile ducts, stricture, cholangiocarcinoma, endoscopic retrograde cholangiopancreatography.

INTRODUCTION

Biliary strictures may arise from benign or malignant causes. Diagnosing malignant biliary strictures (MBS) is complex and requires a multidisciplinary approach, which entails high associated costs[1,2]. Histopathological confirmation is essential to define the most appropriate treatment and to establish patient prognosis[3–6].

The diagnosis of biliary strictures is based on clinical suspicion and imaging studies that guide the acquisition of histological samples[1,3,7]. Although endoscopic retrograde cholangiopancreatography (ERCP) has traditionally been the primary diagnostic method, endoscopic ultrasound (EUS) has redefined its role, particularly in pancreatic cancer and complex biliary drainage[8–10]. Brush cytology during ERCP has low sensitivity but high specificity for the diagnosis of

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cholangiocarcinoma[1,11–14]. Advanced techniques such as cholangioscopy improve diagnostic sensitivity, and interventional radiology becomes relevant when advanced endoscopic options are limited or unavailable[3,15].

In resource-limited settings, a stepwise approach is frequently used, in which advanced diagnostic techniques for MBS are mainly reserved for cases in which conventional methods, such as ERCP and brush cytology, are insufficient[16–19]. However, evidence regarding the effectiveness of this approach in both the short and long term is scarce. In this study, we describe the experience of a tertiary-care hospital in Panama with the implementation of a stepwise approach for diagnosing patients with suspected MBS.

PATIENTS AND METHODS

We conducted a prospective study that included patients with a diagnosis of MBS referred to the Department of Gastroenterology of Complejo Hospitalario Metropolitano de Panamá who underwent biliary drainage by ERCP between June 2021 and June 2023. The study received approval from the institutional bioethics committee. We followed patients who underwent ERCP for 12 months, during which we documented therapeutic and diagnostic procedures, time to histological diagnosis, associated diagnostic costs (including procedures performed), and patient mortality.

All participants in this study were required to have a verified diagnosis of malignant disease. We confirmed the presence of cancer through histopathological samples obtained by various procedures, including ERCP, EUS, computed tomography (CT)-guided biopsy, endoscopy, and surgery. When histology could not be obtained or yielded inconclusive results, we also considered a strong suspicion based on the patient's clinical presentation, CT findings, and ERCP results.

We excluded patients younger than 18 years, patients without an indication for ERCP, and patients with a prior histopathological diagnosis. We categorized patients according to the type of neoplasm causing MBS: pancreatic cancer, cholangiocarcinoma, gallbladder cancer, ampullary cancer, metastases, and lymphoma. We also divided the data into two groups based on stricture location: distal strictures, located below the junction of the cystic duct and the bile duct, and hilar strictures, located above this junction.

Study Variables and Definitions

A gastroenterologist established the diagnosis of malignant biliary stricture using the diagnostic resources available at the institution during patient evaluation. We calculated time to diagnosis as the interval from the patient's first related medical encounter to histopathological confirmation of the diagnosis. We recorded histopathological results, including brush cytology (see the Brush Cytology section), and biochemical parameters such as baseline total bilirubin (BTI_0), alkaline phosphatase (IU/L), albumin (mg/dL), aspartate aminotransferase (AST) (U/L), alanine aminotransferase (ALT) (U/L), and carbohydrate antigen 19-9 (CA 19-9) (U/mL).

For comparative purposes in ROC models, we included patients with benign biliary strictures, defined by the following criteria: absence of an identifiable mass on CT, transabdominal ultrasound, EUS, or magnetic resonance imaging (MRI); absence of distant metastases on imaging studies; no recent (<3 months) history of traumatic or iatrogenic bile duct injury; negative tissue sampling; and no evidence of a tumor mass during a follow-up period of at least 12 months.

For our cost analysis, we carefully documented all procedures performed for each patient. These included endoscopic interventions, imaging studies, interventional radiology approaches, and other relevant procedures (stent placement). We did not collect data on length of hospitalization or on medications used during the treatment process. We assumed that consumables required for ERCP were constant for both plastic stent (PS) placement and uncovered self-expanding metal stent (uSEMS) placement, with the exception of the stents themselves. We determined costs associated with ERCP, percutaneous biopsies performed by interventional radiology, and diagnostic imaging studies based on standardized prices established in Panama by insurance providers for these medical procedures.

Brush Cytology

We used the same ERCP protocols for cytological sample collection in all cases. Under fluoroscopic guidance, we placed a guidewire into the bile duct and advanced it across the stricture. We then introduced a double-lumen cytology brush with a metal guidewire (manufactured by Boston Scientific, Natick, MA, USA; and Cook Medical, Winston-Salem, NC, USA) into the stricture and performed at least eight brush passes. We used two methods: in the first, we employed the cytology brush directly; in the second, we removed the brush head and immersed it in a preservative solution. In addition, we prepared smears and stained them after cytocentrifugation at 1,500 revolutions per minute (rpm) for 5 minutes. To obtain the final cytological diagnosis, we fixed smears and cell pellets in 95% ethanol and stained them using the Papanicolaou method. We classified samples as showing no abnormal cells (benign), atypical cells, suspicious cells, or malignant cells. We considered both suspicious and malignant cells as confirmatory of malignant disease.

Statistical Analysis

We performed the statistical analysis using Stata/SE 16.0 (StataCorp, 4905 Lakeway Dr, College Station, TX, USA). We applied the Kolmogorov-Smirnov test to assess the normality of continuous data and found that our data did not follow a normal distribution.

We summarized continuous variables using the median and interquartile range, and we expressed quantitative variables as percentages. We used the Mann-Whitney test to analyze unpaired continuous variables and the chi-square test to assess differences between qualitative variables. We considered results statistically significant at a two-tailed *p* value <0.05.

We constructed receiver operating characteristic (ROC) curves to determine optimal cutoff values for factors significantly associated with malignant biliary strictures compared with benign biliary strictures, using the trade-off between sensitivity and specificity on the ROC curves. We estimated the accuracy of MBS prediction using the area under the ROC curve (AUC)[19]. Our analysis included laboratory parameters (BTI_0, ALT, AST, alkaline phosphatase, CA 19-9), age, and stricture length. We also generated ROC curves to evaluate our diagnostic performance and accuracy using brush cytology.

RESULTS

We included 147 patients with a diagnosis of malignant biliary stricture (MBS) and 22 patients with benign biliary strictures. Of the MBS cases, 74% were classified as distal strictures and 26% as hilar strictures (p <0.005). Notably, obstructive jaundice was the predominant indication for medical evaluation, observed in 87.7% of patients. Pancreatic cancer was the most prevalent neoplasm (46.2%), followed by cholangiocarcinoma (36.7%) (**Table 1**).

Table 1. Characteristics of patients with malignant biliary strictures according to stricture location

Variable	Total	Distal Stricture (n = 109)	Hilar Stricture (n = 38)	*p*-Value
Age (years)	70.5 (RIC: 60-78)	72 (RIC: 61-79)	66 (RIC: 55-73)	**0.03**
Sex				
- Male	69 (46.9%)	49 (44.9%)	20 (52.6%)	0.414
- Female	78 (53.1%)	60 (55.1%)	18 (47.4%)	
Suspicious clinical presentation				
- Obstructive jaundice	129 (87.7)	99 (91.7%)	30 (76.9%)	0.432
- Choledocholithiasis	2 (1.4%)	1 (0.9%)	1 (2.6%)	
- Cholangitis	15 (10.2%)	8 (7.4%)	7 (17.9)	
- Liver mass	1 (0.7%)	0	1 (2.6%)	
Diagnosis				
- Pancreatic cancer	68 (46.3%)	64 (58.7%)	4 (10.5%)	**0.031**
- Cholangiocarcinoma	54 (36.7%)	27 (25.7%)	27 (71.1%)	
- Gallbladder cancer	6 (4.1 %)	3 (2.8%)	3 (7.9%)	
- Ampullary carcinoma	7 (4.8%)	7 (6.4%)	0	
- NET	2 (1.4%)	2 (1.8%)	0	
- Metastases	7 (4.8%)	2 (1.8%)	5 (13.2%)	
- High-grade lymphoma	3 (2.0%)	3 (2.8%)	0	
Total bilirubin (mg/dL)	17 (12-22.9)	17.5 (12-23.1)	15.2 (10.2-22.4)	0.686
CA 19-9 (U/mL)	337 (61-1515)	219 (42-1425)	679 (35-1945)	**0.018**
Albumin (mg/dL)	3 (2.5-3.5)	2.8 (2.5-4.5)	3 (2.6-3.5)	0.711
Mortality	64 (43.5%)	46 (42.2%)	18 (47.4%)	**0.003**

CA 19-9: carbohydrate antigen 19-9; NET: neuroendocrine tumor; IQR: interquartile range. Author's own research.

Initial laboratory results showed that patients with pancreatic cancer had median total bilirubin and CA 19-9 levels of 16.5 mg/dL (IQR: 10.9–22.3) and 627 U/mL (IQR: 57–1745), respectively. In comparison, patients with cholangiocarcinoma had higher initial bilirubin levels, with a median of 18.5 mg/dL (IQR: 12.6–23.3), and CA 19-9 levels with a median of 356 U/mL (IQR: 78–1825). In cases of ampullary cancer, the median total bilirubin was 8.95 mg/dL (IQR: 5.3–12.6), and the median CA 19-9 was 27 U/mL (IQR: 2.5–156) (**Table 2**).

Diagnostic Methodologies, Timelines, and Costs Associated with Each Type of Neoplasm

Cholangiocarcinoma showed the highest proportion of unconfirmed histopathological diagnoses (39%), followed by pancreatic cancer (21%). The median time to diagnosis was 47 days (IQR: 14–63) for cholangiocarcinoma, 66 days (IQR: 22–114) for pancreatic cancer, and 123 days (IQR: 34–223) for ampullary cancer. The most frequently used diagnostic techniques were brush cytology for cholangiocarcinoma, interventional radiology for pancreatic cancer, and endoscopy with biopsy for ampullary neoplasms (**Figure 1**).

As shown in **Figure 2**, when we evaluated diagnostic costs, cholangiocarcinoma was the most expensive neoplasm to diagnose, with a mean cost of USD 12,095.20 and a median of 1.69 ERCP procedures performed. Pancreatic cancer followed closely, with a mean cost of USD 11,929.20 (1.72 ERCPs), and ampullary cancer, with USD 11,307.00 (2.0 ERCPs). Cost differences among neoplasms were statistically significant (p <0.005).

Brush Cytology

We evaluated the effectiveness of brush cytology, which revealed a low sensitivity of 20% for pancreatic cancer, with a specificity of 81.7%. In contrast, cholangiocarcinoma showed a slightly higher sensitivity of 25.6% and a specificity of 85.3% (**Table 3**).

Table 2. Classification of malignant biliary neoplasms by type and associated clinical characteristics

Variable	Pancreatic Cancer (n = 68)	Cholangiocarcinoma (n = 54)	Gallbladder Cancer (n = 6)	Ampullary Neoplasm (n = 7)	Metastase (n = 7)	Lymphoma (n = 3)	Benign Strictures (n = 22)
Age (years)	60.5 (55-76)	81 (61-81)	63.5 (55-71)	79 (72-82)	59 (52.5-63.5)	58 (57-77)	46 (38-61)
Total bilirubin (mg/dL)	16.5 (10.9-22.3)	18.5 (12.6-23.3)	17.5 (13.6-37.1)	8.95 (5.3-12.6)	15 (12.2-24)	20.5 (7.1-23.7)	3.4 (2.1-5.5)
Alkaline phosphatase	502 (310-739)	518 (339-938)	480 (384-655)	685 (253-685)	388 (298-461)	496 (125-630)	310 (242-381)
CA 19-9 (U/mL)	627 (57-1745)	356 (78-1825)	31.6 (2.1-222)	27 (2.5-156)	297 (233-2220)	194 (173-215)	17 (1.5-31.6)
Albumin (mg/dL)	3.1 (2.6-3.6)	2.7 (2.3-3.1)	3.1 (2.4-3.5)	3.5 (3.4-3.7)	3.5 (3.2-4.1)	2.7 (2.3-3.1)	3.6 (3.3-4.6)
AST (U/L)	151 (110-252)	168 (93-200)	117 (87-175)	114 (26-306)	148 (137-161)	225 (37-279)	89 (110-156)
ALT (U/L)	167 (101-285)	120 (71-190)	95 (83-174)	143 (11-422)	19 (14-33)	110 (60-156)	24 (34-45)
Histopathological confirmation (%)	79%	61%	100%	100%	100%	100%	N/A
Time to diagnosis (days)	66 (22-114)	47 (14-63)	17 (13-96)	123 (34-233)	19 (14-33)	195 (80-586)	N/A
Stricture length (cm)	2.1 (1.7-3)	2 (1.5-3)	3 (1-3.5)	1 (1-1.8)	3 (1.4-3)	3 (1.2-4.1)	1.3 (1-1.8)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CA 19-9: carbohydrate antigen 19-9; N/A: not applicable. Author's own research.

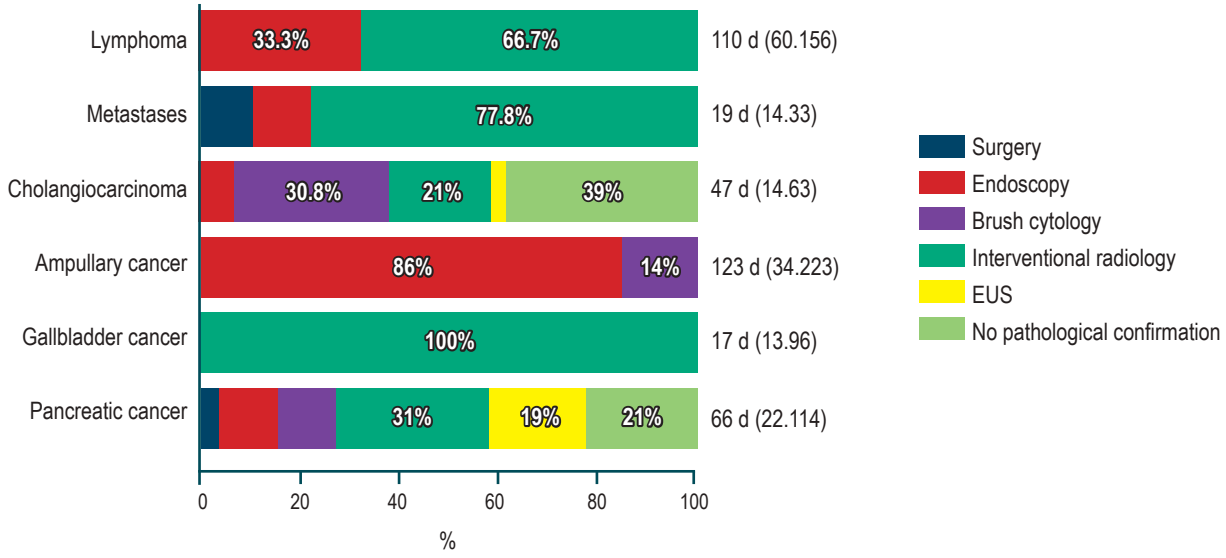


Figure 1. Assessment of diagnostic timelines and modalities according to the type of biliary tract neoplasm. d: days. Author's file.

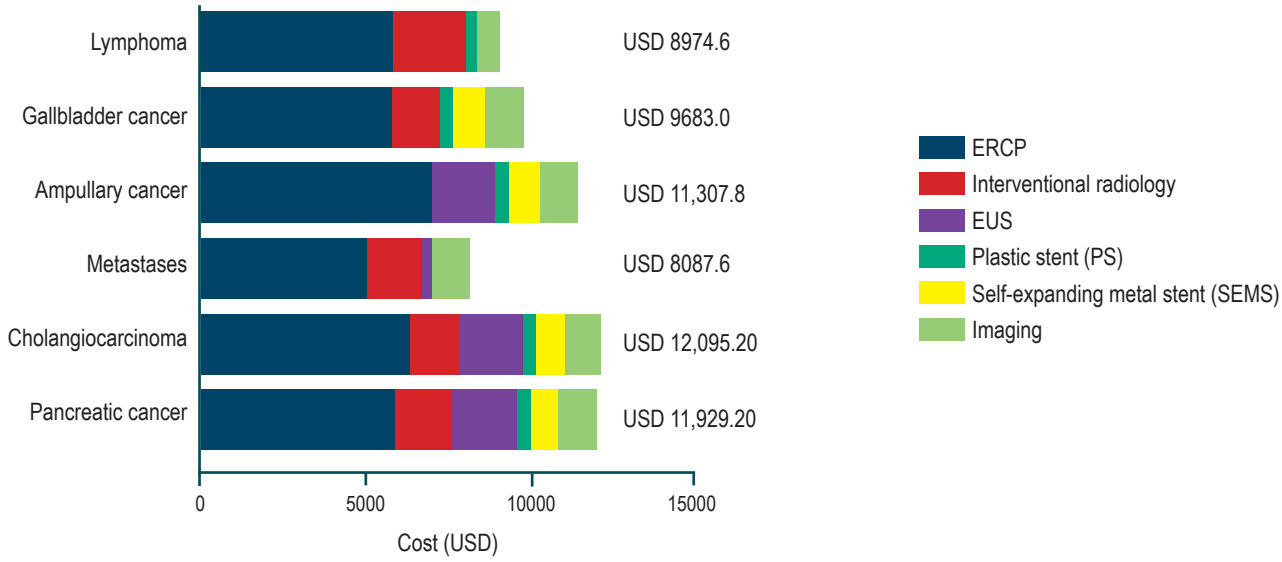


Figure 2. Assessment of diagnostic costs in US dollars for different types of malignant biliary neoplasms. ERCP: endoscopic retrograde cholangiopancreatography; SEMS: self-expanding metal stent; PS: plastic stent; USD: United States dollars; EUS: endoscopic ultrasound. Author's file.

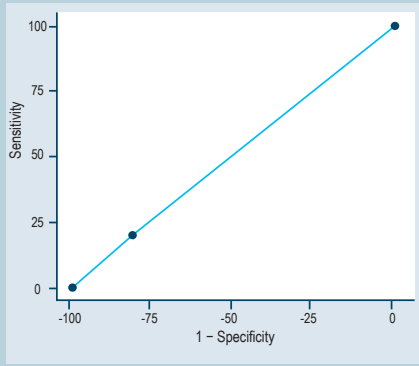
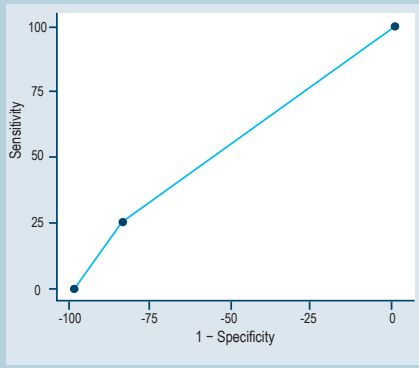
Predictors of Malignant Biliary Strictures

ROC analysis identified predictive variables for malignant biliary strictures, including total bilirubin, CA 19-9 levels, stricture length, and age, all of which showed robust area under the curve (AUC) values. In particular, a total bilirubin cutoff value >8.9 mg/dL yielded a positive predictive value (PPV) of 98%, and a stricture length greater than 1.5 cm also indicated a high PPV of 99%. **Figure 3** provides detailed information on these results, and **Table 4** presents the associated risk increase according to each predictive factor.

DISCUSSION

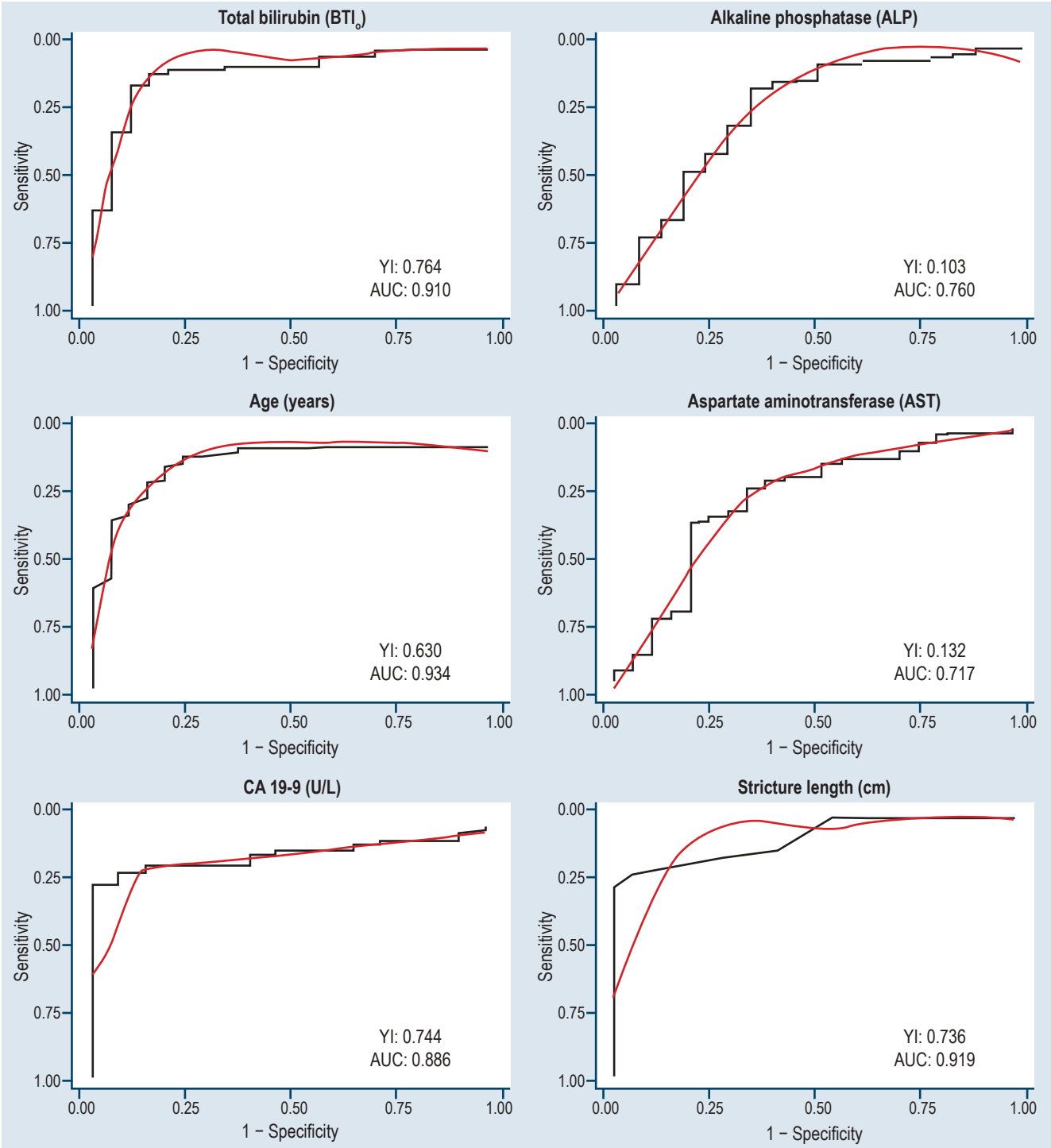
Malignant biliary strictures represent one of the most challenging diagnoses in clinical practice because of the

Table 3. ROC Curves of Cytological Brush STUDIES in Malignant Biliary Strictures

Pancreatic Cancer								
Scale: Cytology Dx								
Cutoff Point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden Index	AUC	Metric Score	ROC Curve: Cytology Dx
1	100%	0%	36.04%	NaN%	0.0000	0.508	1.00	
2	20%	81.69%	38.1%	64.44%	0.0169	0.508	1.02	
Cholangiocarcinoma								
Scale: Cytology Dx								
Cutoff Point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden Index	AUC	Metric Score	ROC Curve: Cytology Dx
1	100%	0%	38.74%	NaN%	0.000	0.554	1.00	
2	25.58%	85.29%	52.38%	64.44%	0.109	0.554	1.11	

AUC: area under the curve; Dx: diagnosis; NaN%: not a number; NPV: negative predictive value; PPV: positive predictive value. Author's own research.

inherent difficulty in obtaining adequate histopathological samples to establish a definitive diagnosis. Although imaging techniques such as magnetic resonance imaging (MRI) and endoscopic procedures such as ERCP and EUS are essential tools in the initial evaluation of biliary strictures, determining the exact etiology remains difficult when there are no obvious findings, such as tumor masses or stones. This study provides relevant evidence in this area by highlighting the difficulties gastroenterologists face in confirming a diagnosis of malignant biliary stricture (MBS) in routine clinical practice, particularly in resource-limited settings. Our results show that ampullary cancer was the etiology associated with the longest mean time to diagnosis. Among the most frequent causes of MBS, cholangiocarcinoma achieved histological confirmation in 61% of cases, whereas pancreatic cancer reached a diagnostic rate of 79%. Patients without a definitive diagnosis required a greater number of procedures, which translated into a significant increase in diagnostic costs. We also identified the following variables as predictors of malignancy in biliary strictures: age at diagnosis ≥47 years, total bilirubin ≥8.9 mg/dL, CA 19-9 ≥35 U/mL, and stricture length ≥1.5 cm.



Variables	Cutoff value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
BTI_0 (mg/dL)	8.9	85	90	98	52	0.910
ALP (IU/L)	110	99	11	88	67	0.760
*ALT (IU/L)	40	97	9	82	50	0.556
AST (IU/L)	37	98	14	83	75	0.717
CA 19-9 (U/mL)	35	81	93	98	40	0.886
Stricture length (cm)	1.5	78	95	99	40	0.919
Age (years)	47	99	63	94	93	0.934

Figure 3. Receiver operating characteristic (ROC) analysis results for predicting malignant biliary strictures. *Analysis not shown in the graph. ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; AUC: area under the curve; BTI_0: baseline total bilirubin; NPV: negative predictive value; PPV: positive predictive value; YI: Youden index. Author's file.

Table 4. Odds Ratios for Variables Associated with Malignant Biliary Strictures

Variable	Odds Ratio	95% CI	*p*-Value*
Cholelithiasis	0.34	0.045-0.932	**0.0001**
CA 19-9 (>34 U/mL)	4.23	1.145-9.92	**0.003**
BTI_0 (>8.9 mg/dL)	3.41	1.322-7.942	**0.021**
AST	1.43	0.034-8.521	0.472
ALT	1.52	0.041-9.328	0.645
Age (>47 years)	4.11	1.56-7.83	**0.0001**
Stricture length (>15 mm)	5.65	2.31-8.94	**0.0031**

*Statistically significant p values are shown in bold. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BTI_0: baseline total bilirubin; CA 19-9: carbohydrate antigen 19-9; CI: confidence interval. Author's own research.

Our findings highlight cholangiocarcinoma and pancreatic cancer as the leading causes of MBS. The median time to histological confirmation of pancreatic cancer was 66 days, and interventional radiology was the most frequently used diagnostic method (31%), whereas EUS was used in only 19% of cases. Despite the presence of a pancreatic mass, histological confirmation was not obtained in 21% of patients. The economic impact was substantial: the average cost of diagnosing pancreatic cancer at our hospital was approximately USD 12,000, excluding additional expenses such as hospitalization, professional fees, or associated complications. Limited availability of supplies for performing EUS-guided fine-needle aspiration (EUS-FNA) required us to rely on interventional radiology as the primary method for obtaining histopathological samples. Previous studies have demonstrated the high efficacy of EUS-FNA in diagnosing pancreatic masses ≥2 cm, with success rates exceeding 90%[10,20,21]. In contrast, ERCP currently plays a limited role and is primarily reserved for biliary drainage[1,22,23]. Both the American Society for Gastrointestinal Endoscopy (ASGE) and the European Society of Gastrointestinal Endoscopy (ESGE) recommend EUS-FNA as the first-line diagnostic approach in distal strictures with a pancreatic mass, and the use of combined methods when such a mass is absent[24,25].

Cholangiocarcinoma was diagnosed predominantly in hilar strictures (71%) and was also the second most frequent cause among distal strictures. Our study demonstrates the diagnostic challenges associated with this entity, as nearly 40% of patients did not achieve histological confirmation despite undergoing multiple diagnostic procedures. The mean time to diagnosis was 47 days, underscoring the need for more effective and timely diagnostic strategies. ERCP with endoscopic brush cytology was performed in 31% of cases and showed a sensitivity of 25.6% and a specificity of 85.3%, values lower than those reported in the literature (sensitivity: 35%–41%; specificity >79%) [11–14]. Many patients required multiple ERCP procedures to achieve a cytological diagnosis, with an estimated average cost of USD 12,095 per case. ESGE guidelines recommend brush cytology and fluoroscopy-guided biopsies for hilar malignant biliary strictures, while reserving EUS for accessible extraluminal lesions[25]. In contrast, the ASGE indicates that cholangioscopy-guided biopsy during ERCP increases diagnostic sensitivity in proximal or non-distal strictures, particularly after an initial nondiagnostic ERCP and in experienced centers. In distal strictures without a visible mass, ERCP combined with cholangioscopy is suggested after prior unsuccessful attempts, although this recommendation is conditional and based on low-quality evidence[24,25].

Standard techniques (brush cytology and biopsy) continue to show low sensitivity (34% and 50%, respectively), whereas cholangioscopy achieves diagnostic accuracies of 80%–85%[3,11,13,14]. Given that 51% of cholangiocarcinomas in our cohort were intrahepatic or perihilar, early use of cholangioscopy—even during the first ERCP—could optimize diagnostic sensitivity and reduce long-term costs.

In this study, we identified significant predictive factors that allow malignant biliary strictures to be distinguished from benign ones. Among these, stricture length emerged as the strongest predictor of malignancy, with an odds ratio of 5.65. These findings are consistent with previous studies indicating that a stricture length greater than 14.5 mm constitutes a robust indicator of malignancy[4,7,26]. Elevated CA 19-9 levels are also widely recognized as biomarkers of pancreatobiliary neoplasms, and our findings confirm that a cutoff value greater than 35 U/mL is closely associated with an increased risk of malignancy. In addition, prior studies have shown that baseline bilirubin levels between 6.0 and 8.4 mg/dL significantly increase the likelihood of a malignant etiology[7,16,27]. Based on these results, we propose that patients presenting with multiple risk factors—such as increased stricture length, elevated CA 19-9 levels, and elevated serum bilirubin—undergo comprehensive diagnostic evaluation before a stricture is classified as benign, in order to optimize early detection of malignancy and reduce diagnostic delay.

Our main limitations were related to the lack of resources for obtaining histopathological diagnoses. In most cases, we opted to perform ERCP with brush cytology and biopsy as the initial diagnostic strategy because access to advanced endoscopic methods, such as cholangioscopy

and EUS, was limited. This situation reflects the challenges of working in a real-world, resource-constrained environment. In addition, our patient selection was restricted to those requiring ERCP, as these were the only patients who could be managed in our department.

This study highlights the diagnostic challenges associated with malignant biliary strictures, particularly the difficulty of obtaining adequate histopathological samples to confirm malignancy. Conventional methods used during ERCP, such as brush cytology and endoscopic biopsy, demonstrated low diagnostic accuracy, leading to the need for additional procedures and increases in diagnostic costs and timelines. Based on our findings, we recommend early integration of advanced techniques, such as EUS and cholangioscopy, into the initial diagnostic algorithm. Implementing this proactive, stepwise approach could increase diagnostic sensitivity, reduce the number of invasive procedures, and optimize the use of hospital resources. Ultimately, systematic application of these strategies has the potential to accelerate definitive diagnosis, improve clinical outcomes, and possibly enhance the prognosis of patients with suspected malignant biliary strictures.

Ethical Statement

This study was approved by the hospital's Bioethics Committee.

Conflict of Interest

The authors declare no potential conflicts of interest.

Funding Sources

This study received no financial support from governmental institutions or private companies.

Use of Artificial Intelligence

No artificial intelligence was used in the preparation of this work.

REFERENCES

1. Elmunzer BJ, Maranki JL, Gómez V, Tavakkoli A, Sauer BG, Limketkai BN, et al. ACG Clinical Guideline: Diagnosis and Management of Biliary Strictures. Am J Gastroenterol. 2023;118(3):405-26. https://doi.org/10.14309/ajg.0000000000002190
2. Lee HJ, Cho KB. Diagnosis of Malignant Biliary Stricture: More is Better. Clin Endosc. 2018;51(2):115. https://doi.org/10.5946/ce.2018.035
3. Rushbrook SM, Kendall TJ, Zen Y, Albazaz R, Manoharan P, Pereira SP, et al. British Society of Gastroenterology guidelines for the diagnosis and management of cholangiocarcinoma. Gut. 2023;73(1):16-46. https://doi.org/10.1136/gutjnl-2023-330029
4. Saluja SS, Sharma R, Pal S, Sahni P, Chattopadhyay TK. Differentiation between benign and malignant hilar obstructions using laboratory and radiological investigations: A prospective study. HPB. 2007;9 (5):373-82. https://doi.org/10.1080/13651820701504207
5. Liao W, Wang Q, Jiang Q, Wu X, Yang Y, Yang A. Enhancing diagnostic strategies for biliary strictures: an evolving landscape. Hepatobiliary Surg Nutr. 2024;13(5):885. https://doi.org/10.21037/hbsn-24-447
6. Dorrell R, Pawa S, Zhou Y, Lalwani N, Pawa R. The diagnostic dilemma of malignant biliary strictures. Diagnostics (Basel). 2020;10(5):337. https://doi.org/10.3390/diagnostics10050337
7. Al-Mofleh IA, Aljebreen AM, Al-Amri SM, Al-Rashed RS, Al-Faleh FZ, Al-Freihi HM, et al. Biochemical and radiological predictors of malignant biliary strictures. World J Gastroenterol. 2004;10(10):1504. https://doi.org/10.3748/wjg.v10.i10.1504
8. Mohamadnejad M, Dewitt JM, Sherman S, Leblanc JK, Pitt HA, House MG, et al. Role of EUS for preoperative evaluation of cholangiocarcinoma: A large single-center experience. Gastrointest Endosc. 2011;73(1):71-8. https://doi.org/10.1016/j.gie.2010.08.050
9. Gonzalo-Marin J, Vila JJ, Perez-Miranda M. Role of endoscopic ultrasound in the diagnosis of pancreatic cancer. World J Gastrointest Oncol. 2014;6(9):360. https://doi.org/10.4251/wjgo.v6.i9.360
10. Rogers HK, Shah SL. Role of Endoscopic Ultrasound in Pancreatic Cancer Diagnosis and Management. Diagnostics 2024, Vol 14, Page 1156. 2024;14(11):1156. https://doi.org/10.3390/diagnostics14111156
11. Shin DW, Moon SH, Kim JH. Diagnosis of Cholangiocarcinoma. Diagnostics (Basel). 2023;13(2):233. https://doi.org/10.3390/diagnostics13020233
12. Van Beers BE. Diagnosis of cholangiocarcinoma. HPB (Oxford). 2008;10(2):87. https://doi.org/10.1080/13651820801992716
13. Weber A, von Weyhern C, Fend F, Schneider J, Neu B, Meining A, et al. Endoscopic transpapillary brush cytology and forceps biopsy in patients with hilar cholangiocarcinoma. World Journal of Gastroenterology: WJG. 2008;14(7):1097. https://doi.org/10.3748/wjg.14.1097

14. Kurzawinski T, Deery A, Davidson BR. Diagnostic value of cytology for biliary stricture. Br J Surg. 1993;80 (4):414-21. https://doi.org/10.1002/bjs.1800800404
15. Siu W, Tang RSY. The Role of Cholangioscopy and EUS in the Evaluation of Indeterminate Biliary Strictures. Gastroenterology Insights 2022, Vol 13, Pages 192-205. 2022;13(2):192-205. https://doi.org/10.3390/gastroent13020020
16. Vasilieva L, Alexopoulou A, Papadhimitriou SI, Romanos A, Xynopoulos D, Dourakis SP. Total bilirubin is a good discriminator between benign and malignant biliary strictures. HPB. 2012;14(1):71. https://doi.org/10.1111/j.1477-2574.2011.00400.x
17. Ballehaninna UK, Chamberlain RS. The clinical utility of serum CA 19-9 in the diagnosis, prognosis and management of pancreatic adenocarcinoma: An evidence based appraisal. J Gastrointest Oncol. 2012;3(2):105-19. https://doi.org/10.3978/j.issn.2078-6891.2011.021
18. Naitoh I, Nakazawa T, Kato A, Hayashi K, Miyabe K, Shimizu S, et al. Predictive factors for positive diagnosis of malignant biliary strictures by transpapillary brush cytology and forceps biopsy. J Dig Dis. 2016;17 (1):44-51. https://doi.org/10.1111/1751-2980.12311
19. Habibzadeh F, Habibzadeh P, Yadollahie M. On determining the most appropriate test cut-off value: the case of tests with continuous results. Biochem Med (Zagreb). 2016;26 (3):297-307. https://doi.org/10.11613/BM.2016.034
20. Viesca MFY, Arvanitakis M. Early Diagnosis And Management Of Malignant Distal Biliary Obstruction: A Review On Current Recommendations And Guidelines. Clin Exp Gastroenterol. 2019;12:415. https://doi.org/10.2147/CEG.S195714
21. Yousaf MN, Chaudhary FS, Ehsan A, Suarez AL, Muniraj T, Jamidar P, Aslanian HR, Farrell JJ. Endoscopic ultrasound (EUS) and the management of pancreatic cancer. BMJ Open Gastroenterol. 2020;7(1):e000408. https://doi.org/10.1136/bmjgast-2020-000408
22. Njei B, McCarty TR, Varadarajulu S, Navaneethan U. Cost utility of ERCP-based modalities for the diagnosis of cholangiocarcinoma in primary sclerosing cholangitis. Gastrointest Endosc. 2017;85(4):773-781.e10. https://doi.org/10.1016/j.gie.2016.08.020
23. Kapoor BS, Mauri G, Lorenz JM. Management of Biliary Strictures: State-of-the-Art Review. Radiology. 2018;289(3):590-603. https://doi.org/10.1148/radiol.2018172424
24. Fujii-Lau LL, Thosani NC, Al-Haddad M, Acoba J, Wray CJ, Zvavanjanja R, et al. American Society for Gastrointestinal Endoscopy guideline on role of endoscopy in the diagnosis of malignancy in biliary strictures of undetermined etiology: methodology and review of evidence. Gastrointest Endosc. 2023;98 (5):694-712.e8. https://doi.org/10.1016/j.gie.2023.06.007
25. Facciorusso A, Crinò SF, Gkolfakis P, Spadaccini M, Arvanitakis M, Beyna T, et al. Diagnostic work-up of bile duct strictures: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2025;57(2):166-85. https://doi.org/10.1055/a-2481-7048
26. Park MS, Kim TK, Kim KW, Park SW, Lee JK, Kim JS, et al. Differentiation of extrahepatic bile duct cholangiocarcinoma from benign stricture: Findings at MRCP versus ERCP. Radiology. 2004;233(1):234-40. https://doi.org/10.1148/radiol.2331031446
27. Garcea G, Ngu W, Neal CP, Dennison AR, Berry DP. Bilirubin levels predict malignancy in patients with obstructive jaundice. HPB. 2011;13(6):426-30. https://doi.org/10.1111/j.1477-2574.2011.00312.x

https://doi.org/10.22516/25007440.1381

Original article

Effect of Rifaximin on Quality of Life in Patients with Irritable Bowel Syndrome and Small Intestinal Bacterial Overgrowth

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Citation:
Hernández-Sampayo F, Yepes-Barreto I, García-del Risco F. Effect of Rifaximin on Quality of Life in Patients with Irritable Bowel Syndrome and Small Intestinal Bacterial Overgrowth. Revista. colomb. Gastroenterol. 2025;40(4):441-449. https://doi.org/10.22516/25007440.1381

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Received: 28/05/2025
Accepted: 09/12/2025

Abstract

Introduction: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder with a multifactorial pathophysiology, including alterations in the gut microbiota. Small intestinal bacterial overgrowth (SIBO) may coexist with IBS and exacerbate symptoms, adversely affecting quality of life. **Objective:** To evaluate the impact of rifaximin therapy on quality of life in patients diagnosed with IBS and SIBO, using the validated IBS-QoL instrument and Rome IV criteria. **Methods:** A quasi-experimental study was conducted at a gastroenterology center in Cartagena, Colombia, between June 2023 and January 2024. Patients with IBS diagnosed through Rome IV criteria and a positive breath test for SIBO were included. Participants received rifaximin 550 mg every 8 hours for 14 days. Quality of life was assessed before and after treatment using the IBS-QoL scale. **Results:** Seventy-one patients with confirmed SIBO were enrolled. The mean age was 48.6 years, and 81.8% were women. Following treatment, a significant improvement in quality-of-life scores was observed (p <0.001), along with a reduction in major symptoms—particularly abdominal distension, bloating, and flatulence. A total of 26.7% of participants reported no improvement. **Conclusion:** The study suggests that rifaximin therapy is associated with symptomatic improvement and enhanced quality of life among patients with IBS and SIBO, with the greatest benefit observed in those presenting with abdominal distension.

Keywords

Irritable bowel syndrome, intestine, quality of life, microbiota.

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic or recurrent abdominal pain associated with alterations in bowel habits, in the absence of a demonstrable organic cause. Worldwide, the prevalence of IBS is estimated at 11.2%, with a predominance in females; in Latin America, it ranges from 6.98% to 24%, depending on the Rome criteria used[(1)]. According to the global epidemiology study conducted by the Rome Foundation, which included 33 countries, the prevalence of IBS using Rome IV criteria is 4.1%, with an estimated prevalence of 4.25% for Latin America and 4.3% for Colombia—figures that are considerably lower than those obtained with Rome III due to the greater diagnostic specificity of Rome IV[(2)].

The diagnosis of IBS is based on the Rome IV criteria, which allow classification according to the predominant symptom pattern into the following subtypes: diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), mixed IBS (IBS-M), or unclassified IBS (IBS-U)[(1)]. IBS is among the ten most common causes of consultation

in gastroenterology and primary care services; it significantly impairs quality of life and generates a high public health cost[3]. It is a multifactorial disease in which interactions among the gut-brain axis, the intestinal microbiota, visceral hypersensitivity, stress, and genetic factors contribute to its development and persistence[4,5].

Recent studies have demonstrated that the intestinal microbiota plays a fundamental role in the pathophysiology of IBS, influencing its clinical course and predisposing to chronicity[6]. Among the proposed mechanisms is intestinal dysbiosis, defined as an imbalance in the composition and function of intestinal bacteria. This alteration may contribute to IBS symptoms; therefore, the presence of small intestinal bacterial overgrowth (SIBO) should be considered a possible contributing factor[7].

SIBO is characterized by abnormal and excessive colonization of bacteria in the small intestine, capable of producing symptoms such as abdominal distension, flatulence, pain, diarrhea, or constipation[8]. The diagnosis of SIBO is established by small intestinal aspirate and culture, which is considered the reference method when bacterial growth of 10^3–10^5 colony-forming units per milliliter (CFU/mL) is observed[9]. However, due to its technical complexity, lactulose or glucose breath tests are commonly used; these measure the concentration of exhaled hydrogen (H_2) and methane (CH_4) after ingestion of the substrate[10].

Several studies have found a high frequency of SIBO in patients with IBS, leading to the proposal that its evaluation be included as part of a comprehensive diagnostic approach[11,12]. Among the treatments used, rifaximin (a non-absorbable antibiotic approved by the Food and Drug Administration [FDA]) has shown efficacy in reducing gastrointestinal symptoms and improving quality of life in patients with IBS associated with SIBO[13–15]. Nevertheless, in Latin America there are few studies evaluating the impact of rifaximin on quality of life in patients with IBS and SIBO, particularly in the Colombian population[16]. Therefore, the aim of the present study is to evaluate the impact of rifaximin treatment on quality of life in patients with IBS and SIBO diagnosed by the lactulose breath test.

MATERIALS AND METHODS

Study Type

We conducted a quasi-experimental, prospective, and analytical study at a medium-complexity gastroenterology center in the city of Cartagena, Colombia, between June 2023 and January 2024. Predefined interventions were applied without a comparator group (placebo or control), and the impact of rifaximin treatment on quality of life was evaluated using pre- and post-intervention measurements.

Study Population

Adult patients (18–75 years) seen in outpatient care with a clinical diagnosis of IBS according to the Rome IV criteria and a positive lactulose breath test for SIBO were included. All patients provided written informed consent prior to participation in the study (**Figure 1**).

Inclusion Criteria

- Age between 18 and 75 years.
- Diagnosis of IBS according to Rome IV criteria.
- Positive lactulose breath test for SIBO.
- Signed informed consent.

Exclusion Criteria

- Diagnosis of neurological, psychiatric, or physical conditions that could hinder participation in clinical assessments (renal, cardiac, or respiratory failure; cancer; human immunodeficiency virus [HIV] infection; pregnancy).
- Use of antibiotics or performance of endoscopic procedures within the four weeks prior to the breath test.
- Baseline hydrogen values greater than 10 parts per million (ppm).
- Lack of treatment adherence or loss to follow-up.

Sample Size Justification

Given that the prevalence of SIBO in patients with IBS is estimated to range from 30% to 50%[6], a minimum sample size of 70 patients with confirmed SIBO was estimated, assuming a 95% confidence interval and an expected error of 10% to detect a significant change in the IBS-QoL scale. The final number of included patients (n = 71) met this estimate.

Diagnostic Procedure and Bias Control

Prior to the breath test, patients were instructed to discontinue antibiotics (at least four weeks before); laxatives, probiotics, fiber supplements, and prokinetic agents (72 hours before); and procedures such as colonoscopy during the preceding month. Certain foods (dairy products, fruits, legumes, onion, and garlic) were restricted for 24 hours before the test, and fasting for at least 14 hours was required. Smoking and chewing gum were prohibited for 12 hours prior to the examination.

Breath Test

The test consisted of oral administration of 10 g of lactulose dissolved in 200 mL of water. Measurements of exhaled

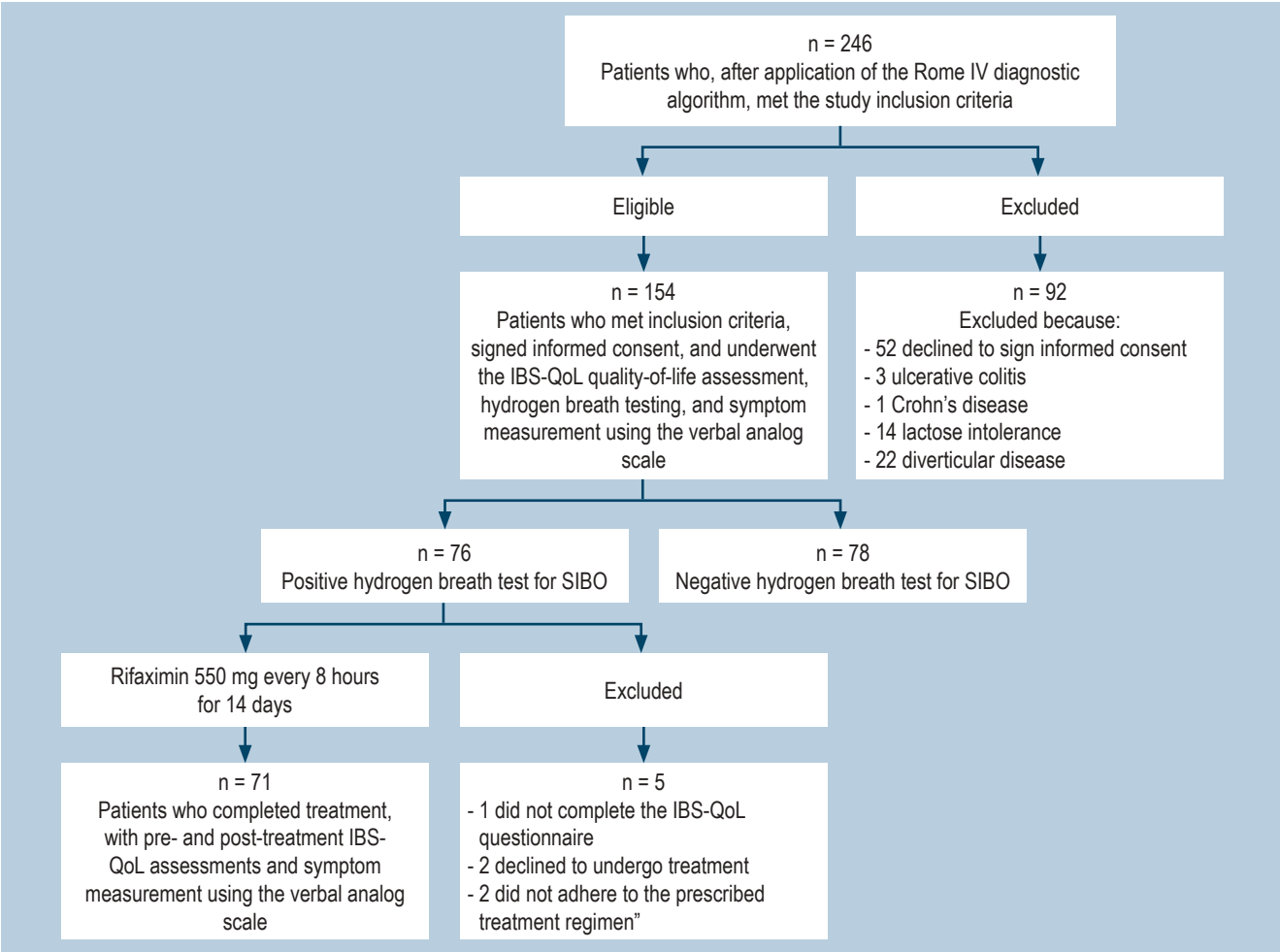


Figure 1. Flow Diagram of Selection and Exclusion of Patients Included in the Study. Author's file.

hydrogen were obtained at 20, 40, 60, 80, 100, 120, 140, 160, and 180 minutes. A test was considered positive if:

- An increase of ≥20 ppm above baseline occurred within the first 80 minutes.
- An elevation of ≥10 ppm was associated with overt clinical symptoms such as pain, abdominal distension, flatulence, defecatory urgency, or bowel movements during the test.

Patients with baseline hydrogen levels >10 ppm were excluded due to the risk of false-positive results.

Intervention

All patients with a positive test were prescribed rifaximin 550 mg every 8 hours for 14 days, in accordance with current FDA recommendations. No concomitant treatments were administered. A post-treatment breath test was not performed; efficacy was assessed based on symptomatic improvement and the quality-of-life score.

Quality-of-life Assessment

The Irritable Bowel Syndrome Quality of Life (IBS-QoL) scale was used. This instrument, validated in Spanish and developed by the MAPI Research Trust group, comprises 34 items across eight dimensions: dysphoria, interference with activities, body image, health worry, food avoidance, social reaction, sexual function, and interpersonal relationships. Scores range from 0 (worst quality of life) to 100 (best quality of life). The scale was administered at baseline (the day of the breath test) and seven days after completion of rifaximin treatment.

Symptom Assessment

Gastrointestinal symptoms (abdominal pain, constipation, diarrhea, stool consistency, abdominal distension, bloating, and flatulence) were assessed using a verbal numerical scale ranging from 1 to 10 points, where 1 represents absence of the symptom and 10 the maximum intensity experienced. Stool consistency was also evaluated on a scale from 1 (very loose) to 10 (very hard) (**Figure 2**).

Statistical Analysis

Quantitative variables were expressed as mean ± standard deviation (SD), and qualitative variables as absolute frequencies and percentages. Paired Student's t tests (pre- vs. post-treatment) and χ^2 tests were used to compare proportions.

To evaluate factors associated with changes in quality of life, simple and multiple linear regression analyses were performed. The dependent variable was the difference between the global pre- and post-treatment scores on the IBS-QoL scale. A p value <0.05 was considered statistically significant. Analyses were conducted using SPSS v15™.

RESULTS

A total of 154 patients with a clinical diagnosis of IBS were evaluated; of these, 76 (49.3%) had a positive breath test for SIBO. Five patients were excluded from the primary analysis: two did not initiate treatment, two did not complete it, and one did not complete the post-treatment questionnaire. The final sample comprised 71 patients.

General Characteristics of the Population

A total of 154 patients with a diagnosis of IBS were included. The mean age was 48.6 years (SD ± 12.4), and 81.8% were women. The most frequent symptoms were abdominal distension (86.4%), abdominal pain (80.5%), flatulence (72.7%), and a sensation of incomplete evacuation (68.8%). Clinical and demographic characteristics are summarized in **Table 1**.

Table 1. Clinical and Demographic Characteristics of Patients with IBS

Variable	Total (%)	Mean ± SD
Age (years)	—	48.6 ± 12.4
Female sex	81.8	—
Abdominal pain	80.5	—
Abdominal distention	86.4	—
Flatulence	72.7	—
Sensation of incomplete evacuation	68.8	—
IBS-D type (diarrhea)	38.3	—
IBS-C type (constipation)	25.9	—
IBS-M type (mixed)	31.1	—
IBS-U type (unclassified)	4.7	—

Author's own research.

Symptoms Associated with the Diagnosis of Small Intestinal Bacterial Overgrowth

Female sex, socioeconomic status, and IBS subtype were not associated with the diagnosis of SIBO. However, the intensity of abdominal distension (7.8 points vs. 6.5 points; $p = 0.005$) and flatulence (7.7 points vs. 6.8 points; $p = 0.049$) was significantly associated with the presence of overgrowth (**Figure 3**).

Changes in quality of life were not associated with the diagnosis of SIBO. Quality-of-life survey results were very similar in both groups (66 points vs. 64.8 points; $p = 0.73$). The food avoidance subscale showed the largest differences between patients with IBS and those with IBS plus SIBO (45.6 points vs. 39.4 points; $p = 0.23$), followed by health worry (55.9 points vs. 51.4 points; $p = 0.28$). The two subscales with the

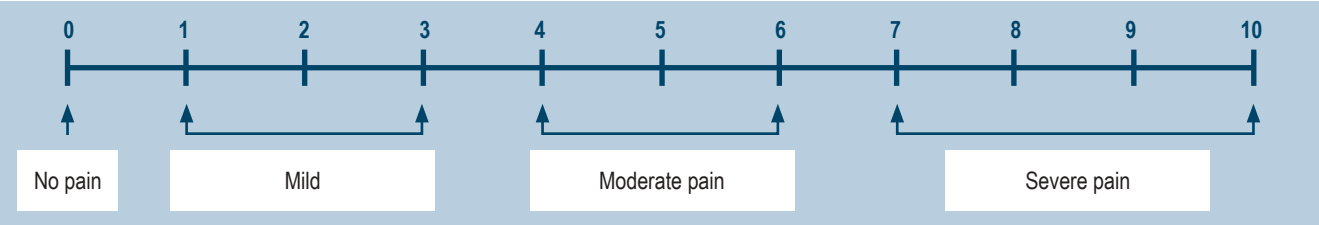


Figure 2. Verbal Numerical Scale. Source: Dolopedia. Unidimensional pain scales [Internet]. Dolopedia; 2024. Available at: https://dolopedia.com/articulo/escalas-unidimensionales-del-dolor[17].

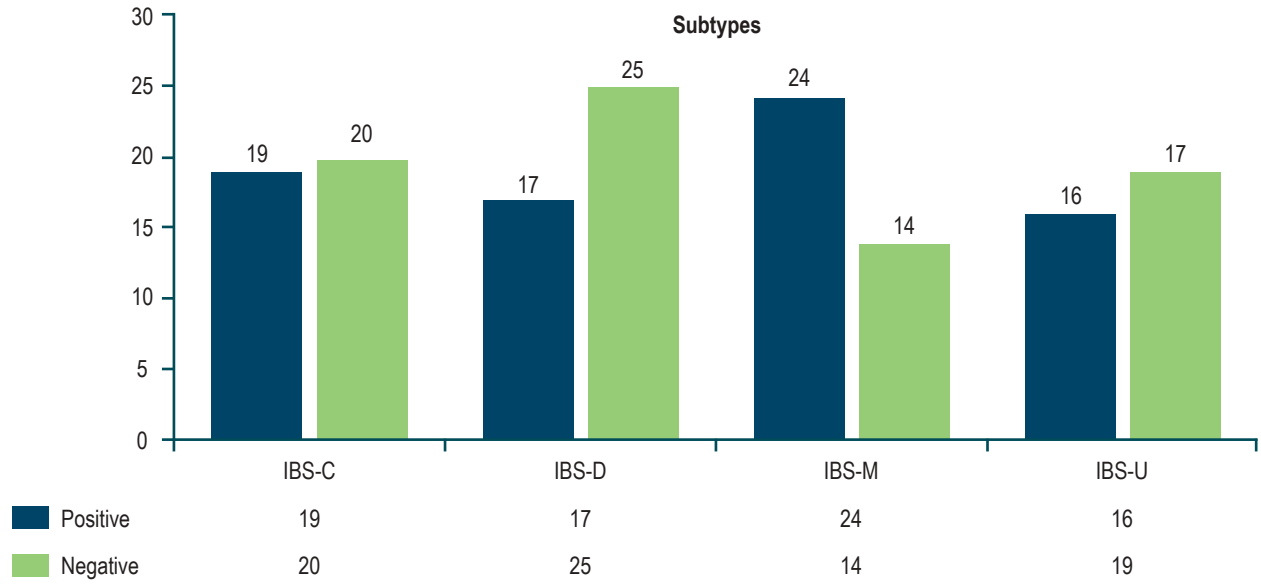


Figure 3. IBS subtype in patients with positive and negative breath tests for SIBO. Author's file.

smallest differences between groups were sexual function (78.04 points vs. 79.2 points; $p = 0.77$) and interpersonal relationships (76.1 points vs. 77.4 points; $p = 0.77$). None of the comparisons reached statistical significance.

Effect of Rifaximin on Quality of Life and Symptom Intensity

A statistically significant improvement ($p < 0.05$) was observed in all symptoms and across all quality-of-life subscales after rifaximin treatment. The symptoms showing the greatest reductions in intensity were abdominal distension (–4.23 points; 95% CI: 3.3–5.09; $p < 0.0001$), bloating (–4.3 points; 95% CI: 3.4–5.1; $p < 0.0001$), and flatulence (–4.26 points; 95% CI: 3.3–5.1; $p < 0.0001$) following completion of treatment (**Table 2**, **Figure 4**).

In the analysis by quality-of-life subscales, a significant improvement ($p < 0.05$) was observed in health worry (+19.9 points; 95% CI: 26.7–13.1; $p = 0.012$), dysphoria (+17.2 points; 95% CI: 22.9–11.6; $p < 0.0001$), food avoi-

Table 2. Comparison of verbal numerical scale and IBS-QoL scores pre- and post-treatment

IBS-QoL Survey	Pre-treatment	Post-treatment	Mean Difference	95% CI	*p*-Value
Interference with activity	66.6 (24.9)	79.9 (18.0)	13.3	19.0 to 7.5	<0.0001
Health worry	50.9 (26.2)	70.8 (21.9)	19.9	26.7 to 13.14	0.012
Social reaction	71.2 (23.4)	87.14 (18.6)	15.9	21.5 to 10.2	<0.0001
Interpersonal relationships	77.11 (26.9)	86.7 (19.4)	9.6	16.06 to 3.1	0.003
Verbal numerical scale					
- Abdominal pain	6 (3.2)	2.9 (2.5)	3.09	2.1 to 4.0	<0.0001
- Constipation	5.7 (3.5)	2.4 (2.3)	3.25	2.33 to 4.1	<0.0001
- Consistency	6.6 (3.0)	4.8 (1.7)	1.87	1.09 to 2.7	<0.0001
- Flatulence	7.6 (2.8)	3.4 (2.6)	4.26	3.3 to 5.1	<0.0001

CI: confidence interval. Author's own research.

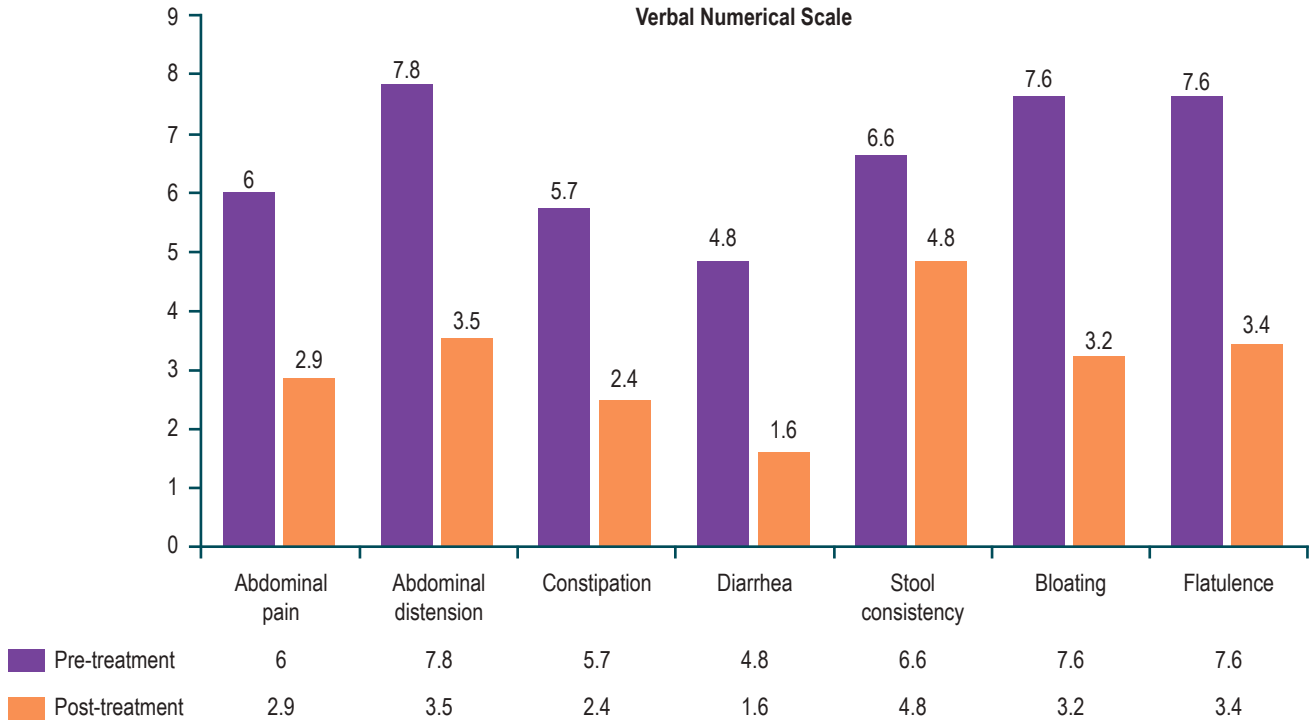


Figure 4. Comparison of gastrointestinal symptom intensity before and after rifaximin treatment according to the verbal numerical scale. Author's file.

dance (+17.0 points; 95% CI: 25.1–8.9; p <0.0001), sexual function (+6.6 points; 95% CI: 13.8–0.4; p = 0.014), and interpersonal relationships (+9.6 points; 95% CI: 16.0–3.1; p = 0.003). The overall quality-of-life assessment showed a mean increase of +15.16 points (95% CI: 20.1–10.3; p <0.0001) in post-treatment results (**Table 3**, **Figure 5**).

Table 3. Univariate analysis of factors associated with changes in quality of life after treatment

Variable	b	95% CI	*p*-Value
Sex	-14.7	-26 to -2.8	0.016
BMI	-0.82	-2.12 to 0.48	0.215
Hypertension	-11.9	-24.02 to 0.12	0.052
Bariatric surgery	5.92	-18.5 to 30.42	0.631
Abdominal pain	1.44	(-0.021 to 2.917)	0.053
Constipation	1.74	(0.39 to 3.084)	0.012
Consistency	1.52	(-0.047 to 3.10)	0.057
Flatulence	0.25	(-1.51 to 2.01)	0.774

Cx: surgery; HTA: arterial hypertension; CI: confidence interval; BMI: body mass index. Author's own research.

Factors Associated with Quality of Life after Treatment

At baseline, the global IBS-QoL survey score was 65.4 ± 22.2 points. The most affected subscales were food avoidance (42.5 points) and health worry (53.7 points), whereas the least affected were sexual function (78.6 points) and interpersonal relationships (76.7 points). These findings reflect a moderate impairment of quality of life prior to treatment.

Although patients with SIBO had lower mean IBS-QoL scores before treatment compared with patients without SIBO, the differences did not reach statistical significance (p >0.05); therefore, no true differences between groups can be established.

After rifaximin treatment, a significant improvement (p <0.05) was observed in the global quality-of-life score and in several subscales. The greatest improvements were recorded in dysphoria (+17.2 points), food avoidance (+17.0 points), health worry (+19.9 points), sexual function (+6.6 points), and interpersonal relationships (+9.6 points). The mean overall improvement was +15.16 points on the IBS-QoL scale.

In the multivariable linear regression analysis, age (b: −0.39; 95% CI: −0.66 to −0.11; p = 0.007), male sex (b: −14.6; 95% CI: −25.4 to −3.8; p = 0.009), and abdominal distension (b: 1.9; 95% CI: 0.16 to 3.6; p = 0.002) were iden-

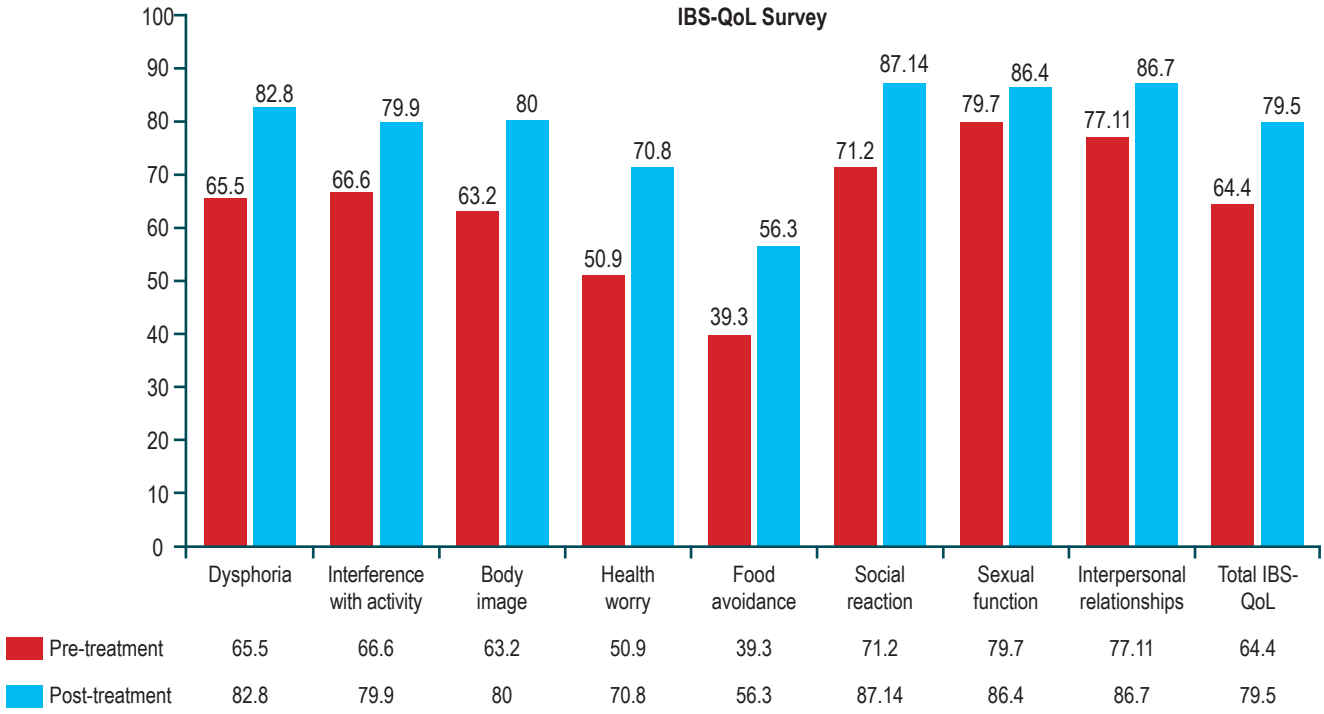


Figure 5. Differences in IBS-QoL quality-of-life scale scores before and after rifaximin treatment. Author's file.

tified as independent predictors of post-treatment quality of life. A total of 26.7% (n = 19) of patients did not respond to treatment or experienced a worsening in quality of life.

DISCUSSION

The World Health Organization (WHO) defines quality of life as an individual's subjective perception of their position in life, considering physical, psychological, and social well-being[18,19]. In the United States, the Bureau of Economic Analysis reported that gastrointestinal diseases such as IBS and SIBO increased their overall medical costs by 104.1% over the past decade, ranking 15th among the costliest conditions, surpassing diseases such as lung cancer, leukemia, or HIV[20].

In our cohort, nearly half of patients with IBS had SIBO, consistent with international studies reporting prevalences between 30% and 60%, regardless of cultural or geographic factors[21]. This similarity supports the hypothesis that SIBO is a condition frequently associated with IBS across different clinical settings. From a pathophysiological standpoint, excessive bacterial growth may produce toxins that increase water secretion, favoring diarrhea; conversely, it may alter motility and slow intestinal transit, resulting in constipation. Shan and colleagues described diarrhea as the predominant SIBO pattern in Eastern populations[8]. In our study, SIBO risk was not associated with any IBS subtype, suggesting that diagnostic evaluation should be actively pursued in all patients, irrespective of clinical classification.

Although variables such as diet or prior antibiotic use were not analyzed, no association was observed between SIBO risk and socioeconomic status, suggesting that factors such as educational level or access to medications may not play a relevant role in its development in this population. Numerous studies have documented a significant reduction in quality of life among patients with IBS, comparable to chronic conditions such as diabetes, hypertension, or kidney disease[18,19,22]. In our study, the most affected subscales were health worry, dysphoria, and food avoidance, likely related to prescribed dietary restrictions (e.g., a low-FODMAP diet)[23]. Consistently, Tuteja and colleagues identified these three dimensions as the most impaired before treatment and those showing the greatest improvement after intervention[16]. The Persian Gulf War veterans clinical trial did not find a significant benefit after rifaximin use[16]; however, lower doses, a small sample size, and a population with potential psychological comorbidities were used, which may explain the differences from our findings.

Analysis of factors associated with quality of life showed that age, male sex, and abdominal distension influenced

treatment response. These findings can be interpreted from behavioral and pathophysiological perspectives: older patients tend to be more concerned about their health, whereas sex-related differences in microbiota composition and treatment adherence may modify clinical response. The absence of a control group represents a relevant limitation due to the risk of selection and confounding biases. Additionally, exclusive use of hydrogen breath testing may have led to underdiagnosis of methane-dependent SIBO; however, previous studies estimate that this subtype accounts for only 14% of patients[21].

Despite these limitations, this study represents the first investigation in Colombia applying Rome IV criteria and the FDA-approved treatment regimen, demonstrating significant improvement in symptoms and quality of life after rifaximin use. Nevertheless, randomized controlled clinical trials are required to confirm these results and to assess the long-term sustainability of the effect.

CONCLUSIONS

This study suggests that patients with irritable bowel syndrome and small intestinal bacterial overgrowth treated with rifaximin (550 mg every 8 hours for 14 days) experience significant improvement in gastrointestinal symptoms and perceived quality of life. The prevalence of SIBO in this cohort was high and consistent with international literature, reinforcing the importance of considering this condition in the diagnostic approach to IBS.

Although the results are promising, methodological limitations—including sample size, absence of a control group, and lack of post-treatment breath testing—preclude establishing firm causal relationships. Therefore, prospective studies and randomized controlled trials are recommended to confirm these findings and to determine the sustained effectiveness of rifaximin treatment.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

Conflict of Interest

We declare that we have no conflicts of interest that could influence or interfere with the content, results, or interpretation of the data presented in this research.

REFERENCES

1. Pontet Y, Olano C. Prevalencia de síndrome de intestino irritable en América Latina. Revista de Gastroenterología del Perú. 2021;41(3):144-149. https://doi.org/10.47892/rgp.2021.413.1154
2. Schmulson MJ, Puentes-Leal GA, Bustos-Fernández L, Francisconi C, Hani A, López-Colombo A, et al. Comparison of the epidemiology of disorders of gut-brain interaction in four Latin American countries: Results of The Rome Foundation Global Epidemiology Study. Neurogastroenterol Motil. 2023;35(6):e14570. https://doi.org/10.1111/nmo.14569
3. Gómez-Álvarez DF, Morales-Vargas JG, Rojas-Medina LM, Mújica-Oviedo SC, Camacho-López PA, Rueda-Jaimes GE. Factores sociosanitarios y prevalencia del síndrome del intestino irritable según los criterios diagnósticos de Roma III en una población general de Colombia. Gastroenterol Hepatol. 2009;32(6):395-400. https://doi.org/10.1016/j.gastrohep.2009.01.177
4. Scarpellini E, Giorgio V, Gabrielli M, Lauritano EC, Pantanella A, Fundarò C, et al. Prevalence of small intestinal bacterial overgrowth in children with irritable bowel syndrome: a case-control study. J Pediatr. 2009;155(3):416-420. https://doi.org/10.1016/j.jpeds.2009.03.033
5. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, et al. Worldwide prevalence and burden of functional gastrointestinal disorders: results of the Rome Foundation Global Study. Gastroenterology. 2021;160(1):99-114.e3. https://doi.org/10.1053/j.gastro.2020.04.014
6. Bourlioux P, Braesco V, Koletzko B, Guarner F. The intestine and its microflora are partners for the protection of the host. Am J Clin Nutr. 2003;78:675-683. https://doi.org/10.1093/ajcn/78.4.675
7. Tojo González R, Suarez Gonzalez A, Rúas Madiedo P, Mancebo Mata A, Pipa Muñiz M, Barreiro Alonso E, et al. Síndrome de intestino irritable: papel de la microbiota y probiótico-terapia. Nutr Hosp. 2015;31(Suppl 1):83-88. https://doi.org/10.3305/nh.2015.31.sup1.8713
8. Shah A, Talley NJ, Jones M, Kendall BJ, Koloski N, Walker MM, et al. Small intestinal bacterial overgrowth in irritable bowel syndrome: a systematic review and meta-analysis of case-control studies. Am J Gastroenterol. 2020;115(2):190-201. https://doi.org/10.14309/ajg.0000000000000504
9. Mishima Y, Ishihara S. Molecular mechanisms of microbiota-mediated pathology in irritable bowel syndrome. Int J

Mol Sci. 2020;21(22):8664. https://doi.org/10.3390/ijms21228664
10. Takakura W, Pimentel M. Small intestinal bacterial overgrowth and irritable bowel syndrome: an update. Front Psychiatry. 2020;11:664. https://doi.org/10.3389/fpsyt.2020.00664
11. Pimentel M, Saad RJ, Long MD, Rao SSC. ACG clinical guideline: small intestinal bacterial overgrowth. Am J Gastroenterol. 2020;115:165-178. https://doi.org/10.14309/ajg.0000000000000501
12. Quera R, Quigley EMM, Madrid AM. Sobrecrecimiento bacteriano intestinal: artículo de revisión. Rev Med Chile. 2005;133:1361-1370. https://doi.org/10.4067/S0034-98872005001100013
13. Blasco-Alonso J, Torcuato Rubio E, Pueyo Agudo E, Polo Hernández FL, Ortiz Pérez P, Martín Masot R, et al. Diagnóstico de sobrecrecimiento bacteriano mediante empleo de prueba de hidrógeno espirado en niños afectos de síndrome de intestino irritable. En: Álvarez Calatayud G, Barros García P, Blanco Rodríguez M, Blasco Alonso J, Bodas Pinedo A, Camarena Grande MC, et al (editores). Libro de Trabajos SEGHNP 2020 [Internet]. Madrid: Ergon; 2020. p. 112 [consultado el 15 de junio de 2024]. Disponible en: https://www.seghnp.org/sites/default/files/2020-09/trabajosSEGHNP2020_0.pdf
14. Giannella RA, Rout WR, Toskes PP. Jejunal brush border injury and impaired sugar and amino acid uptake in the blind loop syndrome. Gastroenterology. 1974;67:965-974. https://doi.org/10.1016/S0016-5085(19)32751-9
15. Avelar-Rodríguez D, Toro-Monjaraz EM, Ramírez-Mayans JA. Sobrecrecimiento bacteriano en el intestino delgado: una causa de dolor abdominal crónico en niños. Bol Med Hosp Infant Mex. 2019;40(2):93-98. https://doi.org/10.18233/APM40No2pp93-981781
16. Tuteja AK, Talley NJ, Stoddard GJ, Verne GN. Double-blind placebo-controlled study of rifaximin and lactulose hydrogen breath test in Gulf War veterans with irritable bowel syndrome. Dig Dis Sci. 2019;64(3):838-845. https://doi.org/10.1007/s10620-018-5344-5
17. Dolopedia. Escalas unidimensionales del dolor [Internet]. Dolopedia; 2024 [consultado el 15 de junio de 2024]. Disponible en: https://dolopedia.com/articulo/escalas-unidimensionales-del-dolor
18. Gómez AJ, Hidalgo P, Alvarado-Bestene J, Rodríguez-Varón A, Cáceres-Méndez EA, Medina M. Impacto en la calidad de vida por la asociación entre trastornos del sueño y síndrome de intestino irritable. Rev Colomb Gastroenterol. 2016;31(1):16-19. https://doi.org/10.22516/25007440.68
19. Castañeda-Sepúlveda R. Irritable bowel syndrome. Med Univ (Méx). 2010;12(46):39-46. https://doi.org/10.1016/S0739-5930(10)79444-7
20. WHOQOL Group. The World Health Organization quality of life assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med. 1995;41(10):1403–1409. https://doi.org/10.1016/0277-9536(95)00112-k
21. Liu ZJ, Wei H, Duan LP, Zhu SW, Zhang L, Wang K. Clinical features of irritable bowel syndrome with small intestinal bacterial overgrowth and a preliminary study of effectiveness of rifaximin. Zhonghua Yi Xue Za Zhi. 2016;96(24):1896-1902. https://doi.org/10.3760/cma.j.issn.0376-2491.2016.24.005.
22. Sánchez JA, Irineo AB, Bernal G. Calidad de vida relacionada con la salud en adultos con síndrome de intestino irritable en un hospital de especialidades de México: estudio transversal. Rev Esp Enferm Dig. 2017;109(4):265-272.
23. Yepes IJ, Múnera MN, Martelo C. Dieta baja en oligosacáridos, disacáridos, monosacáridos y polioles fermentables y calidad de vida en pacientes con síndrome de intestino irritable en Colombia. Biomédica. 2018;38(Suppl 1):54-61.

https://doi.org/10.22516/25007440.1371

Colombian Consensus on the Diagnosis and Management of Eosinophilic Esophagitis in the Pediatric Population: Diagnosis. Part 1

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OPEN ACCESS

Citation:
Vera-Chamorro JF, Zambrano-Pérez CA, Carias-Domínguez AM, Higuera-Carrillo M, Riveros-López JP, García-Paba MB, Peña-Hernández S, Vargas-Sandoval M, Juliao-Baños F, López-Panqueva RP, Triana-Rodríguez GA, Ortiz-Piedrahita C, Chinchilla-Mejía CF, Chapman-Ariza EA, Quintero-Canasto EM, Calderón-Guerrero OG, Puerto-Baracaldo DK, Duarte-Montero D, Vieira MC, Rubinstein E, Vila-Miravet V, Amil-Dias J. Colombian Consensus on the Diagnosis and Management of Eosinophilic Esophagitis in the Pediatric Population: Diagnosis. Part 1. Revista. colomb. Gastroenterol. 2025;40(4):450-462.
https://doi.org/10.22516/25007440.1371

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Received: 26/06/2025
Accepted: 04/11/2025

Abstract

Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated condition characterized by esophageal dysfunction, which may progress to fibrosis or stricture formation without appropriate treatment. **Objective:** To develop evidence-based recommendations through expert consensus for the diagnosis of EoE in individuals younger than 18 years. **Methods:** A multidisciplinary panel of 16 national experts from COLGAHNP—including allergists, pathologists, and adult gastroenterologists—together with four international specialists, formulated 18 clinical questions (8 related to diagnosis and 10 to treatment). A literature search was conducted analyzing clinical practice guidelines, randomized clinical trials, and systematic reviews published over the past decade. Twenty-seven recommendations were developed (12 for diagnosis and 15 for treatment) and submitted for voting using a modified Delphi method across two rounds. The project was sponsored by COLGAHNP. **Results:** All recommendations achieved >90% agreement. EoE should be suspected in patients presenting with esophageal dysfunction and personal or family history of allergic disease. Endoscopy may or may not reveal inflammatory or fibrotic changes (EREFS). At least six esophageal biopsies should be obtained, in addition to initial gastric and duodenal biopsies, given the potential coexistence of other eosinophilic gastrointestinal disorders. Histology typically demonstrates eosinophilic infiltration (≥15 eosinophils per high-power field). Allergy testing should not be routinely used to identify EoE-triggering allergens. A barium esophagram is more sensitive than endoscopy for detecting narrowing or strictures. pH-impedance monitoring, transnasal endoscopy, high-resolution manometry, EndoFLIP, and endoscopic ultrasound have specific indications. **Conclusion:** This consensus provides evidence-based diagnostic recommendations for EoE tailored to patients, families, and healthcare decision-makers within the Colombian and Latin American context.

Keywords

Eosinophilic esophagitis, endoscopy, biopsy, dietary therapy, proton pump inhibitors, budesonide, biologics.

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INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease characterized by intense eosinophilic inflammation associated with esophageal dysfunction, which may progress to tissue remodeling accompanied by subepithelial fibrosis and stricture formation. The estimated incidence ranges from 5 to 10 cases per 100,000 individuals, with a reported prevalence of 0.5–1 per 1,000 inhabitants[1]. Clinical manifestations vary according to age. In children, EoE typically presents with vomiting, heartburn, chest pain, and failure to thrive, whereas in adolescents and adults it is more commonly characterized by dysphagia and food impaction[2]. Colombia is considered a country with a high prevalence of EoE, with reported rates of 18.2 per 1,000 outpatients and 57.7 per 1,000 pediatric patients undergoing endoscopy, ranking as the second highest prevalence in Latin America[3]. According to data collected in 2024 through the REDCap database, 124 patients from nine centers across Colombia were included (male-to-female ratio: 2:1). Age at diagnosis ranged from 3 months to 16 years. The distribution of symptom onset was as follows: <6 months, 17.9%; 6–12 months, 28.2%; and >12 months, 31.6%. The duration of symptoms prior to diagnosis was <1 month in 4.1%, 1–3 months in 15.5%, 3–6 months in 22.7%, and >6 months in 57.7% of cases. Associated factors included a history of atopy—specifically allergic rhinitis (32.9%), asthma (28.2%), food allergy (15.9%), and atopic dermatitis (15.3%)—as well as antibiotic exposure during infancy (41.8%). The most frequent clinical manifestations were abdominal pain (67.7%), nausea (62%), and vomiting (51.2%). Endoscopic findings commonly included longitudinal furrows (76.4%) and whitish exudates (70.5%). The primary treatments administered were proton pump inhibitors (PPIs) in 58.2% of patients, topical corticosteroids in 9.8%, and dupilumab in 0.5%[4]. This consensus is intended for pediatricians, gastroenterologists, allergists, nutritionists, and healthcare payers. Its primary objective is to provide evidence-based recommendations for the diagnosis and management of EoE within the Colombian and broader Latin American context.

METHODOLOGY

A comprehensive literature search was conducted, prioritizing the highest level of available evidence, including clinical practice guidelines (CPGs) assessed using the AGREE II instrument, randomized controlled trials (RCTs), systematic reviews (SRs), and meta-analyses. Searches were performed in PubMed, MEDLINE, Embase, Cochrane Library, and LILACS databases, in both English and Spanish, covering the period from 2014 to 2024. MeSH terms used included *eosinophilic esophagitis, guidelines, pediatric,* and *evidence.* Three clinical practice guidelines were selected as the foundational references for the development of this consensus: two focused on the pediatric population—the guideline jointly issued by the British Society of Gastroenterology (BSG) and the British Society of Pediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN)[5], and the guideline of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)[6]—as well as the Italian consensus on the diagnosis and management of EoE in adults[7]. Additionally, two recent systematic reviews were included: one addressing swallowed topical corticosteroids[8] and another focused on dietary management[9], along with a meta-analysis evaluating pharmacological medical management[10]. These studies were selected based on their methodological rigor and the relevance of their updated evidence.

A multidisciplinary panel comprising 16 experts was convened, including members of the Colombian College of Pediatric Gastroenterology, Hepatology, and Nutrition (COLGAHNP), allergists from the Colombian Association of Allergy, Asthma, and Immunology (ACAAI), national pathologists, adult gastroenterologists from the Colombian Association of Gastroenterology (ACG), and four international experts. The panel formulated 18 clinical questions, eight related to diagnosis and ten related to treatment. Panel members were selected based on their clinical and research expertise in gastroenterology, allergology, and pediatrics, with a minimum of five years of professional practice and affiliations with academic institutions, referral hospitals, and national scientific societies. Four epidemiologists additionally supported the methodological process. All participants conducted a critical appraisal of the available literature to inform the development of the statements and recommendations.

Each statement was accompanied by an assessment of the quality of evidence and the strength of recommendation (strong or weak), following the U.S. Preventive Services Task Force framework (**Table 1**)[11]. A modified Delphi method was applied, consisting of an initial electronic voting round followed by a second hybrid, in-person round. Each recommendation was subjected to voting with three possible responses: disagree, agree, or agree with modifications. Consensus approval required a minimum agreement of 80%, corresponding to a strong recommendation[12]. The response rate was 100% in both rounds. During the first round, agreement exceeding 90% was achieved for all statements. Statements receiving an "agree with modifications" response were discussed collectively, reformulated, and resubmitted for voting during the hybrid meeting until consensus was reached. An update of this consensus is recommended within five years. This

Table 1. Levels of evidence and grades of recommendation

Levels of evidence	
Type I	Evidence obtained from at least one well-designed randomized controlled trial or from a systematic review of randomized clinical trials.
Type II	II-1 Evidence obtained from well-designed prospective controlled studies without randomization. II-2 Evidence obtained from well-designed cohort or case–control observational studies, preferably conducted at multiple centers. II-3 Evidence obtained from case series.
Type III	Opinions of authorities based on clinical experience, expert committee reports, or case reports.
Grades of recommendation	
A	The consensus strongly recommends the intervention. This recommendation is supported by high-quality evidence demonstrating a clear benefit that outweighs potential risks.
B	The consensus recommends routine clinical use of the intervention. This recommendation is supported by moderate-quality evidence demonstrating that the benefits outweigh the risks.
C	The consensus neither recommends for nor against the intervention. No categorical recommendation is made, as the available evidence does not demonstrate a satisfactory risk–benefit relationship. Decisions should be made on a case-by-case basis.
D	The consensus recommends against the intervention or service. This recommendation is supported by at least moderate-quality evidence showing no benefit or indicating that the risks or harms outweigh the benefits.
I	The consensus concludes that the available evidence is insufficient, due to low-quality studies, heterogeneous results, or an inability to determine the balance between risks and benefits.

Adapted from: Harris RP, et al. Am J Prev Med. 2001;20(3 Suppl):21–35[11].

study was sponsored by COLGAHNP, and no conflicts of interest were reported.

DEFINITION OF EOSINOPHILIC ESOPHAGITIS

1. What is the current definition of EoE?

Statement 1

Eosinophilic esophagitis (EoE) is defined as a chronic immune-mediated disease, clinically characterized by esophageal dysfunction and, if left untreated, potentially resulting in fibrosis and stricture formation. Endoscopically, EoE may or may not exhibit signs of inflammation or fibrosis, as assessed by the Endoscopic Reference Score (EREFS). Histologically, it is characterized by esophageal inflammation with eosinophilic infiltration (≥15 eosinophils per high-power field [HPF] or approximately 60 eosinophils/mm^2), along with additional histologic features of esophageal inflammation. EoE may coexist with other eosinophilic gastrointestinal disorders, constituting two associated disease entities. To establish the diagnosis, other causes of esophageal eosinophilia must be excluded. Response to proton pump inhibitors (PPIs) **should not** be considered a diagnostic criterion[5-7,13].

Level of evidence: II-1
Grade of recommendation: A
Level of agreement: 100%

Good Practice Points

The diagnosis of EoE is established by the presence of symptoms of esophageal dysfunction and ≥15 eosinophils per high-power field on esophageal biopsy specimens in at least one histologic sample[13]. Response to PPI therapy is no longer considered a diagnostic criterion and is recommended solely as a tool to guide treatment decisions[13]. Other conditions associated with esophageal eosinophilia but distinct from EoE (non-EoE) must be excluded, including hypereosinophilic syndrome, drug toxicity and hypersensitivity reactions, connective tissue disorders such as Marfan syndrome type II, Netherton syndrome, Loeys–Dietz syndrome, eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome), and graft-versus-host disease[1].

2. What risk factors have been identified as being associated with EoE?

Statement 2

Genetic, gestational, perinatal, and early-life factors have been identified as being associated with the development of EoE. These include maternal use of antibiotics or PPIs, family history of atopy, preterm birth, cesarean delivery, male sex, esophageal atresia, use of PPIs and antibiotics during childhood, the presence of atopic diseases, and autism spectrum disorder. Conversely, *Helicobacter pylori*

infection, pet ownership, and breastfeeding in patients carrying CAPN14 mutations may exert a protective effect. These findings underscore the need for comprehensive and multifactorial approaches to the prevention and management of EoE (**Table 2**)[7,14-35].

Level of evidence: I to II-1
Grade of recommendation: B
Level of agreement: 100%

Good Practice Points

Genetic variants such as CAPN14 and certain genes linked to the 1q21 locus[7,17,18] have been associated with EoE. Environmental factors, including aeroallergens and exposure to pollutants, may contribute to disease relapse. Breastfeeding has demonstrated a protective effect in individuals with genetic susceptibility. The association between EoE and both celiac disease and inflammatory bowel

Table 2. Risk factors associated with eosinophilic esophagitis

Risk factor	OR	Reference
Family history of EoE (first-degree relative)	7.19 (5.65–9.14)	(35)
Family history of EoE (second-degree relative)	1.99 (1.49–2.65)	(35)
CAPN14 mutations	1.98–2.22	(18)
TSLP mutations	1.37, 1.52, 1.85	(18)
Maternal fever	3.18 (1.27–7.98)	(22)
Pregnancy complications	1.4 (1.0–1.9)	(17)
Maternal antibiotic use (increased risk with higher frequency of use)	1.5 (1.2–1.9)	(17)
Maternal proton pump inhibitor use	1.7 (1.0–2.8)	(17)
Preterm birth at 32 weeks	3.2 (1.5–7.1)	(23)
Preterm birth at 33 weeks	3.6 (1.8–7.4)	(23)
Preterm birth at 34 weeks	2.8 (1.7–7.6)	(23)
Cesarean delivery	Ohio: 1.77 (1.01–3.09) Massachusetts: 3.21 (1.2–8.6)	(22)
Neonatal intensive care unit admission	2.8 (1.2–6.6)	(24)
Breastfeeding in patients with CAPN14 polymorphism	0.08 (0.01–0.59)*	(17)
Long-gap esophageal atresia	11.8 (2.5–56.1)	(25)
Allergic rhinitis	5.09 (2.9–8.9)	(26)
Asthma	3.01 (1.9–4.6)	(26)
Food allergy	1.3 (1.2–1.3)	(27)
Celiac disease	0.52 (0.36–0.79)	(28)
Inflammatory bowel disease	7.8 (CD)**, 5.0 (UC)** 11.2 (CD)**, 8.7 (UC)**	(29) (30)
Antibiotic use during childhood	6.0 (1.7–20.8)	(23)
Autism spectrum disorder	3.7 (2.7–5.7)	(31)
Proton pump inhibitor use during childhood	15.9 (9.1–27.7)	(32)
Male sex	2.22 (2.00–2.46)	(33)
Helicobacter pylori infection	0.63 (0.51–0.78)*	(20)
Regions with poorer environmental quality index	1.25 (1.04–1.50)	(34)
Pet ownership	0.58 (0.34–0.97)*	(22)
Achalasia	32.9 (95% CI: 24.8–42.8; $p < 0.001$)***	(19)

* Protective factors for EoE. ** Prevalence ratio (PR). *** Relative risk (RR). CD, Crohn disease; UC, ulcerative colitis; EoE, eosinophilic esophagitis; 95% CI, 95% confidence interval; OR, odds ratio; NICU, neonatal intensive care unit. Table prepared by the authors.

disease suggests potential shared pathogenic mechanisms, although the available evidence remains limited[14-16]. EoE has been described as a cause of achalasia or as a condition associated with achalasia; therefore, exclusion of this diagnosis is strongly emphasized[19]. A potential protective role of *Helicobacter pylori* infection in the development of EoE has been investigated; however, the evidence remains controversial. A systematic review and meta-analysis demonstrated a significant association between *H. pylori* exposure and a reduced likelihood of EoE, with a 37% reduction in risk (odds ratio [OR]: 0.63; 95% confidence interval [CI]: 0.51–0.78)[20,21]. A recent systematic review with meta-analysis has also demonstrated an association between EoE and autism spectrum disorder[31].

CLINICAL MANIFESTATIONS

3. What are the clinical features of patients with EoE?

Statement 3

The symptoms of EoE result from esophageal dysfunction, are nonspecific, and vary in presentation according to patient age and disease phenotype (**Table 3**). Diagnosis requires a high index of suspicion and the active identification of compensatory behaviors, which can be systematically assessed using the IMPACTS acronym (**Table 4**)[36-38].

Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Good Practice Points

EoE should be suspected in any patient presenting with symptoms of esophageal dysfunction and a personal or family history of atopy. Detection depends on the patient's and family's ability to recognize and report symptoms, as well as on a high index of clinical suspicion by the treating physician (**Table 5**)[36,37]. Symptoms do not always correlate with histologic findings and may be explained by fibrotic remodeling or by psychological and food-avoidance behaviors[36].

4. How should symptoms and disease severity in EoE be assessed?

Statement 4

In addition to endoscopic and histologic findings, nutritional status should be assessed, and validated tools should be incorporated to evaluate symptom severity and frequency, such as the Pediatric Eosinophilic Esophagitis Symptom Score (PEESSv2) and the Index of Severity for Eosinophilic Esophagitis (I-SEE), both of which are increasingly used in clinical practice. Periodic assessment of nutritional status and systematic application of these tools allow for longitudinal follow-up and evaluation of clinical response to treatment. Ideally, these instruments should be validated for the Ibero–Latin American context[39-44].

Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Good Practice Points

A linguistically validated Spanish-language tool is available for estimating the severity and frequency of EoE symptoms: PEESSv2, which consists of 20 items assessing four domains—dysphagia, gastroesophageal reflux, nausea or vomiting, and pain[40]. It is available for self-report

Table 3. Clinical presentation of eosinophilic esophagitis according to age and phenotype

Phenotype	Inflammatory	Inflammatory + fibrotic	Fibrotic
Age group	Infant	Preschool/school-age	Adolescent/adult
Symptoms	Feeding difficulties, vomiting and regurgitation, failure to thrive, postprandial cough, abdominal pain	Abdominal, chest, and epigastric pain; GERD-like symptoms; vomiting; dysphagia; food impaction	Dysphagia, food impaction
Endoscopy	Edema, erythema, exudates, linear furrows	Edema, erythema, exudates, non-fixed esophageal rings with longitudinal furrows, strictures	Fixed esophageal rings, strictures
Histology	Mucosal eosinophilia, eosinophilic aggregates, basal zone hyperplasia	Mucosal eosinophilia, eosinophilic aggregates, basal zone hyperplasia, lamina propria fibrosis	Lamina propria fibrosis, basal zone hyperplasia, eosinophilic aggregates, mucosal eosinophilia
Treatment	Medical and dietary	Medical and dietary, esophageal dilation	Esophageal dilation, medical and dietary

Adapted from: Votto M, et al. Front Pediatr. 2022;9:820192[37].

Table 4. Adaptive behaviors that mask symptoms (IMPACTS acronym)

Sigla	Significado	Traducción
I	Imbibe fluids with meals	Drinking liquids with meals
M	Modify food	Modifying food consistency (e.g., cutting into small pieces, pureeing)
P	Prolong meal times	Prolonging meal duration
A	Avoid hard-texture foods	Avoiding hard or solid foods
C	Chew excessively	Excessive chewing
T	Turn away pills and tablets	Refusal of pills or tablets
S	Social avoidance	Reduced social interaction

Adapted from: Hirano I, et al. Gastroenterology. 2020;158(4):840–851[38].

Table 5. Index of Severity for Eosinophilic Esophagitis (I-SEE)

Characteristics	1 point	2 points	4 points	15 points
Symptoms and complications				
Symptoms	Weekly	Daily	Multiple times per day or interfering with social functioning	--
Complications	--	Food impaction requiring emergency department visit or endoscopy (≥18 years)	Food impaction requiring emergency department visit or endoscopy (<18 years) Hospitalization due to esophagitis	Esophageal perforation Malnutrition, failure to thrive Persistent inflammation requiring elemental formula, systemic corticosteroids, or immunomodulators
Inflammatory features				
Endoscopy (edema, furrows, exudates)	Localized	Diffuse	--	--
Histology	15–60 eos/HPF	>60 eos/HPF	--	--
Fibrostenotic features				
Endoscopy (rings, strictures)	Present with easy passage of the endoscope	Present, requiring dilation	--	Endoscope cannot be passed Repeated dilations (≥18 years) At least one dilation (<18 years)
Histology	--	Basal zone hyperplasia or lamina propria fibrosis	--	--

Adapted from: Dellon ES, et al. Gastroenterology. 2022;163(1):59–76[43].

in patients aged 8 to 18 years and for parent-report in patients aged 2 to 18 years[41]. PEESSv2 has been translated and undergone linguistic validation, allowing its use in Spanish; however, cultural validation remains pending[42]. The full version is available for download at: https://eprovide.mapi-trust.org/instruments/pediatric-eosinophilic-esophagitis-symptom-severity-module-version-2.0

The Index of Severity for Eosinophilic Esophagitis (I-SEE) comprises three domains: (1) symptom frequency and presence of complications; (2) inflammatory features, including edema, furrows, or exudates on endoscopy, or marked eosinophilia on biopsy; and (3) fibrostenotic features, either macroscopic (presence of rings or strictures) or microscopic (basal zone hyperplasia or lamina propria fibrosis) (**Table 5**). Based on the total score, disease seve-

rity is classified as inactive (<1), mild (1–6), moderate (7–14), or severe[43]. Higher I-SEE scores (i.e., greater disease severity) have been associated with longer disease duration (8.2 vs. 12.1 years; $p = 0.003$). Additionally, total I-SEE scores have been shown to correlate with genes involved in inflammatory and fibrotic pathways[44].

DIAGNOSIS AND EVALUATION OF THE DISEASE

5. How can the diagnosis of EoE be confirmed by endoscopy?

Statement 5

Esophagogastroduodenoscopy (EGD) should be performed in all patients presenting with symptoms of esophageal dysfunction, such as food impaction and dysphagia (**Tables 3** and **4**), and with a personal or family history of atopy. It is recommended to obtain at least six biopsies in total from the proximal and distal esophagus, even in the absence of macroscopic abnormalities. During the initial endoscopic evaluation, additional biopsies of the stomach and duodenum are advisable to rule out associated eosinophilic gastritis or enteritis. The EoE Endoscopic Reference Score (EREFS) tool should be used to ensure consistent reporting of macroscopic endoscopic findings (**Table 6**)[6,7,38,45-50].

Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Good Practice Points

The use of proton pump inhibitors (PPIs) and corticosteroids may alter eosinophil counts and mask histologic findings; therefore, these medications should be discontinued 3–4 weeks prior to endoscopic evaluation[7]. A minimum of six biopsies is recommended—2 to 4 from the proximal esophagus and 2 to 4 from the distal esophagus and areas of greatest inflammation—even when macroscopic abnormalities are not identified, as 32% to 39% of patients may present with a normal-appearing esophagus, and esophageal eosinophilia exhibits a patchy distribution[45]. Diagnostic sensitivity reaches up to 100% after five biopsies[6,46,47].

The EREFS scoring system allows assessment of macroscopic findings associated with EoE, including inflammatory features such as exudates, edema, and furrows—more frequently observed in young children—and fibrostenotic changes such as rings and strictures, which are typically seen in adolescents and adults (**Table 6**)[38,48]. The presence of eosinophils in other segments of the gastrointestinal tract does not exclude the diagnosis of EoE[6]. Endoscopy plays an important role in the management of esophageal strictures; however, when compared with barium esophagram, it has demonstrated low sensitivity (25%) for their detection[49].

6. What is the role of histology in the diagnosis and follow-up of pediatric patients with EoE?

Statement 6

An intraepithelial eosinophil count of ≥15 eosinophils per high-power field (HPF) (or approximately 60 eosinophils/mm^2) in at least one HPF on esophageal biopsy represents the reference standard, with a sensitivity of 100% and a specificity of 96% for the clinical diagnosis of EoE in patients not previously receiving PPI therapy. Eosinophil activation and other inflammatory features should be assessed through the active use of the Eosinophilic Esophagitis Histology Scoring System (EoEHSS) to provide a more

Table 6. Endoscopic EREFS Score (EoE Endoscopic Reference Score)

	Grade 0	Grade 1	Grade 2	Grade 3
Edema (loss of vascular pattern)	Absent	Loss of clarity or absence of vascular pattern		
Rings (trachealization)	Absent	Mild: ridges	Moderate: distinct rings that do not impair passage of a standard adult diagnostic endoscope (outer diameter 8–9.5 mm)	Severe: rings preventing passage of the endoscope
Exudates (white plaques, exudates)	Absent	Mild: <10% of surface area	Severe: >10% of surface area	
Furrows (vertical lines, grooves)	Absent	Present		
Stricture	Absent	Present		

Adapted from: Hirano I, et al. Gut. 2013;62(4):489–495[50].

comprehensive histologic evaluation of EoE, which has demonstrated a sensitivity of 87%–100% and a specificity of 11%–36%[6,51-53].
Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Good Practice Points

The EoEHSS evaluates eight histologic features: eosinophil density, basal zone hyperplasia, eosinophilic abscesses, eosinophilic surface layering, dilated intercellular spaces, epithelial surface alterations, dyskeratotic epithelial cells, and lamina propria fibrosis. Scoring is based on a 4-point scale, where 0 indicates normal findings or absence of abnormalities and 3 represents the most marked or extensive abnormality[52]. Features may be reported as present or absent; however, a more detailed scoring approach facilitates assessment of improvement, deterioration, and response to therapeutic changes[51]. The EoEHSS is both sensitive and reliable, with scores correlating with clinical symptoms and endoscopic findings[6]. Histopathology reports are encouraged to convert eosinophil counts from eosinophils per HPF to eosinophils per mm^2 or to a standardized HPF, such as that recommended by the Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR)[53], to allow comparability across different microscopes and for collaborative research or consultation: eos/HPF × 1/(HPF area in mm^2) = eos/mm^2[51,52]. An area of 0.27 mm^2 has been used as the standardized HPF area in CEGIR studies[6].

7. What is the role of barium esophagram, esophageal pH/impedance monitoring, unsedated transnasal endoscopy, high-resolution manometry, EndoFLIP, and esophageal endoscopic ultrasound in the diagnosis and evaluation of EoE?

Statement 7.1

In patients with EoE and dysphagia, barium esophagram can identify esophageal narrowing or strictures with greater sensitivity than EGD. Although it is not diagnostic for EoE, it is useful for identifying remodeling sequelae, including ring formation, diffuse mucosal irregularity, fixed strictures, and particularly narrow-caliber esophagus, as well as for excluding other conditions such as achalasia [6,7,49,54,55].
Level of evidence: II-2 and II-3
Grade of recommendation: B
Level of agreement: 100%

Clinical Practice Points

Retrospective studies in patients with EoE and dysphagia have shown that barium esophagram is more sensitive than EGD for identifying esophageal narrowing. It is also useful for assessing alterations in esophageal caliber, detecting strictures, and determining the severity and length of luminal narrowing in areas inaccessible to endoscopy. Although standardized protocols for performing barium esophagram have not been established, reference values for esophageal diameter according to age are available. Its use should be reserved for patients with dysphagia and a reasonable suspicion of stricture in order to avoid unnecessary radiation exposure[6,7,49,54,55].

Statement 7.2

Esophageal pH/impedance monitoring is not recommended for the diagnosis of EoE; however, it may be used in selected cases to identify associated gastroesophageal reflux disease, particularly in symptomatic patients who have achieved histologic remission[6,56,57].
Level of evidence: II-2
Grade of recommendation: C
Level of agreement: 100%

Clinical Practice Points

In esophageal pH/impedance monitoring, increased esophageal acid exposure time and lower baseline impedance have been associated with eosinophilic esophageal infiltration; however, these findings do not correlate with eosinophil counts. Gastroesophageal reflux may play a role in the pathogenesis of EoE, and these tests may help identify patients who require or are more likely to respond to proton pump inhibitor (PPI) therapy. Recent studies in adults suggest that pH/impedance monitoring may serve as a predictive tool for therapeutic response to PPIs[6,56,57].

Statement 7.3

Unsedated transnasal endoscopy is an alternative method for evaluating the esophageal mucosa that reduces costs, procedure time (<2 hours), and risks associated with EGD performed under anesthesiologist-assisted anesthesia. This technique allows assessment of endoscopic findings using a small-caliber endoscope (1.2–2 mm working channel), including EREFS scoring, and permits the acquisition of adequate esophageal biopsies. However, it is operator-dependent[58.59].
Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Clinical Practice Points

Unsedated transnasal endoscopy may serve as an alternative method for long-term follow-up, as it does not require anesthesia, is shorter in duration, more cost-effective, and associated with fewer adverse effects, with visual and his-

tologic results comparable to those of conventional endoscopy. Nevertheless, esophageal visualization is more challenging, and examination of the stomach and duodenum is not feasible; therefore, it is generally used exclusively for esophageal biopsy acquisition. Its use is considered necessary in clinical trials[58,59].

Statement 7.4

High-resolution manometry is a diagnostic tool that allows evaluation of esophageal body motility and function. Its use is recommended in patients with EoE who have persistent dysphagia despite histologic remission and no evidence of fibrostenotic disease or strictures, as esophageal hypomotility patterns—including ineffective esophageal motility, aperistalsis, and frank achalasia—have been described in this population[60].

Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Clinical Practice Points

High-resolution manometry plays a crucial role in patients who remain symptomatic despite adequate control of EoE, as it identifies esophageal motor abnormalities that may require alternative therapeutic approaches. Additionally, high-resolution manometry may increase clinical suspicion of EoE in patients with previously negative endoscopic findings, prompting repeat endoscopy with esophageal biopsies[60].

Statement 7.5

The functional luminal imaging probe (EndoFLIP) is a complementary tool used during endoscopy that allows assessment of esophageal distensibility. A lower distensibility index (DI) measured by EndoFLIP enables differentiation of the fibrostenotic phenotype of EoE from the inflammatory phenotype, although it does not correlate with eosinophil counts[6,61].

Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Clinical Practice Points

EndoFLIP has been evaluated in prospective studies involving patients with a distensibility index <4.5 mm^2/mmHg, where it has been shown to predict ring development within the EREFS classification, abnormal contractility patterns, and ring severity. Furthermore, it enables detection of structural and functional esophageal changes not visible with other diagnostic modalities, such as food impaction[6,61].

Statement 7.6

Esophageal endoscopic ultrasound represents a promising alternative for evaluating pathologic findings and sequelae of EoE using a standard radial endoscope. However, it is not useful for the diagnosis of EoE. Its most relevant role may be the early identification of fibrostenotic phenotypes, although additional studies are required before its routine use can be recommended[6,62-64].

Level of evidence: II-2
Grade of recommendation: B
Level of agreement: 100%

Clinical Practice Points

Ultrasound measurement of the distal esophageal muscle layer and total distal esophageal wall thickness has demonstrated a significant correlation with the EREFS endoscopic score; however, experience in pediatric populations remains limited. In the future, this technique may be useful for assessing treatment effectiveness and phenotype identification when combined with fine-needle biopsy. In adults, distal esophageal wall thickness has been identified as an important factor associated with symptom presence, suggesting that the submucosal layer is the initial site of inflammatory involvement. Regarding cutoff values, thresholds of 2.3 mm for the distance from the mucosal surface to the muscular layer and 3.13 mm for total esophageal wall thickness have been described. In pediatric patients, a case–control study demonstrated significant differences in total esophageal wall thickness between patients with EoE and controls (2.8 mm vs. 2.1 mm; $p = 0.043$), as well as increased combined mucosal and submucosal thickness (1.6 mm vs. 1.1 mm; $p = 0.001$) and muscularis propria thickness (1.2 mm vs. 1.0 mm; $p = 0.043$). Limitations included the need for sedation, lack of equipment appropriately sized for pediatric patients, and the absence of validated standards for measuring esophageal wall thickness and its layers[6,62-64].

8. What is the role of allergy testing in the diagnosis and evaluation of EoE?

Statement 8

Allergy testing—including serum-specific IgE, skin prick testing, and atopic patch testing for foods—should not be used to identify EoE-triggering allergens. Their primary value lies in identifying patients sensitized to foods and those with immediate IgE-mediated hypersensitivity, in order to ensure safe food reintroduction following elimination diets[6,65-67].

Level of evidence: I
Grade of recommendation: C
Level of agreement: 100%

Good Practice Points

Skin testing, food-specific IgE measurements, and atopic patch testing have limited value in identifying triggering allergens, with a positive predictive value below 50%, according to a meta-analysis[6,65]. These tests have demonstrated utility in guiding elimination diets, achieving an effectiveness of 45.7% in children; when all three tests (serum-specific IgE, skin prick testing, and patch testing) are combined, effectiveness increases to 52.7%[66]. They may also identify sensitized patients at risk of immediate hypersensitivity reactions during food reintroduction (6), as well as associations with other allergic comorbidities such as asthma, rhinitis, conjunctivitis, urticaria, and dermatitis[66]. Serum concentrations of food-specific IgG4 may have potential as a noninvasive biomarker, although further studies are required[67].

REFERENCES

1. Dellon ES, Hirano I. Epidemiology and Natural History of Eosinophilic Esophagitis. Gastroenterology. 2018;154(2):319-332.e3. https://doi.org/10.1053/j.gastro.2017.06.067
2. García-Compeán D, González-González JA, González-Moreno EI, Maldonado-Garza HJ. Eosinophilic esophagitis. The North against the South? A bio-economic-social mechanistic approach and clinical implications. Rev Gastroenterol Mex. 2017;82(4):328-36. https://doi.org/10.1016/j.rgmxen.2017.07.005
3. Pierre R, Vieira M, Vázquez R, Ninomiya I, Messere G, Daza W, et al. Prevalencia de esofagitis eosinofílica: estudio multicéntrico en población pediátrica evaluada en 36 centros de gastroenterología de América Latina. Rev Gastroenterol México. 2019;84(4):427-33. https://doi.org/10.1016/j.rgmx.2018.08.001
4. Higuera M, González N, Rivera J, Vera-Chamorro J, Ortiz C, Carias A, et al. Colombian Registry On Clinical, Endoscopic Features, and Treatment of Eosinophilic Esophagitisin Pediatrics. JPGN Reports. 2024;5(S):S94.
5. Dhar A, Haboubi HN, Attwood SE, Auth MKH, Dunn JM, Sweis R, et al. British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. Gut. 2022;71(8):1459-1487. https://doi.org/10.1136/gutjnl-2022-327326
6. Amil-Dias J, Oliva S, Papadopoulou A, Thomson M, Gutiérrez-Junquera C, Kalach N, et al. Diagnosis and management of eosinophilic esophagitis in children: An update from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). J Pediatr Gastroenterol Nutr. 2024;79(2):394-437. https://doi.org/10.1002/jpn3.12188
7. de Bortoli N, Visaggi P, Penagini R, Annibale B, Baiano Svizzero F, Barbara G, et al. The 1st EoETALY Consensus on the Diagnosis and Management of Eosinophilic Esophagitis - Definition, Clinical Presentation and Diagnosis. Dig Liver Dis. 2024;56(6):951-63. https://doi.org/10.1016/j.dld.2024.02.005
8. Chan J, Flynn DM, Gordon M, Parmar R, Moolenschot K, Jackman L, et al. Swallowed topical steroid therapy for eosinophilic oesophagitis in children: practical, evidence-based guidance by the BSPGHAN Eosinophilic Oesophagitis Working Group. BMJ Paediatr Open. 2024;8(1):e002467-e002467. https://doi.org/10.1136/bmjpo-2023-002467
9. Arias Á, Tejera-Muñoz A, Gutiérrez-Ramírez L, Molina-Infante J, Lucendo AJ. Efficacy of Dietary Therapy for Eosinophilic Esophagitis in Children and Adults: An Updated Systematic Review and Meta-Analysis. Nutrients. 2024;16(14):2231. https://doi.org/10.3390/nu16142231
10. Franciosi JP, Gordon M, Sinopoulou V, Dellon ES, Gupta SK, Reed CC, et al. Medical treatment of eosinophilic esophagitis. Cochrane Database Syst Rev. 2023;7(7):CD004065. https://doi.org/10.1002/14651858.CD004065.pub4
11. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al. Current methods of the U.S. preventive services task force: A review of the process. Am J Prev Med. 2001;20(3 Suppl):21-35. https://doi.org/10.1016/S0749-3797(01)00261-6
12. Harris PR, Calderón-Guerrero OG, Vera-Chamorro JF, Lucero Y, Vásquez M, Kazuo Ogata S, et al. Adaptación a la realidad de Latinoamérica de la Guía Clínica NASPGHAN/ESPGHAN 2016 sobre Diagnóstico, Prevención y Tratamiento de Infección por Helicobacter pylori en Pediatría. Rev Chil Pediatría. 2020;91(5):809-27. https://doi.org/10.32641/rchped.v91i5.2579
13. Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. Gastroenterology. 2018;155(4):1022-1033.e10. https://doi.org/10.1053/j.gastro.2018.07.009
14. Litosh VA, Rochman M, Rymer JK, Porollo A, Kottyan LC, Rothenberg ME. Calpain-14 and its association with eosinophilic esophagitis. J Allergy Clin Immunol. 2017;139(6):1762-1771.e7. https://doi.org/10.1016/j.jaci.2016.09.027
15. Arias Á, Lucendo AJ. Epidemiology and risk factors for eosinophilic esophagitis: lessons for clinicians. Expert Rev Gastroenterol Hepatol. 2020;14(11):1069-82. https://doi.org/10.1080/17474124.2020.1806054

16. Shaheen NJ, Mukkada V, Eichinger CS, Schofield H, Todorova L, Falk GW. Natural history of eosinophilic esophagitis: a systematic review of epidemiology and disease course. Dis esophagus. 2018;31(8):doy015. https://doi.org/10.1093/dote/doy015
17. Chang JW, Jensen ET. Epidemiologic and Clinical Clues to the Etiology of Eosinophilic Esophagitis. Immunol Allergy Clin North Am. 2024;44(2):145-55. https://doi.org/10.1016/j.iac.2023.12.003
18. Kottyan LC, Parameswaran S, Weirauch MT, Rothenberg ME, Martin LJ. The Genetic Etiology of Eosinophilic Esophagitis. J Allergy Clin Immunol. 2020;145(1):9-15. https://doi.org/10.1016/j.jaci.2019.11.013
19. Reddy CA, Allen-Brady K, Uchida AM, Peterson KA, Hoffman AM, Souza RF, et al. Achalasia is Strongly Associated With Eosinophilic Esophagitis and Other Allergic Disorders. Clin Gastroenterol Hepatol. 2024;22(1):34-41.e2. https://doi.org/10.1016/j.cgh.2023.06.013
20. Shah SC, Tepler A, Peek RM, Colombel JF, Hirano I, Narula N. Association Between Helicobacter pylori Exposure and Decreased Odds of Eosinophilic Esophagitis-A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2019;17(11):2185-2198.e3. https://doi.org/10.1016/j.cgh.2019.01.013
21. Homan M, Jones NL, Bontems P, Carroll MW, Czinn SJ, Gold BD, et al. Updated joint ESPGHAN/NASPGHAN guidelines for management of Helicobacter pylori infection in children and adolescents (2023). J Pediatr Gastroenterol Nutr. 2024;79(3):758-85. https://doi.org/10.1002/jpn3.12314
22. Jensen ET, Kuhl JT, Martin LJ, Rothenberg ME, Dellon ES. Prenatal, intrapartum, and postnatal factors are associated with pediatric eosinophilic esophagitis. J Allergy Clin Immunol. 2018;141(1):214-22. https://doi.org/10.1016/j.jaci.2017.05.018
23. Jensen ET, Kappelman MD, Kim HP, Ringel-Kulka T, Dellon ES. Early life exposures as risk factors for pediatric eosinophilic esophagitis. J Pediatr Gastroenterol Nutr. 2013;57(1):67-71. https://doi.org/10.1097/MPG.0b013e318290d15a
24. Kurt G, Svane HML, Erichsen R, Heide-Jørgensen U, Sørensen HT, Dellon ES, et al. Prenatal, Intrapartum, and Neonatal Factors Increase the Risk of Eosinophilic Esophagitis. Am J Gastroenterol. 2023;118(9):1558-65. https://doi.org/10.14309/ajg.0000000000002303
25. Dhaliwal J, Tobias V, Sugo E, Varjavandi V, Lemberg D, Day A, et al. Eosinophilic esophagitis in children with esophageal atresia. Dis esophagus Off J Int Soc Dis Esophagus. 2014;27(4):340-7. https://doi.org/10.1111/dote.12119
26. González-Cervera J, Arias Á, Redondo-González O, Cano-Mollinedo MM, Terreehorst I, Lucendo AJ. Association between atopic manifestations and eosinophilic esophagitis: A systematic review and meta-analysis. Ann Allergy, Asthma Immunol. 2017;118(5):582-590.e2. https://doi.org/10.1016/j.anai.2017.02.006
27. Guarnieri KM, Saba NK, Schwartz JT, Devonshire AL, Bufford J, Casale TB, et al. Food Allergy Characteristics Associated With Coexisting Eosinophilic Esophagitis in FARE Registry Participants. J Allergy Clin Immunol Pract. 2023;11(5):1509-1521.e6. https://doi.org/10.1016/j.jaip.2023.02.008
28. Hommeida S, Alsawas M, Murad MH, Katzka DA, Grothe RM, Absah I. The Association Between Celiac Disease and Eosinophilic Esophagitis: Mayo Experience and Meta-analysis of the Literature. J Pediatr Gastroenterol Nutr. 2017;65(1):58-63. https://doi.org/10.1097/MPG.0000000000001499
29. Limketkai BN, Shah SC, Hirano I, Bellaguarda E, Colombel JF. Epidemiology and implications of concurrent diagnosis of eosinophilic oesophagitis and IBD based on a prospective population-based analysis. Gut. 2019;68(12):2152-60. https://doi.org/10.1136/gutjnl-2018-318074
30. Malik A, Liu BD, Zhu L, Kaelber D, Song G. A Comprehensive Global Population-Based Analysis on the Coexistence of Eosinophilic Esophagitis and Inflammatory Bowel Disease. Dig Dis Sci. 2024;69(3):892-900. https://doi.org/10.1007/s10620-024-08283-2
31. Lima RV, Muniz MCR, Barroso LL, Pinheiro MCA, Matos YMT, Nogueira SBR, et al. Autism in patients with eosinophilic gastrointestinal disease: A systematic review with meta-analysis. Pediatr Allergy Immunol. 2024;35(4): e14122. https://doi.org/10.1111/pai.14122
32. Jensen ET, Svane HM, Erichsen R, Kurt G, Heide-Jorgensen U, Sorensen HT, et al. Maternal and Infant Antibiotic and Acid Suppressant Use and Risk of Eosinophilic Esophagitis. JAMA Pediatr. 2023;177(12):1285-93. https://doi.org/10.1001/jamapediatrics.2023.4609
33. Navarro P, Arias Á, Arias-González L, Laserna-Mendieta EJ, Ruiz-Ponce M, Lucendo AJ. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. Aliment Pharmacol Ther. 2019;49(9):1116-25. https://doi.org/10.1111/apt.15231
34. Nance D, Rappazzo KM, Jensen ET, Hoffman K, Cotton CC, Krajewski AK, et al. Increased risk of eosinophilic esophagitis with poor environmental quality as measured by the Environmental Quality Index. Dis Esophagus. 2021;34(12):1-8. https://doi.org/10.1093/dote/doab041
35. Allen-Brady K, Firszt R, Fang JC, Wong J, Smith KR, Peterson KA. Population-based familial aggregation of eosinophilic esophagitis suggests a genetic contribution. J Allergy Clin Immunol. 2017;140(4):1138-43. https://doi.org/10.1016/j.jaci.2016.12.979
36. Matteis A De, Pagliaro G, Corleto VD, Pacchiarotti C, Giulio E Di, Villa MP, et al. Eosinophilic Esophagitis in Children: Clinical Findings and Diagnostic Approach. Curr

Pediatr Rev. 2020;16(3):206-214. https://doi.org/10.2174/1573396315666191004110549
37. Votto M, De Filippo M, Lenti MV, Rossi CM, Di Sabatino A, Marseglia GL, et al. Diet Therapy in Eosinophilic Esophagitis. Focus on a Personalized Approach. Front Pediatr. 2022;9:820192. https://doi.org/10.3389/fped.2021.820192
38. Hirano I, Furuta GT. Approaches and Challenges to Management of Pediatric and Adult Patients With Eosinophilic Esophagitis. Gastroenterology. 2020;158(4):840-51. https://doi.org/10.1053/j.gastro.2019.09.052
39. Martin LJ, Zhang X, Chehade M, Davis CM, Dellon ES, Falk GW, et al. Long-term durability between parent and child patient-reported outcomes in eosinophilic esophagitis. J Allergy Clin Immunol. 2024;154(5):1232-1240.e12. https://doi.org/10.1016/j.jaci.2024.07.011
40. Franciosi JP, Hommel KA, DeBrosse CW, Greenberg AB, Greenler AJ, Abonia JP, et al. Development of a validated patient-reported symptom metric for pediatric eosinophilic esophagitis: qualitative methods. BMC Gastroenterol. 2011;11:126. https://doi.org/10.1186/1471-230X-11-126
41. Martin LJ, Franciosi JP, Collins MH, Abonia JP, Lee JJ, Hommel KA, et al. Pediatric Eosinophilic Esophagitis Symptom Scores (PEESS® v2.0) identify histologic and molecular correlates of the key clinical features of disease. J Allergy Clin Immunol. 2015;135(6):1519-28.e8. https://doi.org/10.1016/j.jaci.2015.03.004
42. Franciosi JP. Pediatric Eosinophilic Esophagitis Symptom Severity Module, version 2.0 distributed by Mapi Research Trust [Internet]. ePROVIDE; 2025 [consultado el 24 de noviembre de 2024]. Disponible en: https://eprovide.mapitrust.org/instruments/pediatric-eosinophilic-esophagitis-symptom-severity-module-version-2.0
43. Dellon ES, Khoury P, Muir AB, Liacouras CA, Safroneeva E, Atkins D, et al. A Clinical Severity Index for Eosinophilic Esophagitis: Development, Consensus, and Future Directions. Gastroenterology. 2022;163(1):59-76. https://doi.org/10.1053/j.gastro.2022.03.025
44. Sato H, Dellon ES, Aceves SS, Arva NC, Chehade M, Collins MH, et al. Clinical and molecular correlates of the Index of Severity for Eosinophilic Esophagitis. J Allergy Clin Immunol. 2024;154(2):375-386.e4. https://doi.org/10.1016/j.jaci.2024.04.025
45. Zambrano LFJ, Arroyave-Benavides J, Jiménez-Uribe AM, Vera-Chamorro JF, Zambrano-Pérez CA, López-Panqueva R del P. Caracterización clínico-patológica de la esofagitis eosinofílica en niños y adolescentes en el Hospital Universitario Fundación Santa Fe de Bogotá. Rev Colomb Gastroenterol. 2019;34(1):23-30. https://doi.org/10.22516/25007440.264
46. Aceves SS, Alexander JA, Baron TH, Bredenoord AJ, Day L, Dellon ES, et al. Endoscopic approach to eosinophilic esophagitis: American Society for Gastrointestinal Endoscopy Consensus Conference. Gastrointest Endosc. 2022;96(4):576-592.e1. https://doi.org/10.1016/j.gie.2022.05.013
47. Nielsen JA, Lager DJ, Lewin M, Rendon G, Roberts CA. The optimal number of biopsy fragments to establish a morphologic diagnosis of eosinophilic esophagitis. Am J Gastroenterol. 2014;109(4):515-20. https://doi.org/10.1038/ajg.2013.463
48. Schoepfer AM, Safroneeva E, Peterson K. Endoscopic Features of Eosinophilic Esophagitis. Immunol Allergy Clin North Am. 2024;44(2):197-204. https://doi.org/10.1016/j.iac.2023.12.007
49. Gentile N, Katzka D, Ravi K, Trenkner S, Enders F, Killian J, et al. Oesophageal narrowing is common and frequently underappreciated at endoscopy in patients with oesophageal eosinophilia. Aliment Pharmacol Ther. 2014;40(11-12):1333-40. https://doi.org/10.1111/apt.12977
50. Hirano I, Moy N, Heckman MG, Thomas CS, Gonsalves N, Achem SR. Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system. Gut. 2013;62(4):489-95. https://doi.org/10.1136/gutjnl-2011-301817
51. Collins MH, Martin LJ, Alexander ES, Todd Boyd J, Sheridan R, He H, et al. Newly developed and validated eosinophilic esophagitis histology scoring system and evidence that it outperforms peak eosinophil count for disease diagnosis and monitoring. Dis Esophagus. 2017;30(3):1-8. https://doi.org/10.1111/dote.12470
52. Collins MH, Arva NC, Bernieh A, Lopez-Nunez O, Pletneva M, Yang GY. Histopathology of Eosinophilic Esophagitis. Immunol Allergy Clin North Am. 2024;44(2):205-21. https://doi.org/10.1016/j.iac.2023.12.008
53. Gupta SK, Falk GW, Aceves SS, Chehade M, Collins MH, Dellon ES, et al. Consortium of Eosinophilic Gastrointestinal Disease Researchers: Advancing the Field of Eosinophilic GI Disorders Through Collaboration. Gastroenterology. 2019;156(4):838-42. https://doi.org/10.1053/j.gastro.2018.10.057
54. Menard-Katcher C, Swerdlow MP, Mehta P, Furuta GT, Fenton LZ. Contribution of Esophagram to the Evaluation of Complicated Pediatric Eosinophilic Esophagitis. J Pediatr Gastroenterol Nutr. 2015;61(5):541-6. https://doi.org/10.1097/MPG.0000000000000849
55. Shahein AR, Krasaelap A, Ng K, Bitton S, Khan M, Manfredi MA, et al. Esophageal Dilation in Children: A State of the Art Review. Vol. 76, Journal of Pediatric Gastroenterology and Nutrition. Lippincott Williams and Wilkins; 2023. p. 1-8. https://doi.org/10.1097/MPG.0000000000003614
56. Eldredge JA, Omari TI, Moore DJ. Pediatric Eosinophilic Esophagitis is Associated With Low Baseline Impedance. J Pediatr Gastroenterol Nutr. 2022;74(5):621-5. https://doi.org/10.1097/MPG.0000000000003396
57. Frazzoni M, Frazzoni L, De Bortoli N, Russo S, Tolone S, Arsiè E, et al. Response of eosinophilic oesophagitis to proton pump inhibitors is associated with impedance-pH para-

meters implying anti-reflux mechanism of action. Aliment Pharmacol Ther. 2021;53(11):1183-9. https://doi.org/10.1111/apt.16371
58. Shaul E, Kennedy KV, Spergel ZC, Daneshdoost S, Mahon M, Thanawala S, et al. Endoscopic and histologic utility of transnasal endoscopy in pediatric eosinophilic esophagitis. J Pediatr Gastroenterol Nutr. 2024;78(5):1155-60. https://doi.org/10.1002/jpn3.12170
59. Nguyen N, Lavery WJ, Capocelli KE, Smith C, DeBoer EM, Deterding R, et al. Transnasal Endoscopy in Unsedated Children With Eosinophilic Esophagitis Using Virtual Reality Video Goggles. Clin Gastroenterol Hepatol. 2019;17(12):2455-2462. https://doi.org/10.1016/j.cgh.2019.01.023
60. Abulawi A, Liu J, Philip S, Josephson M, Abdelwahab H, Feustel PJ, et al. High-Resolution Esophageal Manometric Features in Eosinophilic Esophagitis Patients: A Retrospective Study. Gastro hep Adv. 2022;1(5):703-8. https://doi.org/10.1016/j.gastha.2022.04.020
61. Hoffmann NV, Keeley K, Wechsler JB. Esophageal Distensibility Defines Fibrostenotic Severity in Pediatric Eosinophilic Esophagitis. Clin Gastroenterol Hepatol. 2023;21(5):1188-1197.e4. https://doi.org/10.1016/j.cgh.2022.08.044
62. Ferrelli RS, Machado RS, Ogata SK. Oesophageal wall thickness assessment at endoscopic ultrasound in children and adolescents with eosinophilic oesophagitis: a case-control study. J Ultrasound. 2023;26(4):785-91. https://doi.org/10.1007/s40477-022-00742-8
63. Pytrus T, Akutko K, Kofla-Dłubacz A, Stawarski A. Endoscopic Ultrasonography in Children with Eosinophilic Esophagitis-A Review. Pediatr Rep. 2022;14(1):13-9. https://doi.org/10.3390/pediatric14010003
64. Suzuki Y, Ochiai Y, Hosoi A, Okamura T, Hayasaka J, Mitsunaga Y, et al. Mucosal and Submucosal Thickening of Esophageal Wall Is a Promising Factor in the Development of Symptoms in Eosinophilic Esophagitis. Gut Liver. 2024;18(1):50-9. https://doi.org/10.5009/gnl220490
65. Lucendo AJ. Meta-Analysis-Based Guidance for Dietary Management in Eosinophilic Esophagitis. Curr Gastroenterol Rep. 2015;17(10):464. https://doi.org/10.1007/s11894-015-0464-y
66. Pitsios C, Vassilopoulou E, Pantavou K, Terreehorst I, Nowak-Wegzryn A, Cianferoni A, et al. Allergy-Test-Based Elimination Diets for the Treatment of Eosinophilic Esophagitis: A Systematic Review of Their Efficacy. J Clin Med. 2022;11(19):5631. https://doi.org/10.3390/jcm11195631
67. Lim AHW, Ngoi B, Perkins GB, Wong S, Whitelock G, Hurtado P, et al. Outcomes of Serum Food-Specific Immunoglobulin G 4 to Guide Elimination Diet in Patients With Eosinophilic Esophagitis. Am J Gastroenterol. 2024;119(6):1066-73. https://doi.org/10.14309/ajg.0000000000002678

https://doi.org/10.22516/25007440.1399

Review article

Gastric Cancer: Detection and Prevention

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OPEN ACCESS

Citation:
Oliveros-Wilches R, Facundo-Navia H, Pinilla-Morales R, Bonilla A, Aguirre G. Gastric Cancer: Detection and Prevention. Revista. colomb. Gastroenterol. 2025;40(4):463-471.
https://doi.org/10.22516/25007440.1399

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Received: 20/06/2025
Accepted: 15/12/2025

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Abstract

Models for both primary and secondary prevention of gastric cancer have been proposed. However, at least in Western countries, these strategies have not been widely implemented at a scale sufficient to achieve the anticipated public health impact. This article offers a reflective overview of the disease's natural history, primary and secondary prevention concepts, risk-stratification strategies, and screening approaches, with particular emphasis on endoscopy and eradication of *Helicobacter pylori.* The article also discusses considerations for regions with intermediate incidence rates. Several of these strategies have been successfully adopted in other parts of the world as global prevention measures aimed at reducing the current and future burden of gastric cancer.

Keywords

Gastric cancer, screening, early detection, disease prevention, *Helicobacter pylori*, risk factors.

INTRODUCTION

Gastric cancer (GC) is a public health problem because its morbidity and mortality rates remain very high and continue to rise worldwide. Prevention is the key to reducing its incidence and mortality[1]. By 2022, gastric cancer was the fifth most common cancer globally and the fifth leading cause of cancer-related death, with 968,350 new cases and 659,853 related deaths, respectively[2].

In Colombia, according to Globocan 2022, it is the fourth most common cancer in men and women combined, the third in men, the fifth in women, and the leading cause of cancer-related mortality in men. Gastric cancer risk is defined based on the age-standardized annual incidence rate. A region is considered high risk when the annual incidence exceeds 20 cases per 100,000 inhabitants, intermediate risk when incidence ranges between 10 and 20 cases per 100,000 inhabitants, and low risk when it is <10 cases per 100,000 inhabitants[2–5].

Colombia has an intermediate incidence of 17.4 per 100,000 inhabitants and a mortality rate of 13.4 per 100,000 inhabitants[4]. However, there are high-risk and low-risk areas in different regions of the country[6]. Although its incidence has gradually decreased, gastric cancer continues

to represent a major disease burden and an epidemiological challenge worldwide[3–5].

NATURAL COURSE OF GASTRIC CANCER

Gastric carcinogenesis is a progressive, long-term process resulting from the interaction of infectious, environmental, dietary, and genetic factors. Correa's model describes a well-established sequence that progresses from chronic non-atrophic gastritis to atrophic gastritis, intestinal metaplasia, dysplasia, and finally gastric adenocarcinoma[7,8]. Among environmental factors, high salt intake and consumption of salt-preserved foods such as smoked or dried meat and fish, combined with low fiber, fruit, and vegetable intake, significantly increase the risk of non-cardia GC[9]. However, the most important and widely recognized confirmed risk factor for GC is *Helicobacter pylori* infection. In recent years, a causal relationship has been firmly established between the chronic inflammatory process of the gastric mucosa triggered by this bacterium and subsequent gastric carcinogenesis[10]. Because this process can take decades to develop, we can improve early detection by identifying precancerous lesions and implementing endoscopic surveillance in high-risk patients, allowing us to diagnose malignancies at early, operable stages with better prognosis. In a large 10-year follow-up study, progression rates for patients with atrophic gastritis, intestinal metaplasia, low-grade dysplasia, or high-grade dysplasia were estimated at 0.8%, 1.8%, 4.0%, and 33.0%, respectively[9].

Despite recognition of the long, insidious course preceding cancer development, acceptance of the concept that gastric cancer can be prevented through detection and eradication of *H. pylori* has been slow[11]. *H. pylori* infection is the main trigger for GC regardless of histologic phenotype. Other conditions, including older age, high salt intake, diets low in fruits and vegetables, smoking, alcohol consumption, and family history, also contribute to gastric carcinogenesis[3]. Diffuse-type GC is genetically determined and less associated with environmental factors. Nevertheless, development of these tumors is also associated with *H. pylori* infection, which accounts for 90% of non-cardia GC cases and is recognized as the primary target for prevention strategies[3].

Countries with high gastric cancer incidence must recognize the immediate need to reduce mortality directly through endoscopic detection of premalignant lesions and, in addition, establish detection and treatment of *H. pylori* infection as a secondary strategy to reduce future risk[12]. Risk stratification can help identify high-risk groups and determine more intensive screening approaches and prioritization of diagnostic examinations[5].

PREVENTION

Primary cancer prevention through eradication or mitigation of modifiable risk factors represents the best opportunity to reduce the future burden of this disease. Reducing this burden will not only improve health and well-being, but will also decrease pressure on fiscal resources allocated to oncology services and the health sector as a whole[13].

Cancer prevention is not only the most effective strategy to reduce future incidence; it is also highly cost-effective. According to the WHO, every dollar invested in preventive interventions against noncommunicable diseases, including cancer, can generate an average return of seven dollars in health and economic benefits, while tobacco control programs have demonstrated savings of up to fifty dollars for every dollar invested[13,14].

Cancer prevention measures require a coordinated effort both within and beyond the health sector. These measures include targeted policies designed to reduce exposure to cancer-causing risk factors, such as tobacco and alcohol consumption, and ensuring access to vaccines that prevent cancer-related infections, such as hepatitis B and human papillomavirus (HPV)[13].

GC is associated with poor survival, with 5-year survival ranging between 20% and 40%. This unfavorable prognosis is mainly related to late-stage diagnosis. In contrast, early GC carries an excellent prognosis, with a 5-year survival rate above 90%[3,10].

Prevention strategies for GC must encompass all stages of primary and secondary prevention: maintaining a healthy lifestyle with an adequate diet, avoiding alcohol and tobacco consumption, and engaging in physical activity; screening for *H. pylori* infection and ensuring its eradication; early diagnosis of premalignant lesions, and risk stratification in patients older than 45 years through upper gastrointestinal endoscopic screening. Once high-risk individuals are identified, we must provide endoscopic surveillance and timely treatment according to disease evolution[15].

The absence of symptoms is a key feature of early-stage gastric cancer. High-definition white-light endoscopy performed by trained personnel can identify precancerous lesions as well as early-stage tumors. More advanced endoscopic techniques, such as chromoendoscopy or magnification endoscopy, are used in patients in whom a lesion has already been identified with white light, in order to achieve optical diagnosis of precancerous changes, estimate depth of invasion, and define appropriate margins for potential endoscopic resection[15].

Screening strategies must be adapted to the real conditions of each region. Although several validated tools exist for accurate GC diagnosis, identifying a universal

modality for population screening remains challenging[2]. An endoscopy-based screening program imposes a substantial socioeconomic burden due to the need for specific technical resources and highly trained personnel[3]. Such a strategy is cost-effective only in regions with high GC incidence and is focused exclusively on secondary prevention (early detection), without addressing primary prevention[3]. Despite awareness of this situation, there is still no universally accepted prevention strategy, and incidence and mortality have not been successfully reduced. Global gastric cancer prevention efforts must increase their level of effectiveness[15].

ENDOSCOPIC SCREENING AND RISK STRATIFICATION

The risk of developing gastric cancer is directly proportional to the severity of mucosal atrophy. The total gastric surface area ranges from 220 ± 27 cm^2 to 536 ± 25 cm^2. We identify the severity of gastric mucosal atrophy in biopsy samples according to the morphological visual analogue scale, based on the degree of reduction in the number of gastric glands. Through endoscopic visualization, we can estimate the surface area of atrophic stomach mucosa using the Kimura–Takemoto classification, from C1 to O3[15].

Histological risk stratification for GC involves assessing the extent and severity of atrophic gastritis and intestinal metaplasia[5]. In Asian countries, the extent of atrophy is assessed endoscopically by direct mucosal observation using the Kimura–Takemoto classification. In Western settings, histologic classification from systematic biopsies of the antrum, incisura, and corpus is preferred, and pathologists report findings using the Operative Link on Gastritis Assessment (OLGA) or Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) systems. Both approaches require endoscopy performed in a clean stomach with sufficient observation time. One approach requires biopsies from specific sites, while the other requires expertise in endoscopic classification. We should use these examinations in combination[1,7,15].

The OLGA system is based on a combination of atrophy scores using samples taken from antral and oxyntic mucosa (Sydney protocol). Combined score values express the severity of atrophy, which parallels GC risk (OLGA stages 0, I, and II: low risk; OLGA III and IV: high GC risk). Prospective studies support the prognostic value of staging atrophic gastritis and its usefulness in clinical practice[7].

Currently, screening programs are implemented in high-risk areas. Meta-analyses indicate that endoscopic screening in high-risk Asian populations may reduce GC mortality by up to 40%[3]. In Japan, screening programs began in 1983 using indirect radiology in individuals older than 40 years, with annual frequency. When abnormalities such as stenosis, deformity, rigidity, barium retention, gastric area irregularities, fold changes, or suspected polypoid lesions are detected, endoscopy is required to verify or confirm findings. This approach significantly reduced mortality[3]. In the 2014 and 2018 Japanese guidelines, endoscopy was approved as an alternative screening method. The screening age threshold was increased to 50 years, with intervals of 2 to 3 years (**Table 1**)[3].

South Korea launched its national screening campaign in 2001 in asymptomatic adults aged 40 to 74 years, offering either barium studies or endoscopy depending on patient preference and comorbidities. There has been a marked preference for endoscopy, increasing from 31.2% in 2002 to 72.6% in 2011. In Korea, endoscopy is cost-effective,

Table 1. Screening Programs for Gastric Cancer in High-Risk Countries

	Japan	South Korea	China	China
Year of implementation	1983	1999	2008	2012
Coverage	National	National	High-risk groups, rural areas	High-risk groups, urban areas
Strategy	Indirect radiology, endoscopy	Indirect radiology, endoscopy	Endoscopy	Questionnaire, endoscopy
Starting age	>50 years	>40 years	40–69 years	40–69 years
Screening interval	Every 2–3 years	Every 2 years	Individuals with severe chronic atrophic gastritis or intestinal metaplasia: endoscopy every 3 years	Individuals with severe atrophic gastritis or intestinal metaplasia: endoscopy every 3 years Dysplasia: endoscopy within 3–6 months

Adapted from: Januszewicz W, et al. Cancers (Basel). 2023;15(3):664.[3]

and program participation increases by 4.3% annually[3]. In China, screening began in 2008 in high-risk areas, initially rural and subsequently urban (2012), targeting individuals aged 40 to 69 years. This strategy is repeated every two years and is cost-effective[3].

It is clear that these screening programs are indicated for high-risk groups. The question that follows is: what type of program should be implemented for populations at low or intermediate risk? Some authors recommend endoscopy for individuals in these groups who have additional risk factors—for example, those who have lived in high-incidence regions for more than three years, individuals older than 50 years, men, tobacco and alcohol users, those with high salt intake, *H. pylori* infection, or a family history of GC[3].

SCREENING AND TREATMENT STRATEGY FOR *HELICOBACTER PYLORI* INFECTION

According to the World Health Organization (WHO), *H. pylori* is a class I carcinogen and remains the principal global risk factor for GC. Several noninvasive tests are available to detect this pathogen, including fecal antigen testing, the urea breath test, and serologic tests (e.g., anti–*H. pylori* IgG). These tests enable straightforward access to a "test-and-treat" approach, making this strategy a preferred method for primary GC prevention in high-incidence regions[3,5]. *H. pylori* screening identifies individuals with infection, who then become targets for eradication therapy[3].

Successful eradication therapy has been shown to cure gastric mucosal inflammation and thereby prevent its progression to preneoplastic lesions. In fact, the latest Kyoto consensus recommendations for high-risk regions support active and early detection of *H. pylori* infection together with treatment, before chronic inflammation and its complications develop[3,16].

The "test-and-treat" strategy for *H. pylori* infection has already been established in several countries and has contributed to decreasing incidence in some regions. In Western countries, this strategy is currently used most frequently in patients with dyspeptic symptoms and has been shown to reduce the cost of dyspepsia evaluations in general health care. With this in mind, using a broader testing framework (that also includes asymptomatic individuals) at the population level may represent a feasible strategy within health care systems[3].

The International Agency for Research on Cancer (IARC) has recommended developing appropriate GC prevention policies, including *H. pylori* eradication therapy, in countries with high GC incidence[5,17]. It has been estimated that if all *H. pylori* infections were eradicated, approximately 89% of noncardia GC, 29% of cardia GC, and 74% of gastric lymphoma cases could be prevented. In 2014, the IARC working group emphasized the need to allocate additional medical resources to GC control and recommended that countries explore the feasibility of implementing population-based *H. pylori* screening and eradication programs[1,5,11,17].

In Japan, eradication therapy for *H. pylori*–related chronic gastritis (*H. pylori* gastritis) was approved under the national health insurance plan in February 2013. If the incidence of *H. pylori* gastritis can be reduced through eradication therapy, the incidence of atrophic gastritis—a premalignant condition for GC—will also decline[17,18]. Consequently, in recent years we have witnessed a paradigm shift from cancer detection toward cancer prevention.

Population-based strategies for primary prevention depend on local prevalence and cost-effectiveness relationships. In high-incidence regions, *H. pylori* eradication is the most effective strategy for preventing GC. A meta-analysis including 6,497 subjects from six randomized controlled trials demonstrated reduced GC incidence in *H. pylori*–infected individuals who received eradication therapy compared with placebo or untreated controls after 4 to 14.7 years of follow-up (odds ratio [OR], 0.66; 95% confidence interval [CI], 0.46–0.95)[17,18]. Similar results were reported in another meta-analysis by Chen and colleagues, which included 10 analyses from eight randomized clinical trials, totaling 7,955 participants. The risk of cancer development was lower in the eradication group compared with controls, with a pooled relative risk (RR) of 0.64 (95% CI: 0.48–0.85). However, in subgroup analyses of patients with intestinal metaplasia or dysplasia, this difference was not observed (RR = 0.88; 95% CI: 0.59–1.31)[18,19]. Therefore, the preventive benefit of eradication is limited to *H. pylori*–infected patients without advanced precancerous conditions at baseline[10,15,19,20].

In high-incidence settings, both endoscopic screening and *H. pylori* "test-and-treat" strategies represent cost-effective models[3]. China historically has had high GC incidence and high *H. pylori* prevalence. Nearly half of all new GC cases and GC-related deaths worldwide attributable to *H. pylori* infection occurred in China[12]. With the publication of five Chinese consensus reports on *H. pylori* management and active public dissemination of *H. pylori*–related knowledge, diagnostic and therapeutic practices among clinicians have become more standardized[12]. In 2013, the Fourth Chinese National Consensus Report on the treatment of *H. pylori* infection was published, including indications, diagnosis, and treatment recommendations[12].

In 2018, the Fifth Chinese National Consensus Report on the management of *H. pylori* infection was published. Raising awareness regarding the prevention and treatment of *H. pylori* infection among the Chinese population was also essential. Most surveyed individuals (87.0%) and

physicians (82.2%) supported a national *H. pylori* screening plan to prevent GC[12]. In Changle, Fujian Province, 1,630 asymptomatic *H. pylori*–infected individuals were randomly assigned to receive either eradication therapy or placebo and were followed for 26.5 years (1994–2020). Participants who received eradication therapy had a lower incidence of GC than their placebo counterparts (hazard ratio: 0.57; 95% CI: 0.33–0.98), and the benefit was more evident in participants without premalignant gastric lesions or dyspeptic symptoms at baseline[12,20,21].

The gastric cancer incidence rate in the Matsu Islands had been the highest among all Taiwanese populations, with a standardized incidence rate exceeding 50 per 100,000 person-years. To control the gastric cancer burden, a mass eradication program for *H. pylori* infection was developed in 2004. Residents aged 30 years or older were eligible to participate, based on a cost-effectiveness analysis predicting the superiority of early *H. pylori* eradication[12,22]. Participants underwent the C13 urea breath test, and those who tested positive received one or two courses of standardized triple- or quadruple-therapy regimens, validated through a randomized trial confirming eradication[12]. The prevalence of *H. pylori* infection rapidly declined from 63% to 10%, with a reinfection rate of less than 1% per person-year. By 2016, the program resulted in a 53% reduction in gastric cancer. By 2023, fewer than 6 per 100,000 residents were being diagnosed with gastric cancer, and by 2025, incidence and mortality rates are expected to decrease by 68% and 39%, respectively (**Table 2**)[1,8,12,17].

At the general population level, *H. pylori* screening and treatment strategies are most cost-effective in young adults in regions with high GC incidence and are preferably recommended before the development of atrophic gastritis and intestinal metaplasia[8,17].

RISK PREDICTION MODELS AND RISK FACTORS

An effective way to improve the critical situation of gastric cancer (GC) diagnosis and treatment in China was to implement screening in patients at high risk for GC. Current national GC screening guidelines in China recommend screening from age 40 onward for all members of high-risk populations (those who have lived in high-incidence regions for more than three years or who have *H. pylori* infection, a positive family history of GC, or other GC risk factors, among others). It is estimated that more than 300 million individuals were classified as high risk and required upper gastrointestinal endoscopy, which was likely unfeasible in clinical practice. Therefore, a practical risk prediction rule was needed to more accurately stratify GC risk within the Chinese high-risk population[12].

From 2015 to 2017, the China Alliance for the Prevention and Treatment of Early Gastrointestinal Cancer conducted a nationwide, multicenter cross-sectional study to identify high-risk individuals prior to endoscopy, recruiting 14,929 persons aged 40–80 years who attended hospitals for screening gastroscopy[22,23]. Seven variables—age, sex, PG I/II ratio, G-17 level, *H. pylori* infection, and consumption of pickled and fried foods—were evaluated to predict risk, with scores ranging from 0 to 25[21,22]. Risk categories were defined as low, intermediate, and high when the scores ranged from 0–11, 12–16, and 17–25, respectively. A total of 66.7% were classified as low risk, 27.6% as intermediate risk, and 5.7% as high risk. The prevalence of GC was 1.2%, 4.4%, and 12.3%, respectively (p <0.001). Notably, 70.8% of patients with advanced gastric cancer (AGC) and 70.3% of patients with early gastric cancer (EGC) were diagnosed when endoscopy was performed in the intermediate- and high-risk groups identified by the scoring system.

Table 2. *Helicobacter pylori* Screening Programs Worldwide

Country	Starting Age (years)	Program Start Year	Screening Interval	Strategy	Outcome
Japan	20	2013	Once	Diagnosis, *H. pylori* detection, and endoscopic screening	6% reduction in mortality in 2016
Republic of Korea	40-65	2014	Once	Breath test	Reduced GC incidence through *H. pylori* eradication
China	18	2022	Once	Family-based breath testing	Prevention of intrafamilial *H. pylori* transmission and consequent reduction in GC incidence
Taiwan	30	2004	Every 2 years	Breath test	53% reduction in GC incidence and 25% reduction in mortality

GC: gastric cancer. Adapted from: Conti CB, et al. Int J Environ Res Public Health. 2023;20(3):2149.[1]

Endoscopy requirements could be reduced by up to 66.7%, corresponding to the low-risk proportion. This study was successfully developed and validated nationwide[12,24].

SCREENING PROGRAM AND *HELICOBACTER PYLORI*

To implement a screening program of this scale, we need a structure in which collaboration among health policy makers, frontline general practitioners, and the population is guided and monitored through multiple quality indicators[11].

Screening everyone simultaneously is unrealistic for several reasons; in particular, it would impose a substantial burden on subsequent treatment and follow-up. Therefore, the program should be defined as a continuous process rather than a "one-time" project, with balanced costs relative to potential health care expenditures[11]. In regions where gastric cancer is a major public health concern, the proportion of individuals infected with *H. pylori* tends to be high[24,25]. Combining *H. pylori* eradication with endoscopic screening has shown promise in reducing GC incidence in high-incidence populations[24].

The Maastricht IV European *Helicobacter* Study Group (EHSG) report supported Asian expert opinions with the following statements:

- *H. pylori* infection is the most consistent risk factor for GC; therefore, eradication is the most promising strategy to reduce GC incidence (level of evidence: 1a).
- GC risk can be reduced most effectively by providing eradication therapy before preneoplastic conditions develop (level of evidence: 1a).
- *H. pylori* eradication to prevent GC should be implemented in high-risk populations (level of evidence: 1c)[24,25].

There is also evidence on combining *H. pylori* infection screening with fecal occult blood testing to identify patients eligible for eradication therapy. This approach has been shown to increase individual participation, and although a direct association between infection and increased endoscopic findings of precancerous lesions has not yet been demonstrated, adding risk factor identification will likely help us select patients for endoscopic assessment (**Table 3**)[25,26].

APPLICABILITY IN INTERMEDIATE-RISK REGIONS

Gastric cancer (GC) screening programs should not be implemented in countries with low or intermediate risk[3]. Colombia is considered an intermediate-incidence country overall, but certain municipalities in departments such as Boyacá and Nariño have very high incidence rates[4,26,27]. In most countries, incidence varies geographically and correlates with the prevalence of *H. pylori* infection[11]. A test-and-treat strategy for *H. pylori* reduces future GC incidence, but it does not help to reduce current GC mortality[2,3]. This tool provides the greatest benefit in individuals at higher risk and has been considered cost-effective based on a willingness-to-pay threshold for gains in life-years[5].

H. pylori infection is the main cause of GC, but it is not an adequate standalone predictor of cancer development. Approximately 90% of noncardia GC cases are related to *H. pylori* infection[28]; however, among 100 infected patients, only one will develop GC. Since only a very small proportion of infected individuals will develop cancer in the future, not all infected subjects will require treatment. Treating everyone after detection would lead to unnecessary therapies and related adverse effects, such as antibiotic resistance, obesity, and increased risk of other diseases[2].

When we encounter a patient from an intermediate-incidence GC region with a positive *H. pylori* test, should we always treat them? The answer is not always. The magnitude of the protective effect of *H. pylori* eradication also depends on baseline risk[5].

In the initial patient evaluation, we must define individual risk. If the patient is young (symptomatic or asymptomatic), we should treat them. Younger individuals benefit most from *H. pylori* eradication because it cures *H. pylori*–related gastritis, reduces GC risk, and decreases transmis-

Table 3. Intervention Strategies for Gastric Cancer Screening

High-Risk Areas	Low- or Intermediate-Risk Areas
Endoscopic screening; assess cost-effectiveness	Targeted endoscopic screening in at-risk individuals
Diagnosis and treatment of *H. pylori*	*H. pylori* "test-and-treat" strategy for at-risk individuals (e.g., family history of GC, precancerous gastric lesions, *H. pylori* infection)
Population: above 40 or 50 years	*H. pylori* stool antigen testing combined with a colorectal cancer screening program using fecal occult blood testing (FOBT)

CRC: colorectal cancer; GC: gastric cancer; FOBT: fecal occult blood test. Adapted from: Januszewicz W, et al. Cancers (Basel). 2023;15(3):664.[3]

sion to their children[5,28]. If the subject is a first-degree relative of a patient diagnosed with GC, we should treat them. It is estimated that 20% of GC patients have a family history of GC, which confers a 2- to 10-fold increased risk[9]. If the patient comes from a high-risk region, we should treat them. If the patient is otherwise low risk but has lived in a high-risk area for at least three years, we should treat them. At the individual level, *H. pylori* eradication reduces the risk of metachronous gastric cancer in patients with early GC after curative endoscopic resection[5,6,9,10].

H. pylori eradication does not increase the risk of gastroesophageal reflux disease, and there is no evidence that it increases the risk of metabolic syndrome, autoimmune disease, or inflammatory bowel disease (IBD)[5]. A retrospective cohort study showed an association between *H. pylori* eradication and a significantly higher risk of IBD and certain autoimmune diseases[29]. However, large-scale prospective studies are needed to clarify the impact of eradication on the incidence of these diseases in adults[5]. Gut microbiota diversity is lower in infected individuals compared with uninfected individuals, and gradual recovery is achieved within two to three months after treatment[5,28].

CONCLUSIONS

Prevention and screening strategies for GC must be adapted to the epidemiological conditions of each region. In high-incidence countries, implementing population-based endoscopic screening programs is a priority to enable earlier diagnoses and reduce mortality. Furthermore, when *H. pylori* prevalence is high, screening and eradication strategies emerge as key complementary measures to reduce future GC incidence. Conversely, in intermediate- or low-risk regions, it is more efficient to focus screening endoscopy on individuals with risk factors—for example, those older than 50 years, men, smokers, or individuals with a family history of gastric cancer—rather than implementing universal screening.

Ultimately, primary prevention (dietary improvements, *H. pylori* eradication, tobacco control, among others) and secondary prevention (early detection through endoscopy supported by risk-stratification models) are not mutually exclusive; instead, they must be integrated in a complementary manner.

GC has received very limited attention in terms of preventive action policies. An integrated and sustained approach, adapted to the characteristics and resources of each community, is essential to effectively reduce the global burden of GC. It is imperative that health authorities and health systems develop policies and programs that combine detection and prevention in a cost-effective manner, ensuring long-term implementation in accordance with local epidemiological needs.

REFERENCES

1. Conti CB, Agnesi S, Scaravaglio M, Masseria P, Dinelli ME, Oldani M, Uggeri F. Early Gastric Cancer: Update on Prevention, Diagnosis and Treatment. Int J Environ Res Public Health. 2023;20(3):2149. https://doi.org/10.3390/ijerph20032149
2. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63. https://doi.org/10.3322/caac.21834
3. Januszewicz W, Turkot MH, Malfertheiner P, Regula J. A Global Perspective on Gastric Cancer Screening: Which Concepts Are Feasible, and When? Cancers (Basel). 2023;15(3):664. https://doi.org/10.3390/cancers15030664
4. Laudano O RAMJP. Prevención del cáncer gástrico: contexto y experiencia latinoamericana. Acta Gastroenterol Latinoam. 2024;54(4):299-399. https://doi.org/10.52787/agl.v54i4.456
5. Hamashima C. Forthcoming Step in Gastric Cancer Prevention: How Can Risk Stratification Be Combined with Endoscopic Screening for Gastric Cancer? Gut Liver. 2022;16(6):811-824. https://doi.org/10.5009/gnl210313
6. Bedoya Á, Sansón F, Yépez Fuertes Y, Santacruz C, Cifuentes Y, Calvache D, et al. Prevalencia y severidad de las lesiones precursoras de malignidad en una área de alto riesgo de cáncer gástrico. Pasto 2012;27(4): 275-281.
7. Rugge M SESMBLMP. Gastritis: the clinic pathological spectrum. Dig Liver Dis. 2021;53(10):1237-46. https://doi.org/10.1016/j.dld.2021.03.007
8. Liou JM, Malfertheiner P, Lee YC, Sheu BS, Sugano K, Cheng HC, et al. Screening and eradication of *Helicobacter pylori* for gastric cancer prevention: the Taipei global consensus. Gut. 2020;69(12):2093-2112. https://doi.org/10.1136/gutjnl-2020-322368
9. Marqués-Lespier JM, González-Pons M, Cruz-Correa M. Current Perspectives on Gastric Cancer. Gastroenterol Clin North Am. 2016;45(3):413-28. https://doi.org/10.1016/j.gtc.2016.04.002
10. Venerito M, Vasapolli R, Malfertheiner P. Helicobacter pylori and Gastric Cancer: Timing and Impact of Preventive Measures. Adv Exp Med Biol. 2016;908:409-18. https://doi.org/10.1007/978-3-319-41388-4_20

11. Chiang TH, Cheng HC, Chuang SL, Chen YR, Hsu YH, Hsu TH, et al. Mass screening and eradication of Helicobacter pylori as the policy recommendations for gastric cancer prevention. J Formos Med Assoc. 2022;121(12):2378-2392. https://doi.org/10.1016/j.jfma.2022.08.012
12. Hu Y, Zhu Y, Lu NH. The management of *Helicobacter pylori* infection and prevention and control of gastric cancer in China. Front Cell Infect Microbiol. 2022;12:1049279. https://doi.org/10.3389/fcimb.2022.1049279
13. Safarty D. Preventing cancer: the only way forward. Comment. Lancet. 2022;20(400):540-1. https://doi.org/10.1016/S0140-6736(22)01430-1
14. GBD 2019 Cancer Risk Factors Collaborators. The global burden of cancer attributable to risk factors, 2010-19: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;400(10352):563-591. https://doi.org/10.1016/S0140-6736(22)01438-6
15. Kotelevets SM. Global strategy for prevention of gastric cancer. World J Clin Cases. 2024;12(30):6353-7. https://doi.org/10.12998/wjcc.v12.i30.6353
16. Sugano K, Tack J, Kuipers EJ, Graham DY, El-Omar EM, Miura S, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut. 2015;64(9):1353-67. https://doi.org/10.1136/gutjnl-2015-309252
17. Tsuda M, Asaka M, Kato M, Matsushima R, Fujimori K, Akino K, et al. Effect on Helicobacter pylori eradication therapy against gastric cancer in Japan. Helicobacter. 2017;22(5):e12415. https://doi.org/10.1111/hel.12415
18. Ford AC, Forman D, Hunt RH, Yuan Y, Moayyedi P. Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomised controlled trials. BMJ. 2014;348:g3174. https://doi.org/10.1136/bmj.g3174
19. Chen HN, Wang Z, Li X, Zhou ZG. Helicobacter pylori eradication cannot reduce the risk of gastric cancer in patients with intestinal metaplasia and dysplasia: evidence from a meta-analysis. Gastric Cancer. 2016;19(1):166-75. https://doi.org/10.1007/s10120-015-0462-7
20. Yan L, Chen Y, Chen F, Tao T, Hu Z, Wang J, et al. Effect of Helicobacter pylori Eradication on Gastric Cancer Prevention: Updated Report From a Randomized Controlled Trial With 26.5 Years of Follow-up. Gastroenterology. 2022;163(1):154-162.e3. https://doi.org/10.1053/j.gastro.2022.03.039
21. Chiang TH, Chang WJ, Chen SLS, Yen AMF, Fann JCY, Chiu SYH, et al. Mass eradication of Helicobacter pylori to reduce gastric cancer incidence and mortality: A long-term cohort study on Matsu Islands. Gut. 2021;70(2):243-50. https://doi.org/10.1136/gutjnl-2020-322200
22. Cai Q, Zhu C, Yuan Y, Feng Q, Feng Y, Hao Y, et al. Development and validation of a prediction rule for estimating gastric cancer risk in the Chinese high-risk population: A nationwide multicentre study. Gut. 2019;68(9):1576-87. https://doi.org/10.1136/gutjnl-2018-317556
23. Oliveros Wilches R, Facundo Navia H, Bonilla Castañeda AD, Pinilla Morales RE. Factores de riesgo para cáncer gástrico: ¿cuál es su papel?. Rev Colomb Gastroenterol. 2021;36(3):366-7. https://doi.org/10.22516/25007440.656
24. Fock KM. Review article: the epidemiology and prevention of gastric cancer. Aliment Pharmacol Ther. 2014;40(3):250-60. https://doi.org/10.1111/apt.12814
25. Lee YC, Chiang TH, Chiu HM, Wu MS, Yeh YP, Hsiu-Hsi Chen T; et al. Community-Based Gastric Cancer Screening Coupled With a National Colorectal Cancer Screening Program: Baseline Results. Gastroenterology. 2021;160(6):2159-2161.e4. https://doi.org/10.1053/j.gastro.2021.01.008
26. Arias Sosa LC, 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):181-9.
27. Bedoya-Urresta Á, Yépez Y, Calvache D, Cifuentes Y, Lucero N, González P, et al. Proyecto Urkunina 5000-Investigación de la prevalencia de lesiones precursoras y del efecto de la erradicación de Helicobacter pylori como prevención primaria del cáncer gástrico en el departamento de Nariño. Revista Colombiana de Cirugía. 2018;33(4):345-52. https://doi.org/10.30944/20117582.81
28. Leja M. Where are we with gastric cancer screening in Europe in 2024? Gut. 2024;73(12):2074-82. https://doi.org/10.1136/gutjnl-2024-332705
29. Lin KD, Chiu GF, Waljee AK, Owyang SY, El-Zaatari M, Bishu S, et al. Effects of Anti-Helicobacter pylori Therapy on Incidence of Autoimmune Diseases, Including Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol. 2019;17(10):1991-1999. https://doi.org/10.1016/j.cgh.2018.12.014

https://doi.org/10.22516/25007440.1140

Review article

Research and Publication. Part 8. Basic Ethical Principles in Clinical Research: Essential Bioethical Considerations in Biomedical Investigation: Foundations, Standards, and Indispensable Practices

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OPEN ACCESS

Citation:
Granada-Copete AM. Research and Publication. Part 8. Basic Ethical Principles in Clinical Research: Essential Bioethical Considerations in Biomedical Investigation: Foundations, Standards, and Indispensable Practices. Revista. colomb. Gastroenterol. 2025;40(4):472-476.
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Received: 30/07/2025
Accepted: 17/11/2025

Abstract

Biomedical research is a continuously evolving field whose primary purpose is to address current health needs. Today, the availability of advanced technoscientific tools offers new opportunities to improve diagnostic and therapeutic capabilities. This article outlines the fundamental ethical principles that govern clinical research, emphasizing their historical development, key international and national regulatory frameworks, and the contemporary challenges posed by emerging technologies such as artificial intelligence and personalized medicine. The seven criteria proposed by Emanuel et al.[1] are presented as a cornerstone for the ethical assessment of biomedical research protocols. The article also highlights the importance of bioethics training, the strengthening of Research Ethics Committees (RECs), and the cultivation of a broader culture of scientific integrity.

Keywords

Bioethics, clinical research protocol, ethics committees, informed consent, scientific integrity.

INTRODUCTION

Biomedical research has evolved as an essential tool for improving public health; however, it has also generated ethical challenges that require systematic reflection. Its impact is far-reaching and, therefore, integrating bioethics at every stage of the research process is an obligation to ensure respect for human rights, transparency, and justice. Bioethics in research is not limited to the individual protection of participating subjects; it extends to a social and collective responsibility regarding how knowledge is produced, how derived benefits are distributed, and who participates in decision-making. For these reasons, it is indispensable to analyze not only regulatory frameworks but also the philosophical foundations that underpin ethical practices in biomedical contexts. Accordingly, the question that explains the research ecosystem is: why is it necessary to integrate bioethics into biomedical research? In this regard, a brief historical overview is presented to highlight certain requirements necessary to comply with research ethics and scientific integrity.

Throughout history, in light of advances in knowledge and techno-scientific developments—which today enable and challenge the use of artificial intelligence, gene therapy, and personalized medicine, among others—research methodologies have been transformed, making it increasingly important to remain attentive to their impacts on human beings and, by extension, on humanity as a whole.

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METHODOLOGY

This work was conducted as a narrative, documentary-type review, grounded in a hermeneutic and deliberative bioethical approach. Primary and secondary sources were analyzed, including international codes (Nuremberg, Helsinki, Belmont, CIOMS), academic literature, and national regulatory frameworks, with the aim of identifying tensions between classical ethics and the emerging demands of contemporary biomedical research.

METHODOLOGICAL LIMITATIONS

The review does not include empirical data, which limits the practical corroboration of the findings. Nevertheless, this approach allows for a critical and cross-cutting understanding of the current ethical-regulatory framework, appropriate for the conceptual analysis of applied bioethics.

ETHICAL FOUNDATIONS OF CLINICAL RESEARCH

From its earliest beginnings, biomedical research has required the presentation of a methodology to carry out the best possible research project. While this is true, in its early stages research was not structured in this manner, as experiments were conducted without clearly defined objectives and hypotheses that could readily demonstrate such methodology as a requirement for compliance with biomedical research standards. This changed particularly following the recognition of the experiments conducted during the Second World War and the subsequent trial of physicians in Nuremberg, which prompted the implementation of methodological and ethical criteria in the conduct of biomedical research. It was then that international declarations emerged to guide biomedical research, such as the Nuremberg Code (1949)[2] and the Declaration of Helsinki (1964), along with its most recent update (2024)[3].

The Declaration of Helsinki is a set of ethical principles established by the World Medical Association (WMA) to guide medical research involving human participants. Its primary objective is to protect the dignity, rights, and well-being of individuals who participate in medical research. To this end, it requires the protection of life and health and respect for participant autonomy, and it promotes the minimization of risks and harms. Likewise, it fosters scientific integrity and ensures access to benefits, which is reflected in the research protocol and the informed consent process. Research protocols must be evaluated by a Research Ethics Committee (REC) and approved prior to the initiation of a study, thereby ensuring the transparent publication of research results. In its final section, the Declaration refers to interventions that are not approved in clinical practice. The Belmont Report[4], the International Ethical Guidelines for Biomedical Research (CIOMS)[5], the Declaration of Taipei[6], among others, constitute recommendations to which countries adhere through their internal regulations.

The regulatory framework that has gained the greatest visibility is the implementation of Good Clinical Practice (GCP) for research involving human beings and biomedical products, proposed by the World Health Organization (WHO) and the International Council for Harmonisation (ICH). These practices establish standards and guidelines for GCP. Accordingly, in Colombia, the National Institute for the Surveillance of Medicines and Foods (INVIMA), through Resolution 2378 of 2008[7], implemented GCP and required that, in order to conduct research, researchers must be members of a Research Ethics Committee or belong to a research center in order to obtain GCP certification.

Considering the regulatory framework and its evident appropriation for scientific production, it is essential to recognize the importance and sensitivity of scientific integrity. Today, there are publications reporting research retractions for various reasons; among the most frequent are plagiarism, misconduct, errors, fabrication, and duplication, all of which relate to scientific integrity. These issues generally arise from methodological doubts, problematic results, and ethical concerns that necessitate review, drawing attention to their increasing frequency. This underscores the importance of mitigating such issues through education and awareness regarding publication ethics and the responsible conduct of research by researchers and journal editorial teams[8].

The Belmont Report (1979)[4] promotes ethical principles and guidelines for the protection of human beings in research, which are reflected in informed consent. This document evidences the ethical and transparent process through which the autonomy of the research participant is recognized, freely, voluntarily, and consciously, as an expression of participatory acceptance in the research. Informed consent constitutes the informational evidence provided to the participant regarding the objectives of the research, and it is the responsibility of the principal researchers to inform the REC of how this information will be conveyed, whether through a clearly defined and robust encounter, requiring clear and accessible language delivered through videos or written texts. The informed consent document is validated by the signature of the participant, the principal researcher, and two witnesses, in accordance with Colombian regulations (Resolution 8430 of 1993 of the Ministry of Health, which establishes standards for health research)[9], thereby ensuring participant autonomy, the adequacy of the information provided, and respect for participant rights—fundamental requirements for obtaining informed consent. In addition, Law 23 of 1981[10], in

Article 10, establishes that informed consent must be obtained for any medical or surgical treatment that may physically or psychologically affect the patient. With respect to research, this medical ethics law refers to the recommendations of the WMA in Article 54, which states: "with regard to biomedical research in general, therapeutic research in humans, and the application of new technologies, whether for diagnostic purposes (…)". For this reason, the scope of the regulatory framework cannot be disregarded.

JUSTIFICATION OF ITS CURRENT RELEVANCE

Within this broad context that defines and shapes biomedical research, research ethics constitutes an indispensable requirement due to the direct involvement of human beings and the contribution of bioethics to understanding the care of life. Accordingly, it calls for reflection on all components of research and their future impacts. An additional component that strengthens the work of the researcher is scientific integrity, which aims to maintain trust and credibility in science through good practices in the generation and appropriation of knowledge[11].

ETHICAL CRITERIA FOR RESEARCH PROJECTS

Emanuel and colleagues[1] propose seven criteria for considering clinical research to be ethical, as presented in **Table 1**.

These criteria constitute the minimum ethical framework for designing and evaluating clinical research projects, and they are particularly useful for Research Ethics Committees when analyzing complex protocols with innovative methodologies or involving emerging technologies. In addition, they provide concrete guidance for researchers and promote an ethics of shared responsibility. Given the diversity of methodologies in biomedical research, adjustments in ethical evaluation are required, which invariably demand deliberative reflection within the research context.

CONTEMPORARY CHALLENGES AND NEW BIOETHICAL CONSIDERATIONS

Current challenges include research conducted in public health emergency contexts, as well as the use of artificial intelligence (AI), big data, genomics, and personalized medicine. These technologies require new ethical and legal regulations. The United Nations Educational, Scientific and Cultural Organization (UNESCO)[12] has issued recommendations, and in Colombia, CONPES 3975 of 2019[13] establishes guidelines for the use of AI.

The use of AI in ethical evaluation by Research Ethics Committees (RECs) raises new questions regarding algorithmic transparency, consent, and equity. For example, a lack of understanding of AI models by researchers or reviewers may lead to decisions based on opacity or unidentified biases. This reinforces the need for continuous training in the ethics of technology and for interdisciplinary technical evaluation.

Genetic research, gene editing (such as the use of CRISPR-Cas9), and data biobanks also demand new bioethical considerations, particularly with respect to privacy, broad consent, and future data use. Protection of the right not to know and the ethical management of the return of results have become key issues. It is crucial to anticipate potential dilemmas before they arise, fostering a prospective or anticipatory bioethics[14].

Current techno-scientific advances reconfigure traditional notions of consent, risk, and justice. The expansion of genetic biobanks, AI applied to health, and gene editing through technologies such as CRISPR-Cas9 generate unprecedented tensions with respect to classical principles.

Table 1. Ethical Criteria for Ethical Clinical Research according to Emanuel and Colleagues[1]

No.	Ethical Criteria	Summary Description
1	Social or scientific value	Research must contribute relevant knowledge to public health or science.
2	Scientific validity	The methodological design must be rigorous and appropriate to answer the research question.
3	Fair participant selection	Inclusion must be just and avoid the exploitation of vulnerable populations.
4	Favorable risk-benefit balance	Risks must be reasonable in relation to the expected benefits.
5	Independent review	An ethics committee must review and approve the protocol prior to its execution.
6	Informed consent	Participants must freely agree after understanding risks, benefits, and alternatives.
7	Respect for participants	Includes confidentiality, voluntary withdrawal, and access to results.

Adapted from: Emanuel EJ, et al. JAMA. 2000;283(20):2701-11[1].

Autonomy requires reinterpretation in light of broad and ongoing consent for secondary data use. Beneficence and non-maleficence face the epistemic uncertainty of new techniques, and justice takes on a global dimension in the context of unequal access to advanced therapies. These challenges call for an anticipatory bioethics capable of collectively deliberating on the limits and purposes of science.

RECOMMENDATIONS

- Strengthen bioethics training for researchers, including the ethics of technology, global justice, and cultural pluralism.
- Consolidate the role of ethics committees as active deliberative bodies with technical competence.
- Promote community participation in the research process, not only as subjects but as deliberative actors.
- Ensure effective communication among researchers, RECs, and regulatory entities.
- Foster scientific integrity at all stages of research, from design to publication and dissemination of results.
- Promote public policies that update regulatory frameworks in line with techno-scientific transformations.
- Include mechanisms for continuous monitoring and ethical audits to strengthen accountability in clinical research.

CONCLUSIONS

Clinical research must be conducted ethically and responsibly. Respect for human dignity, protection against harm, the pursuit of social benefits, and justice in participant selection are indispensable pillars. Good practices must be reflected in informed consent, transparency of results, confidentiality, and ethical oversight. The principal researcher is responsible for maintaining the methodological and ethical integrity of the study.

Bioethics, as a reflective discipline, must critically and constructively accompany the constant transformation of biomedical research. In the face of new challenges such as AI and gene editing, it is essential to promote an anticipatory ethics grounded in respect, precaution, and inclusion. Only in this way can a culture of trust and responsibility in the production of scientific knowledge be strengthened.

Ethical Considerations

This article corresponds to a narrative, documentary-type review grounded in a hermeneutic and deliberative bioethical approach. No human beings or animals were involved in the collection or analysis of data; therefore, approval by a research ethics committee was not required.

I declare that I have conflicts of interest related to the preparation, content, or publication of this manuscript. Compliance with the principles of academic integrity, transparency, and responsible citation of all sources used is guaranteed.

Likewise, the use of the ChatGPT tool (OpenAI) is declared solely as support for style review and text organization, with the author retaining full intellectual and academic responsibility for the content.

REFERENCES

1. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA. 2000;283(20):2701-11. https://doi.org/10.1001/jama.283.20.2701
2. The Nuremberg Code (1947). BMJ [Internet]. 1996;313(7070):1448. https://doi.org/10.1136/bmj.313.7070.1448
3. World Medical Association. The World Medical Association-Declaración de Helsinki de la AMM – Principios éticos para las investigaciones médicas con participantes humanos [Internet]. WMA; 2024 [consultado el 20 de junio de 2025]. Disponible en: https://www.wma.net/es/policies-post/declaracion-de-helsinki-de-la-amm-principios-eticos-para-las-investigaciones-medicas-en-seres-humanos/
4. The Belmont Report. Ethical Principles and Guidelines for the Protection of Human Subjects of Research [Internet]. US Department of Health and Human Services; 1979 [consultado el 20 de junio de 2025]. Disponible en: https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html
5. Organización Panamericana de la Salud y Consejo de Organizaciones Internacionales de las Ciencias Médica. Pautas éticas internacionales para la investigación relacionada con la salud con seres humanos [Internet]. 4.ª edición. Ginebra: Consejo de Organizaciones Internacionales de las Ciencias Médicas (CIOMS); 2016 [consultado el 20 de junio de 2025]. Disponible en: https://cioms.ch/wp-content/uploads/2017/12/CIOMS-EthicalGuideline_SP_INTERIOR-FINAL.pdf
6. World Medical Association. Declaración de Taipéi [Internet]. WMA; 2016 [consultado el 28 de junio de 2025]. Disponible en: https://www.wma.net/es/que-hacemos/etica-medica/declaracion-de-taipei/
7. Ministerio de la Protección Social. Resolución 2378 de 2008, por la cual se adoptan las buenas prácticas clínicas para las instituciones que conducen investigación con

medicamentos en seres humanos [Internet]. INVIMA; 2008 [consultado el 28 de junio de 2025]. Disponible en: https://www.invima.gov.co/biblioteca/resolucion-2378-2008-buenas-practicas-clinicas
8. Sharma P, Sharma B, Reza A, Inampudi KK, Dhamija RK. A systematic review of retractions in biomedical research publications: reasons for retractions and their citations in Indian affiliations. Humanit Soc Sci Commun. 2023;10(1):597. https:// doi.org/ 10.1057/s41599-023-02095-x
9. Ministerio de Salud de Colombia. Resolución 8430 de 1993, por la cual se establecen las normas científicas, técnicas y administrativas para la investigación en salud [Internet]. MinSalud; 1993 [consultado el 28 de junio de 2025]. Disponible en: https://www.minsalud.gov.co/sites/rid/lists/bibliotecadigital/ride/de/dij/resolucion-8430-de-1993.pdf
10. Congreso de Colombia. Ley 23 de 1981, por la cual se dictan normas en materia de ética médica [Internet]. Función Pública; 1981 [consultado el 28 de junio de 2025]. Disponible en: https://www.funcionpublica.gov.co/eva/gestornormativo/norma.php?i=68760
11. Colciencias. Política de ética, bioética e integridad científica [Internet]. Colombia: Colciencias; 2017 [consultado el 28 de junio de 2025]. Disponible en: https://minciencias.gov.co/sites/default/files/upload/noticias/politica-etica.pdf
12. UNESCO. Recomendación sobre la ética de la inteligencia artificial. París: UNESCO; 2022 [consultado el 28 de junio de 2025]. Disponible en: https://unesdoc.unesco.org/ark:/48223/pf0000381137_spa
13. Departamento Nacional de Planeación. CONPES 3975: Política nacional para la transformación digital e inteligencia artificial [Internet]. Bogotá: DNP; 2019 [consultado el 28 de junio de 2025]. Disponible en: https://colaboracion.dnp.gov.co/CDT/Conpes/Econ%C3%B3micos/3975.pdf
14. Hernández Flórez LJ. El uso de la Inteligencia Artificial en los Comités de Ética en Investigación-CEI [Internet]. Aipocrates; 2025 [citado 22 de junio de 2025]. Disponible en: https://aipocrates.blog/2025/04/27/el-uso-de-la-inteligencia-artificial-en-los-comites-de-etica-en-investigacion-cei/

https://doi.org/10.22516/25007440.1294

Case report

Nodular Lymphoid Hyperplasia, An Uncommon Benign Entity Associated with Gastrointestinal Bleeding: Report of Two Cases

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Citation:
González-Soriano LS, Delgado-Marrugo RD, Frías-Ordoñez JS, Olaya-Morales N, Alarcón-Nieto MC, Ruiz-Morales OF, Gómez-Zuleta MA. Nodular Lymphoid Hyperplasia, An Uncommon Benign Entity Associated with Gastrointestinal Bleeding: Report of Two Cases. Revista. colomb. Gastroenterol. 2025;40(4):477-485.
https://doi.org/10.22516/25007440.1294

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Received: 22/10/2024
Accepted: 04/04/2025

Abstract

Introduction: Nodular lymphoid hyperplasia (NLH) is a benign condition characterized by diffuse hyperplasia of lymphoid follicles in the gastrointestinal tract, predominantly in the small intestine. In adults, it is rare, with an unknown sex distribution and a broad clinical spectrum ranging from asymptomatic presentation to nonspecific symptoms such as abdominal pain, flatulence, chronic diarrhea, malabsorption with weight loss, and even gastrointestinal bleeding. Diagnosis is based on characteristic endoscopic findings showing innumerable 2–10 mm nodules, along with histologic confirmation. NLH carries a potential risk for malignant transformation, and its optimal management remains uncertain. **Case presentation:** We describe two male patients in their second and third decades of life who presented with gastrointestinal bleeding and were ultimately diagnosed with NLH following endoscopic and histopathological evaluation. Notably, one patient had a significant surgical history, including appendectomy followed by right colectomy with end-to-end anastomosis for an appendiceal mass during childhood. The second patient presented with coexisting medication-induced liver injury. Both were managed conservatively. **Conclusions:** NLH should be considered in the differential diagnosis of gastrointestinal bleeding given its variable clinical spectrum. Its presence often reflects an underlying condition, most commonly related to immune system disorders. NLH is generally an incidental finding, and management focuses on treating the associated pathology while maintaining vigilant follow-up due to its potential for malignant transformation and the lack of standardized guidance regarding management and surveillance.

Keywords

Benign neoplasms, gastrointestinal hemorrhage, endoscopy, diagnosis, lymphoid tissue, case reports.

INTRODUCTION

Nodular lymphoid hyperplasia (NLH) is a rare, benign condition characterized by the presence of multiple small nodules, measuring between 2 and 10 mm in diameter, with diffuse hyperplasia of lymphoid follicles in the lamina propria and submucosa of the gastrointestinal tract[1]. It mainly involves the small intestine and is less commonly found in the colon and stomach[1,2]. The exact etiology is unknown; however, associations have been described with certain conditions such as immunoglobulin deficiency syndromes, *Helicobacter pylori* (*H. pylori*) infection, giardiasis, human immunodeficiency virus (HIV) infection, and celiac disease[2–5]. Its incidence and sex distribution are unknown. It can occur at any age, although it is more common in children[6]. Two types have been described—focal and diffuse—with the diffuse form being the most common. Clinical presentation is variable, ranging from asymptomatic cases to nonspecific

symptoms such as abdominal pain and flatulence, as well as chronic diarrhea, malabsorption syndromes with weight loss, and even gastrointestinal bleeding[2].

Diagnosis is established based on the classic endoscopic findings of innumerable nodules measuring 2–10 mm, along with histological confirmation showing hyperplastic B-cell follicles in the mucosa and submucosa with mitotically active germinal centers and well-defined lymphocytic mantles. These follicles are cytologically polymorphic and demonstrate lymphocytic polyclonality, confirmed by immunohistochemical or molecular analysis[2,6]. There is no specific treatment, and management is directed toward the associated condition[6]. Given the high risk of extraintestinal and intestinal lymphomas[1,7], NLH represents a risk factor for both intestinal and extraintestinal lymphoma, making diagnosis and follow-up crucial[1]. In adults, NLH infrequently causes gastrointestinal bleeding; the main presentations described include massive obscure bleeding[8,9], recurrent bleeding[10,11], and hematochezia[12]. It has been reported predominantly in immunocompromised patients and less frequently in immunocompetent individuals, and in a few cases no association with an underlying condition has been identified[6]. No association with post-surgical states has been established. Consequently, significant gaps remain in the understanding of this entity. We present two cases and discuss relevant clinical findings, which included gastrointestinal bleeding as the presenting manifestation, in which potential related stimuli—HIV, giardiasis, *H. pylori* infection, and celiac disease—were ruled out, as well as immunocompromise. One case had a history of prior ileocolonic surgery. These represent uncommon associations based on what has been reported to date.

CASE PRESENTATION

Case 1 Presentation

A 24-year-old male patient was admitted with a six-day history of episodes of hematochezia, followed by the onset of melena and epigastric pain, associated with asthenia, adynamia, and nausea. His medical history was notable for appendectomy at eight years of age, with subsequent right hemicolectomy and end-to-end anastomosis due to an appendiceal phlegmon in the setting of complicated acute appendicitis. On admission, he exhibited signs of low cardiac output, including mucocutaneous pallor, a heart rate of 128 beats/minute, and hypotension, with no other relevant findings. Vasopressor support was required, and acute anemia was documented, necessitating transfusional support (**Table 1**). Upper gastrointestinal endoscopy was performed, revealing erythematous corpoantral gastropathy and duodenal ulcers covered with fibrin. Colonoscopy was also performed and showed findings suggestive of nodular lymphoid hyperplasia (NLH) (**Figure 1**). Given these findings and the patient's young age, it was considered appropriate to exclude the presence of lesions in other segments of the small intestine; therefore, antegrade enteroscopy was performed, with no lesions identified in the proximal jejunum.

Table 1. Laboratory Studies Performed during Hospitalization and Outpatient Follow-up

Test	Admission	Follow-up at 41 Days
Leukocytes	4800/µL	4280/µL
Hemoglobin	9.1 g/dL	13 g/dL
Hematocrit	26%	39%
Platelets	250,000 µL	356,000 µL
Acute-phase reactants		
- CRP	1 mg/L	
Coagulation		
- PT	12 seconds	
- INR	1,03	
- PTT	28 seconds	
Renal function		
- Creatinine	1,07 g/dL	
Liver function		
- AST	13 U/L	
- ALT	18 U/L	
- Direct bilirubin	0.14 mg/dL	
- Indirect bilirubin	0.63 mg/dL	
- Total bilirubin	0.77 mg/dL	
Electrolytes		
- Sodium	141 mmol/L	
- Potassium	4.28 mmol/L	
Infectious studies		
- Hepatitis B	Negative	
- Hepatitis C	0.08	
- VDRL	Non-reactive	
- HIV	Negative	

ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; CRP: C-reactive protein; PT: prothrombin time; PTT: partial thromboplastin time; VDRL: Venereal Disease Research Laboratory; HIV: human immunodeficiency virus. Author's own research.

Because NLH was identified in the context of gastrointestinal bleeding, the question arises as to whether this represents the cause of bleeding or an incidental finding. In this case, bleeding was secondary to duodenal ulcers, whereas NLH was found in the colon; therefore, its relationship to the hemorrhagic event is not conclusive.

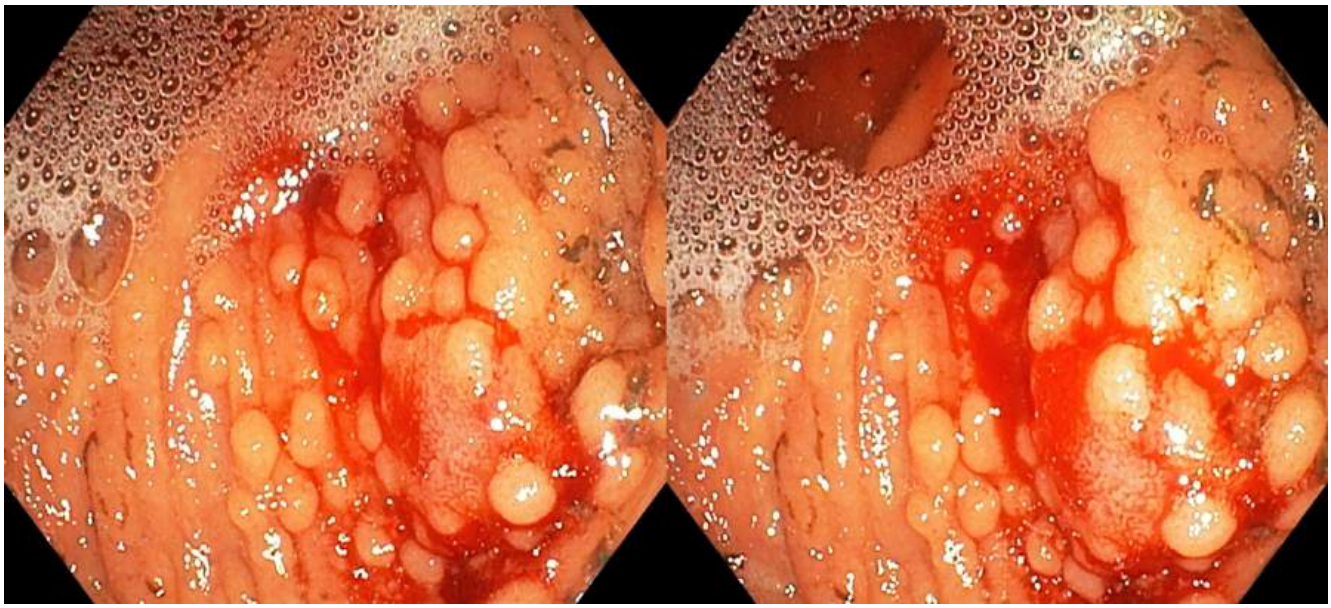


Figure 1. Colonoscopy showing multiple nodular and polypoid lesions, more than 30 in number, involving 100% of the circumference, with diameters ranging from 2 to 10 mm and an extension of approximately 8 cm at the level of the enterocolonic anastomotic loop. Biopsies were obtained. Author's file.

Regarding the patient's immune status, this possibility was explored because NLH has been described in immunocompromised patients. However, a history of appendectomy with right hemicolectomy does not necessarily imply immunosuppression. Although appendectomy may be associated with alterations in intestinal mucosal immunity due to the loss of lymphoid tissue of the appendix, this does not categorize all appendectomized patients as immunocompromised. In this case, it was considered appropriate to evaluate other possible causes of immunosuppression.

The patient subsequently showed an optimal clinical course, with no further need for transfusional support. He was discharged after five days and, at discharge, received empirical therapy for *H. pylori*, despite the absence of histological documentation, given the clinical context. Nevertheless, it was considered necessary to exclude other possible causes of duodenal ulcers before initiating this treatment.

At 41 days, he was evaluated on an outpatient basis, with no recurrence of gastrointestinal bleeding or anemia, and a histopathological report was obtained concluding reactive NLH (**Figure 2**). Given the presentation of this disease in immunocompromised patients, an evaluation for acquired or congenital etiologies was performed, with negative results for HIV infection and hepatitis B and C viruses. In addition, immunoglobulin levels were requested and are pending. To date, the patient has not presented recurrence of symptoms during six months of outpatient follow-up.

Case 2 Presentation

A 19-year-old patient was admitted to the emergency department with a four-month history of episodes of abdominal colic associated with abdominal distension and, occasionally, episodes of hematemesis and hematochezia. There was no relevant past medical history. On admission, vital signs were normal, and no significant findings were observed on physical examination. Laboratory tests showed no anemia and no abnormalities in the hepatic profile (**Table 2**).

Initial studies included an upper gastrointestinal endoscopy performed at admission, which demonstrated erythematous antral gastritis, with no findings suggestive of NLH, as well as a contrast-enhanced abdominal computed tomography (CT) scan without pathological findings. Given the persistence of abdominal pain, lack of therapeutic response to opioid analgesia, and inconclusive initial studies, an exploratory laparotomy was performed, with no evidence of surgical pathology to explain the pain.

Four days after the initial endoscopy, further endoscopic evaluation was undertaken. The second upper gastrointestinal endoscopy identified nodular-appearing mucosa at the level of the gastric antrum, with marked extrinsic compression of the posterior wall of the gastric body, a finding that had not been reported on the initial endoscopic study or the initial CT scan. Additionally, colonoscopy revealed findings suggestive of NLH in the distal ileum and right

colon, prompting biopsy sampling (**Figure 3**). Given the findings on upper gastrointestinal endoscopy, endoscopic ultrasound was performed, which identified gastric compression, possibly secondary to hepatomegaly.

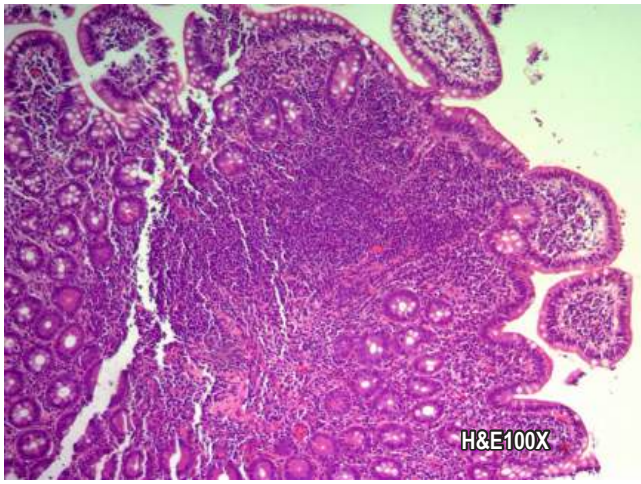


Figure 2. Ileal mucosa with dense lymphoid infiltrate in the lamina propria forming lymphoid follicles with active germinal centers. The epithelium shows mild villous atrophy with an increased number of intraepithelial lymphocytes. Author's file.

During the clinical course, elevated transaminase levels were identified, with predominance of alanine aminotransferase (ALT) and an R ratio of 4.8 (mixed pattern), associated with hepatomegaly on ultrasonography. Given the suspicion of hepatitis, studies for viral, autoimmune, metabolic, and infiltrative etiologies were ordered (**Table 2**), all of which were negative. A liver biopsy was performed, revealing foci of hemorrhagic necrosis and ischemia with minimal acute inflammation. Autoimmune hepatitis was initially considered; therefore, treatment with prednisolone 40 mg/day was initiated and serological studies were expanded (**Table 2**). Once the autoimmune workup was confirmed to be negative, this diagnosis was ruled out, corticosteroid therapy was tapered, and the clinical picture was considered more likely to correspond to drug-induced liver injury, specifically attributed to prolonged exposure to opioids (tramadol).

Subsequently, the patient continued to experience intermittent abdominal pain. A repeat contrast-enhanced abdominal CT scan demonstrated ileal stenosis, a finding that had not been visualized on the prior study. Repetition of the CT scan was deemed necessary to assess the evolution of the clinical course in the setting of persistent symptoms; subsequently, magnetic resonance enterography was performed, with no areas of obstruction identified. Given the unclear etiology of the abdominal pain and the absence of lesions on endoscopic studies, magnetic resonance entero-

Table 2. Laboratory Studies Performed during Hospitalization

Test	Results
Leukocytes	4,200/mm^3
Hemoglobin	15 g/dL
Hematocrit	44%
Platelets	196,000 µL
Acute-phase reactants	
- CRP	0.6 mg/dL
Coagulation	
- PT	11.9 s
- INR	1.06
- PTT	36.6 s
Renal function	
- Creatinine	0.9 mg/dL
- BUN	12 mg/dL
Liver function	
- AST	58 U/L
- ALT	129 U/L
- Total bilirubin	0.2 mg/dL
- Direct bilirubin	0.0 mg/dL
- Indirect bilirubin	0.2 mg/dL
- LDH	147 U/L
Electrolytes	
- Sodium	136 mEq/L
- Potassium	4.3 mEq/L
- Chloride	102 mEq/L
Infectious	
- Hepatitis B	0.68
- Hepatitis C	0.08
- Hepatitis A	15
- VDRL	Non-reactive
- HIV	Negative
Non-infectious	
- Ceruloplasmin	11.5 mg/mL
- Ferritin	119 ng/mL
- Transferrin saturation	41%
- Total iron	148 µg/dL
- Copper	70 µg/mL
- Fecal calprotectin	119 ng/mL
- Urinary porphobilinogen	0.5 mg/24 h
Autoimmunity	
- Immunoglobulin G	9895 mg/L
- Antinuclear antibodies	Negative
- Smooth muscle antibodies	Negative
- Extractable nuclear antibodies	Negative
- Anti-liver/kidney microsomal antibodies	Negative

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; INR: international normalized ratio; LDH: lactate dehydrogenase; CRP: C-reactive protein; PT: prothrombin time; PTT: partial thromboplastin time; VDRL: Venereal Disease Research Laboratory; HIV: human immunodeficiency virus. Author's own research.

graphy, and CT imaging, video capsule endoscopy (VCE) was indicated (**Figure 4**). This study ruled out involvement of the stomach, duodenum, and jejunum and identified NLH limited to the ileum (**Figure 5**) in a patient without immunocompromise and without association with infectious processes.

The patient demonstrated an adequate clinical course and was discharged after 10 days, without recurrence of

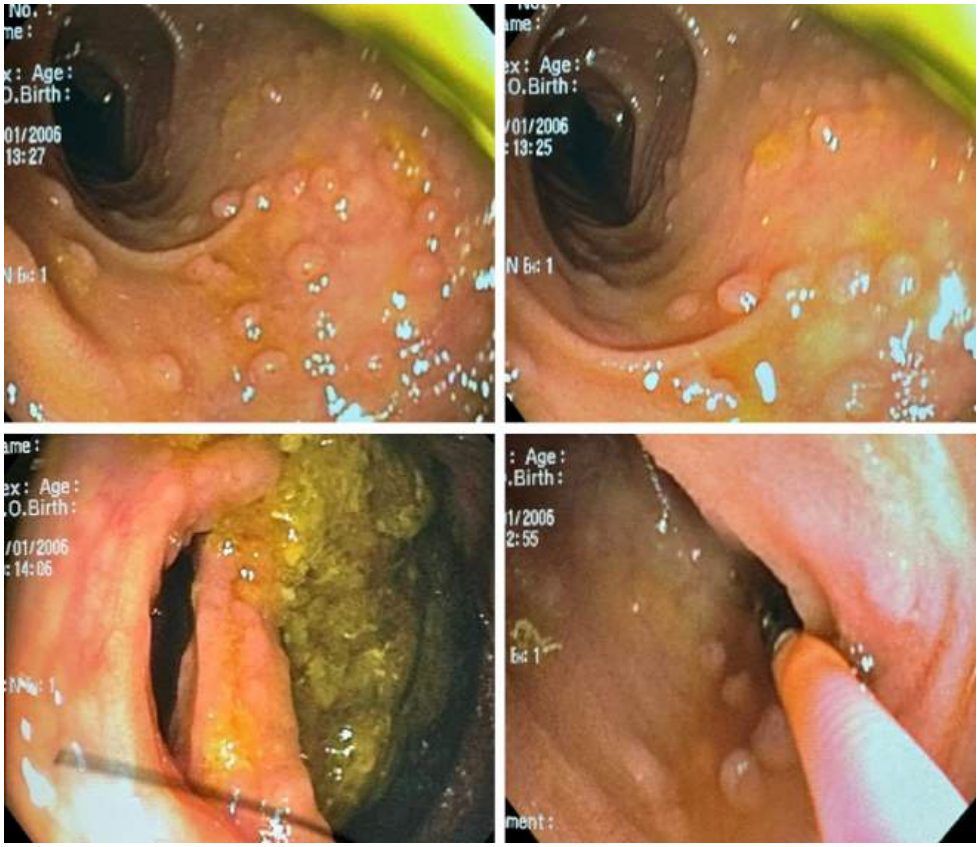


Figure 3. Colonoscopy showing multiple nodular lesions, more than 30 in number, involving 100% of the circumference, with diameters ranging from 2 to 10 mm and an extension of approximately 8 cm at the level of the distal ileum, ileocecal valve, cecum, and ascending colon. Biopsies were obtained. Author's file.



Figure 4. Video capsule endoscopy showing multiple nodular lesions with complete circumferential involvement, predominantly in the distal ileum, ileocecal valve, cecum, and ascending colon. Author's file.

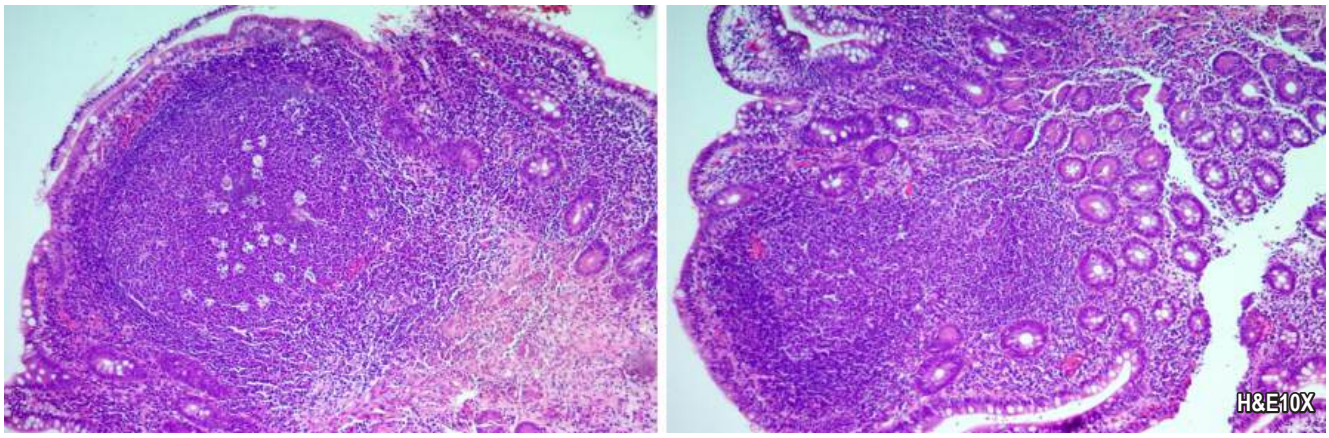


Figure 5. Ileal biopsy showing evidence of chronic inflammatory infiltrate, presence of lymphoid follicles with reactive germinal centers, and increased lymphocytic infiltrates within the villi, findings consistent with reactive nodular lymphoid hyperplasia. Author's file.

symptoms. Outpatient follow-up was scheduled for six months later.

DISCUSSION

Several features of these cases are noteworthy and warrant analysis in light of current knowledge. One of the characteristics that make these cases unique is that they involved young adults presenting with gastrointestinal bleeding. In one patient, there was a prior surgical history involving the ileum and proximal colon, in addition to the age at presentation and the absence of associated secondary pathology. Conversely, some typical features were also observed, including documentation of lesions predominantly involving the ileum and, in one case, achievement of clinical stability without recurrence of gastrointestinal bleeding following empirical therapy for *H. pylori*.

The proposed classification of NLH includes diffuse NLH and focal forms, which mainly affect the terminal ileum, rectum, or other areas of the digestive tract[13–15]. In adults, management is guided by the presence or absence of immunodeficiency[16], although NLH is usually associated with immunodeficiency and giardiasis[3]. In states of immunodeficiency, its presentation has been proposed to result from a compensatory state of intestinal lymphoid tissue with inadequate function, leading to the accumulation of plasma cell precursors due to defects in B-cell maturation and development[17]. Conversely, in the absence of immunodeficiency, NLH has been proposed to arise from immune stimulation of intestinal lymphoid tissue by antigenic triggers, possibly infectious, resulting in repetitive stimulation and eventual hyperplasia of lymphoid follicles[18]. Of the cases described, one corresponded to focal NLH with ileal involvement and absence of immunodeficiency; the other more likely represented diffuse NLH with gastric and ileal involvement, in which the main infectious agents associated with NLH were ruled out. This raises several hypotheses regarding prior noxious exposures related to the presentation in both cases: in one, ileal and proximal colon resection with end-to-end anastomosis; in the other, the inability to exclude unidentified infectious insults or antigenic stimulation during early life. Nor could the hypothesis proposed by Chiaramonte and colleagues[7] be excluded, in which NLH represents a transitional stage in the development of a malignant lesion or, possibly, an early-stage lymphoma.

The spectrum of entities associated with NLH is broad and includes selective immunoglobulin A (IgA) deficiency, celiac disease, common variable immunodeficiency, HIV infection, *H. pylori* infection, and giardiasis[3]. Many of these conditions have been described in both immunocompromised and immunocompetent patients; therefore, in the initial diagnostic approach, investigations are directed toward these etiologies. Conditions related to immunodeficiency have been described predominantly with diffuse involvement[6], showing classic endoscopic findings in the jejunum, ileum, and rectum, whereas giardiasis and *H. pylori* infection have been mainly associated with classic endoscopic findings in the stomach, duodenum, and proximal jejunum[3,6,19]. An association between NLH and non-exophytic colonic neoplasms, adenomas, and adenocarcinomas has also been suggested, with these entities showing classic endoscopic findings particularly in the terminal ileum[20]. It should also be noted that in other cases no association with any of these entities has been described, and the clinical and endoscopic behavior in such cases is even less well understood[21].

In both cases described, classic endoscopic findings were predominantly identified in the ileum; therefore, extended endoscopic and imaging studies were performed due to suspicion of neoplasia or adenomas in locations not assessable by initial endoscopic methods. It should also be noted that the decision to initiate empirical therapy for *H. pylori* in one of the described cases was supported by endoscopic findings of duodenal ulcers in the context of gastrointestinal bleeding, rather than by suspicion of NLH.

Both cases presented with gastrointestinal bleeding at onset. This clinical manifestation is unusual in the literature to date regarding NLH; moreover, in adults, this form of presentation is less well characterized than in the pediatric population[6,8,11]. Among bleeding manifestations, the best-described in adult NLH is hematochezia, followed to a lesser extent by obscure-origin bleeding and massive bleeding[9,22]. One of the patients described had duodenal ulcers with signs of recent bleeding, which was associated with greater severity of the bleeding episode requiring transfusional support. In both cases, ileal involvement by NLH was documented by colonoscopy with distal ileoscopy and by VCE.

Common causes of mid-gastrointestinal bleeding include angiodysplasias, intestinal tumors, ulcers, erosions, and entero-vascular fistulas[23]. In addition, NLH should be considered as a differential diagnosis after these entities in the context of overt obscure gastrointestinal bleeding in adults[22]. Definitive management in the setting of gastrointestinal bleeding remains highly debated in the literature to date and depends on the severity of the clinical presentation. Greater experience exists in pediatric patients, with therapeutic options ranging from conservative medical management to more radical approaches, including surgical or interventional treatment, the choice of which varies on a case-by-case basis[8,9]. In both cases, supportive care and clinical surveillance with symptomatic management were provided, with no other associated conditions identified. Treatment is directed toward management of associated conditions, as this disorder alone generally does not require intervention[24]. Surgical management represents a controversial measure and may result in unnecessary radical resections due to diagnostic difficulty[2].

In the cases described, periodic outpatient follow-up was considered and, depending on clinical evolution, additional imaging or endoscopic studies were to be considered. Currently, there is no consensus regarding follow-up in NLH; however, surveillance is recommended given the risk of malignant transformation[2]. Regarding the preferred modality for follow-up, imaging studies such as computed tomography enterography or barium contrast series may be useful; however, these modalities have limitations for the early detection of precancerous or cancerous lesions[25]. VCE and double-balloon enteroscopy represent excellent options for follow-up in NLH and are particularly useful for ruling out complications and determining disease extent[26]. However, they are not formally indicated for diagnosis or routine follow-up, and when considered, their limitations must be taken into account, including availability, cost, and the need for experienced personnel to perform them[2]. The duration and interval of follow-up have also not been defined. Consequently, follow-up in NLH represents a challenge in clinical practice due to the scarcity of recommendations or guidelines, limited information regarding its association with malignant conditions, and the lack of a single preferred modality. Therefore, decisions regarding follow-up should be guided by multiple factors, including age, the presence of alarm signs and symptoms, the type of NLH involvement documented, the presence of related secondary pathology, and associated immunocompromise.

CONCLUSIONS

NLH is a benign condition, infrequent in adults, with a variable clinical spectrum, whose presence usually indicates an underlying cause, most often related to immune system disorders. Management is focused on treatment of the associated condition, and NLH has been associated with malignant transformation. It represents a challenge in clinical practice, given the difficulty of diagnosis—which must be supported by endoscopic and histopathological findings—the limited information available on multiple aspects of the disease, and the absence of guidelines for standardized management and follow-up. Therefore, definitive decisions regarding treatment and follow-up should be guided by multiple factors that vary on a case-by-case basis.

DECLARATIONS

Ethical Approval and Participant Consent

This report was approved by the patient and their family.

Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Data and Material Availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Conflict of Interests

The authors declared no competing interests.

Funding

The authors received no financial support.

Author Contributions

All authors analyzed and interpreted the patient data, wrote the manuscript, analyzed and interpreted the images, and contributed to manuscript preparation. All authors read and approved the final manuscript.

REFERENCES

1. Pellegrini JR Jr, Russe-Russe J, Arias J, Prasandhan S. A Rare Case of Diffuse Nodular Lymphoid Hyperplasia With Rectal Involvement. Cureus. 2022;14(5):e24671. https://doi.org/10.7759/cureus.24671
2. Elkholy S, Mogawer S, Farag A. Nodular lymphoid hyperplasia of the gastrointestinal tract: A comprehensive review. Acta Gastroenterol Belg. 2017;80(3):405-10.
3. Khuroo MS, Khuroo NS, Khuroo MS. Diffuse duodenal nodular lymphoid hyperplasia: A large cohort of patients etiologically related to Helicobacter pylori infection. BMC Gastroenterol. 2011;11:1-2. https://doi.org/10.1186/1471-230X-11-36
4. Baran B, Gulluoglu M, Akyuz F. Nodular lymphoid hyperplasia of duodenum caused by Giardiasis. Clin Gastroenterol Hepatol. 2013;11(10):23333704. https://doi.org/10.1016/j.cgh.2012.12.019
5. Molaei M, Kaboli A, Fathi AM, Mashayekhi R, Pejhan S, Zali MR. Nodular lymphoid hyperplasia in common variable immunodeficiency syndrome mimicking familial adenomatous polyposis on endoscopy. Indian J Pathol Microbiol. 2009;52(4):530-3. https://doi.org/10.4103/0377-4929.56152
6. Albuquerque A. Nodular lymphoid hyperplasia in the gastrointestinal tract in adult patients: A review. World J Gastrointest Endosc. 2014;6(11):534-40. https://doi.org/10.4253/wjge.v6.i11.534
7. Chiaramonte C, Glick SN. Nodular lymphoid hyperplasia of the small bowel complicated by jejunal lymphoma in a patient with common variable immune deficiency syndrome. AJR Am J Roentgenol. 1994;163(5):1118-9. https://doi.org/10.2214/ajr.163.5.7976886
8. Shuhaiber J, Jennings L, Berger R. Nodular lymphoid hyperplasia: A cause for obscure massive gastrointestinal bleeding. J Pediatr Surg. 2005;40(4):E17-9. https://doi.org/10.1016/j.jpedsurg.2005.01.029
9. Jones DR, Hoffman J, Downie R, Haqqani M. Massive gastrointestinal haemorrhage associated with ileal lymphoid hyperplasia in Gaucher's disease. Postgrad Med J. 1991;67(787):479-81. https://doi.org/10.1136/pgmj.67.787.479
10. Freiman JS, Gallagher ND. Mesenteric node enlargement as a cause of intestinal variceal hemorrhage in nodular lymphoid hyperplasia. J Clin Gastroenterol. 1985;7(5):422-4. https://doi.org/10.1097/00004836-198510000-00010
11. Ersoy E, Gündodu H, Uraş NS, Aktimur R. A case of diffuse nodular lymphoid hyperplasia. Turkish J Gastroenterol. 2008;19(4):268-70.
12. Bharadhwaj G, Triadafilopoulos G. Endoscopic appearances of colonic lymphoid nodules: New faces of an old histopathological entity. Am J Gastroenterol. 1995;90(6):946-50.
13. Ranchod M, Lewin KJ, Dorfman RF. Lymphoid hyperplasia of the gastrointestinal tract. A study of 26 cases and review of the literature. Am J Surg Pathol. 1978;2(4):383-400. https://doi.org/10.1097/00000478-197812000-00005
14. Rambaud JC, De Saint-Louvent P, Marti R, Galian A, Mason DY, Wassef M, et al. Diffuse follicular lymphoid hyperplasia of the small intestine without primary immunoglobulin deficiency. Am J Med. 1982;73(1):125-32. https://doi.org/10.1016/0002-9343(82)90938-X
15. Hermans PE, Huizenga KA, Hoffman HN, Brown AL Jr, Markowitz H. Dysgammaglobulinemia associated with nodular lymphoid hyperplasia of the small intestine. Am J Med. 1966;40(1):78-89. https://doi.org/10.1016/0002-9343(66)90189-6
16. Ward EM, Wolfsen HC. Review article: The non-inherited gastrointestinal polyposis syndromes. Aliment Pharmacol Ther. 2002;16(3):333-42. https://doi.org/10.1046/j.1365-2036.2002.01172.x
17. Hermans PE, Diaz-Buxo JA, Stobo JD. Idiopathic late-onset immunoglobulin deficiency. Clinical observations in 50 patients. Am J Med. 1976;61(2):221-37. https://doi.org/10.1016/0002-9343(76)90173-X
18. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 8-1997. A 65-year-old man with recurrent abdominal pain for five years. N Engl J Med 1997;336(11):786-93. https://doi.org/10.1056/NEJM199703133361108
19. Rubio-Tapia A, Hernández-Calleros J, Trinidad-Hernández S, Uscanga L. Clinical characteristics of a group of adults with nodular lymphoid hyperplasia: A single center experience. World J Gastroenterol. 2006;12(12):1945-8. https://doi.org/10.3748/wjg.v12.i12.1945
20. Rubio CA. Nonprotruding colorectal neoplasms: Epidemiologic viewpoint. World J Surg. 2000;24(9):1098-103. https://doi.org/10.1007/s002680010147
21. Monsanto P, Lérias C, Almeida N, Lopes S, Cabral JE, Figueiredo P, et al. Intestinal nodular lymphoid hyperplasia and extraintestinal lymphoma - a rare association. Acta Gastroenterol Belg. 2012;75(2):260-2.

22. Buscaglia J, Carroll C, Daniels J, Marohn M. Benign lymphoid hyperplasia: a rare cause of obscure overt bleeding in an adult. Gastrointest Endosc. 2007;66(6):1248-50. https://doi.org/10.1016/j.gie.2007.04.004
23. Bashir RM, Al-Kawas FH. Rare causes of occult small intestinal bleeding, including aortoenteric fistulas, small bowel tumors, and small bowel ulcers. Gastrointest Endosc Clin N Am. 1996;6(4):709-38. https://doi.org/10.1016/S1052-5157(18)30337-4
24. Schwartz DC, Cole CE, Sun Y, Jacoby RF. Diffuse nodular lymphoid hyperplasia of the colon: Polyposis syndrome or normal variant? Gastrointest Endosc. 2003;58(4):630-2. https://doi.org/10.1067/S0016-5107(03)01969-2
25. Elkholy S. Diffuse Nodular Lymphoidhyperplasia with Selective IgA Deficiency Syndrome Presenting with Intestinal Lymphoma. MOJ Clin Med Case Reports. 2016;4(5):116-8. https://doi.org/10.15406/mojcr.2016.04.00105
26. Said-Criado I, Gil-Aguado A. Nodular lymphoid hyperplasia in common variable immunodeficiency. Lancet. 2014;383(9911):23870815. https://doi.org/10.1016/S0140-6736(13)60256-1

https://doi.org/10.22516/25007440.1299

Case report

Liver Transplantation as Treatment for Budd–Chiari Syndrome: Case Report

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Citation:
Montenegro AA, Florez-de-Moya HY, Gómez DM, Rico-Juri JM, Zapata M, Urrego J, Bustamante-Cristancho LA. Liver Transplantation as Treatment for Budd–Chiari Syndrome: Case Report. Revista. colomb. Gastroenterol. 2025;40(4):486-491. https://doi.org/10.22516/25007440.1299

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Received: 05/11/2024
Accepted: 30/05/2025

Abstract

Background: Polycythemia vera is a myeloproliferative neoplasm that leads to hyperviscosity, blood stasis, and a high risk of thrombotic complications. When these events affect the hepatic veins, they give rise to Budd–Chiari syndrome, characterized by elevated portal capillary hydrostatic pressure, predisposing patients to ascites, variceal bleeding, and hepatic dysfunction. Liver transplantation is considered in two principal clinical scenarios: fulminant hepatic failure and progressive cirrhosis, particularly when TIPS is not feasible. **Case summary**: We report the case of a 40-year-old woman with polycythemia vera and Budd–Chiari syndrome who, despite successful recanalization of the hepatic veins through anticoagulation, experienced clinical deterioration with progressive portal hypertension and refractory ascites. Her severity score and clinical decline (Rotterdam index 2.7 = class III, poor 3-month prognosis) supported the decision to proceed with a deceased-donor liver transplant, which was successfully performed. Sequential use of antiplatelet therapy, hydroxyurea, and anticoagulation prevented thrombotic complications without inducing bleeding. Outpatient follow-up showed no clinical signs of portal hypertension, including ascites or variceal bleeding. **Conclusion:** Budd–Chiari syndrome secondary to myeloproliferative disorders is uncommon, and its management must be individualized according to disease stage, comorbidities, and institutional expertise to achieve optimal patient outcomes.

Keywords

Polycythemia vera, Budd–Chiari syndrome, liver transplantation, acute myeloid leukemia secondary to myelodysplastic syndrome.

INTRODUCTION

Polycythemia vera is considered a myeloproliferative neoplasm characterized by the clonal expansion of an abnormal hematopoietic stem cell, resulting in elevated blood cell counts—predominantly red blood cells—which leads to hyperviscosity and blood stasis and, consequently, a predisposition to thrombotic complications[1] affecting both the arterial and venous vascular systems[2]. When the thrombotic event involves the inferior vena cava or the hepatic veins, it constitutes Budd-Chiari syndrome, which is characterized by a hemodynamic disturbance secondary to increased portal capillary hydrostatic pressure. This results in sinusoidal dilatation and leakage of fluid into the interstitial space, with a consequent increase in portal pressure and a reduction in hepatic perfusion, leading to cellular hypoxic injury[3].

Budd-Chiari syndrome is one of the indications for liver transplantation, usually associated with two forms

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of disease presentation: fulminant hepatitis or cases of progressive cirrhosis, particularly when transjugular intrahepatic portosystemic shunt (TIPS) placement is not feasible[4]. We present a case of cirrhosis due to Budd-Chiari syndrome in a patient who was not a candidate for TIPS because of recanalization of the hepatic veins resulting from anticoagulation therapy.

CLINICAL CASE

We report the case of a 40-year-old female patient with no significant past medical history, who had been diagnosed with Janus kinase 2 (JAK2)-positive polycythemia vera 12 years earlier. Four years prior to the current clinical presentation, partial thrombosis of the portal vein and hepatic veins was documented (**Figure 1**). She was therefore treated with anticoagulation using warfarin (2.5 mg five days per week alternating with 5 mg two days per week), without achieving adequate control of the international normalized ratio (INR) during follow-up. Anticoagulation was subsequently switched to apixaban, in combination with hydroxyurea (500 mg daily). Ten months later, a repeat abdominal computed tomography scan demonstrated recanalization of the portal vein thrombosis and a high suspicion of recanalization of the hepatic vein thrombosis, which was later confirmed by cavography.

Despite continued anticoagulation and evidence of recanalization of the hepatic vein thrombosis, over the last four months the patient progressively developed symptoms consistent with large-volume ascites (greater than 10 liters), requiring frequent drainage (approximately every two weeks). This was accompanied by marked weight loss (approximately 15 kg over the same period) and an episode of hepatic encephalopathy classified as grade III according to the West Haven criteria, which required hospitalization in the intensive care unit, in addition to several grade I–II episodes managed on an outpatient basis. During hepatology follow-up, liver cirrhosis was diagnosed based on the clinical presentation, laboratory findings (**Table 1**), and imaging studies (transient elastography showing 14.16 kPa, compatible with cirrhosis; reference >11.9 kPa). Other etiologies were ruled out, including alcoholic liver disease, metabolic dysfunction-associated fatty liver disease, and autoimmune or infectious liver disease (negative antinuclear and anti-smooth muscle antibodies, negative hepatitis B surface antigen, and negative hepatitis C antibodies). Given advanced liver dysfunction associated with encephalopathy and a Rotterdam score of 2.7, the patient was classified as class III (poor three-month prognosis). Evaluation for liver transplantation was therefore pursued, and the possibility of TIPS placement was ruled out. In a multidisciplinary meeting, she was listed for transplantation with a Child-Pugh class B (9 points) and a MELD-Na score of 16.

Three months after being placed on the waiting list, a graft from a deceased donor became available. Intraoperative findings revealed changes consistent with severe portal hypertension, including the presence of splenorenal and retroperitoneal shunts and recanalization of the umbilical veins, as well as hepatomegaly, with a liver weight of 2,780 g. Orthotopic liver transplantation was performed without recorded complications (total ischemia time of 10 hours and 29 minutes; warm ischemia time of 35 minutes).

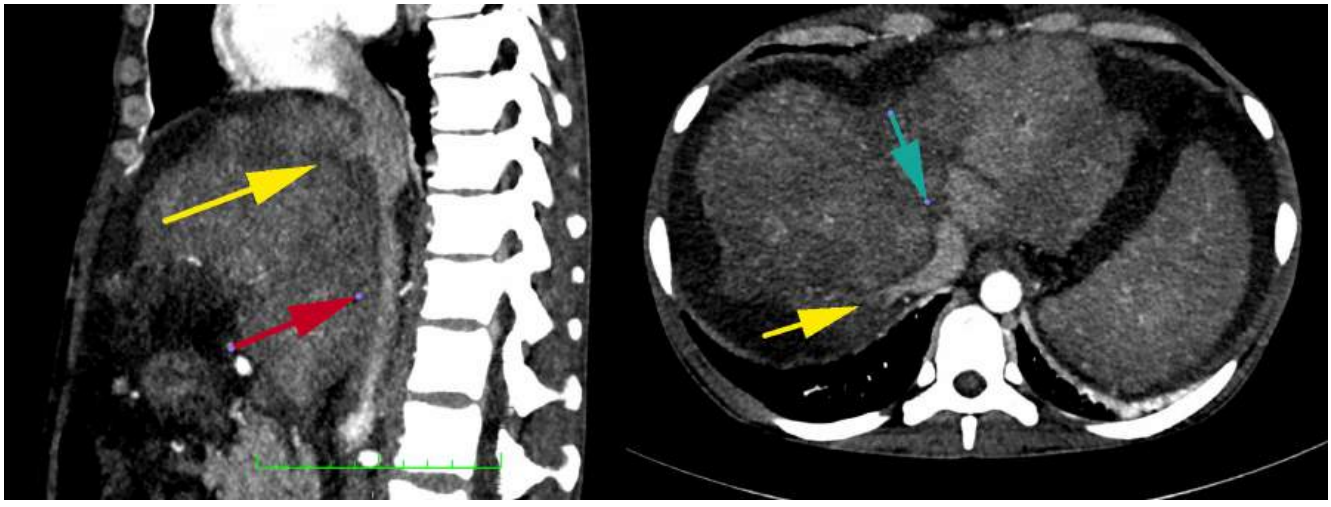


Figure 1. Abdominal CT Angiography Acquired in the Arterial Phase. The right hepatic vein shows flow interruption, suggesting chronic-appearing occlusion (yellow arrow). The middle hepatic vein also shows flow interruption, suggesting chronic-appearing occlusion (green arrow). The retrohepatic inferior vena cava shows reduced caliber without thrombosis or occlusion (red arrow). Author's file.

Table 1. Paraclinical Follow-up and Portal Doppler after Transplantation

	Outpatient Follow-up	Day 1	Day 3	Day 5
ALT (U/L)	22	623	366	230
AST (U/L)	17	1087	159	51
INR	1.35	2.83	1.42	-
Total bilirubin (mg/dL)	0.30	2.89	0.58	0.56
Direct bilirubin (mg/dL)	0.15	2.45	0.40	0.3
Hemoglobin (g/dL)	11	10.7	7.6	7.7
Creatinine (mg/dL)	0.66	0.65	0.82	0.85
Tacrolimus levels (ng/mL)	NA	-	-	5.0
Portal Doppler hepatic artery RI	NA	0.62 (12 h)	0.6 (24 h)	0.67 (48 h)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; RI: resistance index; NA: not applicable. Author's own research.

Postoperatively, the patient was transferred to the intensive care unit with invasive mechanical ventilatory support and vasopressors. She subsequently showed satisfactory evolution, with withdrawal of ventilatory support and complete discontinuation of vasopressors after 48 hours in the unit. Immunosuppression was administered according to the institutional protocol (tapering doses of methylprednisolone and tacrolimus). During the first 24 hours, antiplatelet therapy with acetylsalicylic acid (ASA) (100 mg/day) and hydroxyurea 500 mg/day was indicated. Enoxaparin (40 mg subcutaneously once daily) was initiated within the first 48 hours, with no evidence of bleeding complications.

After completing 48 hours in the intensive care unit, transfer to the general ward was indicated. Her clinical course was satisfactory, with improvement in cytolysis, cholestasis, and liver function parameters (**Table 1**). Given the high thromboembolic risk, serial portal Doppler evaluations were performed at 12, 24, and 48 hours in the unit, all showing normal findings (**Table 1**). She was discharged on postoperative day five with instructions for outpatient medical management, including prednisolone 20 mg/day, extended-release tacrolimus 2 mg/day, hydroxyurea 500 mg/day, ASA 100 mg/day, trimethoprim/sulfamethoxazole 160/800 mg three times per week, enoxaparin 40 mg subcutaneously once daily for one month, fluconazole 200 mg/day for 21 days, and furosemide 40 mg/day.

At the two-month follow-up visit, the patient showed adequate clinical progression, with no new episodes of ascites, variceal bleeding, or hepatic encephalopathy. At the most recent follow-up, a weight gain of 1 kg compared with her previous weight was documented.

DISCUSSION

Polycythemia vera is considered a myeloproliferative neoplasm characterized by the clonal expansion of an abnormal hematopoietic stem cell, resulting in elevated blood cell counts—predominantly red blood cells—most commonly due to different mutations in the JAK2 tyrosine kinase gene. Approximately 97% of these mutations correspond to JAK2 V617F, which results from a somatic guanine-to-thymine mutation involving exon 14 of the JAK2 gene. This leads to a nucleotide change at position 1849 and the substitution of valine by phenylalanine at codon 617[5,6]. The pathophysiological consequence is stasis due to hyperviscosity and an increased risk of thrombotic events associated with blood stasis. Thrombotic events usually occur in the venous system and are more prevalent in women, whereas arterial thrombosis is less frequent[2]. In the present case, the diagnosis of polycythemia vera was supported by the course of erythrocytosis, thrombotic phenomena, and the presence of a JAK2 mutation; accordingly, the patient was being followed on an outpatient basis by hematology.

Budd-Chiari syndrome is defined as hepatic venous outflow obstruction, leading to hypotrophy or atrophy of the affected hepatic segment and hypertrophy of the remaining segments, with symptoms that depend on the extent of the obstructive involvement. The consequence of this obstruc-

tion is a hemodynamic disturbance caused by increased portal capillary hydrostatic pressure, which alters vascular pressure gradients. These hemodynamic changes translate into sinusoidal dilatation and leakage of fluid into the interstitial space, passing through the hepatic capsule when lymphatic drainage capacity is exceeded, with a consequent increase in portal pressure and a reduction in hepatic perfusion, resulting in cellular hypoxic injury[3]. In the present case, thrombosis of the hepatic veins established the diagnosis of Budd-Chiari syndrome, and the patient also developed symptoms related to clinically evident portal hypertension due to the presence of large-volume ascites.

Budd-Chiari syndrome is one of the indications for liver transplantation and is usually associated with two forms of disease presentation. The first is fulminant hepatitis with secondary cirrhosis, which results from acute obstruction of hepatic venous outflow, leading to hepatic congestion and rapid-onset dysfunction. The second presentation is subacute, consisting of gradually developing liver injury, likely because some patients develop intrahepatic and portosystemic collaterals and may therefore remain asymptomatic for prolonged periods[4]. When symptoms of portal hypertension develop, clinical manifestations such as persistent ascites, esophageal varices, or variceal bleeding may occur[7]. The reported case fits the second form of presentation, given its chronic course and the presence of portal hypertension associated with portosystemic collaterals. In this patient, recanalization of the hepatic veins was confirmed by cavography, likely related to chronic anticoagulation; however, the clinical course suggests progressive disease characterized by persistent ascites and other complications, such as spontaneous bacterial peritonitis or hepatic encephalopathy. This indicates that the patient developed liver cirrhosis, probably secondary to Budd-Chiari syndrome, which did not resolve despite recanalization of the hepatic veins.

Recent publications suggest that the prognosis of patients undergoing liver transplantation for Budd-Chiari syndrome is comparable to that of other etiologies[8], provided that anticoagulant therapy is maintained postoperatively[9]. However, in patients with myelodysplastic syndromes, outcomes appear to be somewhat less favorable in terms of survival[10]. In this regard, one study followed 14 patients after liver transplantation indicated for Budd-Chiari syndrome and reported three postoperative deaths due to primary graft nonfunction, heart failure, and intra-abdominal sepsis; another patient died from recurrence of Budd-Chiari syndrome 19 months after transplantation. Early complications described included gastrointestinal bleeding, cholangitis and mechanical ileus, fistula and intra-abdominal abscess, pleural effusion, and surgical site infection. Three patients required intervention with endoscopic retrograde cholangiopancreatography and stent placement for biliary leaks. Nevertheless, one- and five-year survival rates were 87% and 71%, respectively[11], making liver transplantation an attractive therapeutic alternative for patients with fulminant liver failure and for those with portal hypertension refractory to medical management, particularly when TIPS is not feasible.

For the reported case, the indication for liver transplantation without TIPS was based on three main reasons. First, follow-up imaging studies demonstrated recanalization of the hepatic veins, suggesting that the clinical deterioration was most likely related to liver cirrhosis as a consequence of Budd-Chiari syndrome. Second, the clinical course was associated with hepatic encephalopathy, which could worsen with the use of TIPS. Finally, the third argument was related to the deterioration in quality of life in a young patient, in whom recurrent episodes of large-volume ascites and an episode of encephalopathy translate into increased mortality. It should be noted that, in this context, liver transplantation carries a higher risk of hepatic vascular thrombosis (arterial, venous, and portal) compared with liver transplantation for other etiologies; likewise, survival is lower than that observed for other indications for liver transplantation. Despite this, in several scenarios it becomes the only therapeutic alternative with acceptable survival rates. Recent literature has shown that 10-year survival after liver transplantation is not modified by prior TIPS placement or the absence thereof[12], allowing us to infer that appropriate patient selection based on disease assessment, comorbidities, and the experience of the treating center is critical when choosing the optimal therapy.

In the country, few studies have been published with follow-up of patients with Budd-Chiari syndrome. The first study characterized a cohort of 31 patients in the city of Bogotá, identifying a prothrombotic factor as the main etiology and, secondarily, myelodysplastic syndrome. In that cohort, 80% of patients received anticoagulation, 19% underwent TIPS, and 16% underwent liver transplantation. The reported mortality was 25.8%, with a mean survival of 337 days, compared with the death of two patients who underwent liver transplantation (12.5%)[13]. A second patient cohort was published in the city of Medellín, describing a subacute presentation of this condition in 35 patients; only 20 patients received recanalization treatment by different methods, and of these, only 20% underwent orthotopic liver transplantation[14]. In the present case report, survival of 12 months has been observed at the time of reporting, in the absence of complications such as portal hypertension, hepatic encephalopathy, or spontaneous bacterial peritonitis. Likewise, no complications such as vascular thrombosis have been recorded during the postoperative follow-up period.

In the post-liver transplantation follow-up of patients with polycythemia vera and Budd-Chiari syndrome, efforts focus on preventing recurrence of thrombotic events through the use of anticoagulants or antiplatelet agents. Lifelong anticoagulation with low-molecular-weight heparin has been considered, with warfarin as an alternative, adjusted to maintain an INR of 2–3[3]. However, during a mean follow-up of 28.2 months in 16 patients, several thrombotic events were reported (three in the portal vein, one in the hepatic artery, and one in the axillary vein), along with an even more concerning rate of hemorrhagic complications of 44%[15]. Additionally, reports have described management with hydroxyurea and aspirin instead of anticoagulant therapy in patients with documented myelodysplastic disorders, based on the theoretical cause of qualitative and quantitative platelet abnormalities. In these reports, aspirin was administered at a dose of 325 mg/day and hydroxyurea at doses ranging from 500 to 1,500 mg/day, initiated four to seven days after transplantation, with excellent long-term outcomes: 90% of treated patients did not develop new thrombotic events during up to 59.9 months of follow-up, and a 15-year survival rate of 73% was reported[15,16]. In the present case, early initiation of ASA, thromboprophylaxis with low-molecular-weight heparins, and hydroxyurea was chosen, with no documented recurrence of thrombotic events during the 12 months of postoperative follow-up, in the absence of bleeding and with a satisfactory clinical course that allowed hospital discharge on the fifth postoperative day after liver transplantation.

CONCLUSION

Polycythemia vera is associated with thrombotic phenomena, occasionally involving the hepatic veins and resulting in Budd-Chiari syndrome. This rare entity is associated with portal hypertension and complications such as variceal bleeding and hepatic encephalopathy. Treatment should be individualized according to disease progression, comorbidities, and the experience of the treating center. We present a case of liver cirrhosis due to Budd-Chiari syndrome successfully treated with liver transplantation.

REFERENCES

1. Iurlo A, Cattaneo D, Bucelli C, Baldini L. New perspectives on polycythemia vera: From diagnosis to therapy. Int J Mol Sci. 2020;21(16):1-16. https://doi.org/10.3390/ijms21165805
2. Tefferi A, Rumi E, Finazzi G, Gisslinger H, Vannucchi AM, Rodeghiero F, et al. Survival and prognosis among 1545 patients with contemporary polycythemia vera: An international study. Leukemia. 2013;27(9):1874-81. https://doi.org/10.1038/leu.2013.163
3. Correa-Gaviria S, Ramírez AC, Espinoza-Herrera YP, Restrepo-Gutiérrez JC. A Review of Budd Chiari Syndrome. Rev Colomb Gastroenterol. 2016;31(3):242-52.
4. Min AD, Atillasoy EO, Schwartz ME, Thiim M, Miller CM, Bodenheimer HC Jr, et al. Reassessing the role of medical therapy in the management of hepatic vein thrombosis. Liver Transpl Surg. 1997;3(4):423-9. https://doi.org/10.1002/lt.500030410
5. Tefferi A. Myeloproliferative neoplasms: A decade of discoveries and treatment advances. Am J Hematol. 2016;91(1):50-8. https://doi.org/10.1002/ajh.24221
6. Pardanani A, Lasho TL, Finke C, Hanson CA, Tefferi A. Prevalence and clinicopathologic correlates of JAK2 exon 12 mutations in JAK2V617F-negative polycythemia vera. Leukemia. 2007;21(9):1960-3. https://doi.org/10.1038/sj.leu.2404810
7. Pedersen MR, Molloy P, Wood D, Seetharam A. Direct intrahepatic portocaval shunt for treatment of portal thrombosis and Budd-Chiari syndrome. Ann Hepatol. 2016;15(1):127-30. https://doi.org/10.5604/16652681.1184288
8. Aktas H, Ozer A, Yilmaz TU, Keceoglu S, Can MG, Emiroglu R. Liver transplantation for Budd-Chiari syndrome: A challenging but handable procedure. Asian J Surg. 2022;45(7):1396-402. https://doi.org/10.1016/j.asjsur.2021.09.007
9. Dongelmans E, Erler N, Adam R, Nadalin S, Karam V, Yilmaz S, et al. Recent outcomes of liver transplantation for Budd-Chiari syndrome: A study of the European Liver Transplant Registry (ELTR) and affiliated centers. Hepatology. 2024;80(1):136-51. https://doi.org/10.1097/HEP.0000000000000778
10. Ibach M, Eurich D, Dobrindt E, Lurje G, Schöning W, Öllinger R, et al. Orthotopic liver transplantation for Budd-Chiari syndrome: Observations from a 30-year liver transplant program. Medicina (Kaunas). 2021;57(8):821. https://doi.org/10.3390/medicina57080821
11. Doğrul AB, Yankol Y, Mecit N, Kanmaz T, Acarlı K, Kalayoğlu M. Orthotopic liver transplant for Budd-Chiari Syndrome: An analysis of 14 cases. Exp Clin Transplant. 2016;14(6):641-5. https://doi.org/10.6002/ect.2015.0026
12. Alqahtani SA, Schneider C, Sims OT, Gurakar A, Tamim H, Bonder A, et al. Liver Transplantation for Budd-Chiari Syndrome in the MELD Era. Transplant Direct.

2022;8(12):e1407.
https://doi.org/10.1097/TXD.0000000000001407
13. Morales Cruz XP, Rojas Kozhakin DV. Características clínicas, manejo y sobrevida de pacientes con síndrome de Budd-Chiari en un centro de hepatología colombiano. [Tesis de grado]. [consultado el 24 de agosto de 2024]. Repositorio Universidad del Rosario. 2022. https://doi.org/10.48713/10336_38068
14. Muñoz-Maya O, Vergara-Cadavid JA, Cajiao-Castro L, Santos OM, Marín-Zuluaga JI, Restrepo-Gutiérrez JC. Síndrome de Budd-Chiari: etiología, manejo y resultados en una cohorte de 35 pacientes del Hospital Pablo Tobón Uribe. Rev. colomb. Gastroenterol. 2019;35(3):280-6. https://doi.org/10.22516/25007440.431
15. Melear JM, Goldstein RM, Levy MF, Molmenti EP, Cooper B, Netto GJ, et al. Hematologic aspects of liver transplantation for Budd-Chiari syndrome with special reference to myeloproliferative disorders. Transplantation. 2002;74(8):1090-5. https://doi.org/10.1097/00007890-200210270-00006
16. Pavri TM, Herbst A, Reddy R, Forde KA. Budd-Chiari syndrome: A single-center experience. World J Gastroenterol. 2014;20(43):16236-44. https://doi.org/10.3748/wjg.v20.i43.16236

https://doi.org/10.22516/25007440.1300

Case report

NSAID-Induced Esophagitis: An Uncommon Cause of Severe Eosinophilic Infiltration

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OPEN ACCESS

Citation:
Aliaga Ramos J, Arantes V. NSAID-Induced Esophagitis: An Uncommon Cause of Severe Eosinophilic Infiltration. Revista. colomb. Gastroenterol. 2025;40(4):492-496.
https://doi.org/10.22516/25007440.1300

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Received: 12/11/2024
Accepted: 06/05/2025

Abstract

Background: Drug-induced esophagitis is an underdiagnosed condition, largely due to the inadequate clinical assessment these patients often receive. A thorough medical history is essential for establishing a correct diagnosis. Early identification is crucial for proper management and counseling, helping to prevent recurrent episodes that may significantly impair quality of life. Upper endoscopy and histopathological examination are fundamental to clarifying the diagnosis and excluding other conditions with similar presentations. Severe eosinophilic infiltration, although uncommon in drug-induced esophagitis, may resemble other disorders such as eosinophilic esophagitis. **Case report:** We present the case of a young patient who developed severe dysphagia following exposure to nonsteroidal anti-inflammatory drugs (NSAIDs). Upper endoscopy revealed pronounced inflammation with marked eosinophilic infiltration on histopathological evaluation. Symptoms resolved fully after discontinuing NSAIDs and initiating proton pump inhibitor therapy, with no recurrence over the medium- to long-term follow-up. **Conclusions:** Drug-induced esophagitis should be recognized as a potential cause of severe eosinophilic infiltration and may even mimic the endoscopic and histologic profile traditionally associated with other conditions, such as eosinophilic esophagitis.

Keywords

Esophagitis, nonsteroidal anti-inflammatory agents, eosinophilic esophagitis.

INTRODUCTION

Several drugs have now been identified as responsible for the development of esophagitis of varying degrees of severity, the most common being antibiotics (primarily tetracyclines) and nonsteroidal anti-inflammatory drugs (NSAIDs). There is no consensus defining the clinical-epidemiological profile of this condition; however, most studies agree that an atopic component in genetically predisposed individuals is a frequent feature in this group of patients[1–9].

The most characteristic clinical presentation of this condition is retrosternal pain and dysphagia of recent onset following ingestion of the potentially causative drug. In most cases, the disease is self-limited and without serious complications; however, certain pharmacologic groups, such as NSAIDs, have been associated with more severe (gastrointestinal bleeding and/or esophageal stricture) and prolonged symptoms. Upper gastrointestinal endoscopy is currently considered the best diagnostic modality to characterize and analyze the esophageal lesions produced. The most frequent findings include superficial ulcers with regular margins and an inflammatory appearance, generally located in the middle and upper thirds of the esophagus, classically described in the literature as "kissing ulcers," often accompanied by erythematous and congestive areas. However, it is unusual to find whitish longitudinal furrows,

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which represent the endoscopic manifestation of severe eosinophilic infiltration of the esophageal mucosa[10–13].

Histologic examination is very useful because it helps exclude other entities such as malignant neoplasms. In most cases, it shows only an acute inflammatory reaction composed of a marked neutrophilic infiltrate, with a severe eosinophilic component being rarely observed in the examined samples[14–18].

Here, we present a case of NSAID-induced esophagitis that exhibited a severe eosinophilic inflammatory component with endoscopic representation and responded successfully to treatment with proton pump inhibitors in association with withdrawal of the offending drug.

CASE DESCRIPTION

A 23-year-old male patient with a history of allergic rhinitis presented with the sudden onset, following the use of NSAIDs (naproxen) prescribed for an odontogenic condition, of moderate-intensity retrosternal burning pain associated with dysphagia for both solid and liquid foods (Atkinson dysphagia scale: 4). The complete blood count showed peripheral blood eosinophils of 395.5 eosinophils/μL (normal range: ≤500 eosinophils/μL) and a serum immunoglobulin E (IgE) level of 189.8 IU/mL (normal range: 0–99.9 IU/mL).

Upper gastrointestinal endoscopy revealed a superficial ulcer with an inflammatory appearance and regular, congestive margins, located in the middle third of the esophagus and involving approximately 40% of the circumference (**Figure 1A**). Multiple whitish exudates were also observed in the lower third of the esophagus, associated with erosions and erythematous areas (**Figures 1B** and **1C**).

Histologic analysis showed a marked eosinophilic infiltrate (20 eosinophils/HPF), predominantly involving the epithelium, lamina propria, and submucosa (**Figure 2**). NSAIDs were discontinued, and treatment with proton pump inhibitors was initiated, with clinical, endoscopic, and histologic remission observed after eight weeks, without recurrence.

DISCUSSION

At present, there is limited scientific evidence demonstrating the true clinical impact of this condition in the affected population. Likewise, there are no international consensuses that clearly define diagnostic and therapeutic guidelines for drug-induced esophagitis. Our study consolidates the knowledge established to date, but with an atypical endoscopic-histologic profile, mimicking other clinical entities associated with esophageal eosinophilia.

A major challenge for the gastroenterologist is distinguishing drug-induced esophagitis from eosinophilic esophagitis when atypical variations are present in some cases. The most recent guidelines on the diagnosis and treatment of eosinophilic esophagitis have clearly established the endoscopic and histologic criteria for identifying this condition[1–5]. However, to date, there is no international consensus defining the parameters for drug-induced esophagitis, as most of the available scientific evidence is based solely on case reports[6–13]. Consequently, when a combination of similar endoscopic and histologic criteria exists for these two cli-

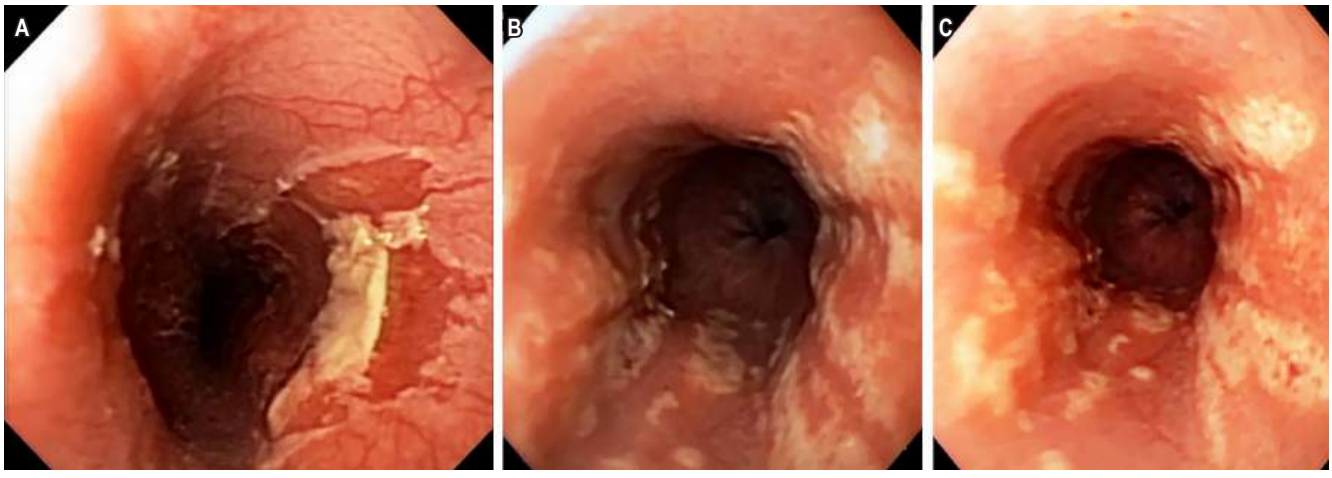


Figure 1. A. Esophageal ulcer. **B, C.** Whitish exudates. Author's file.

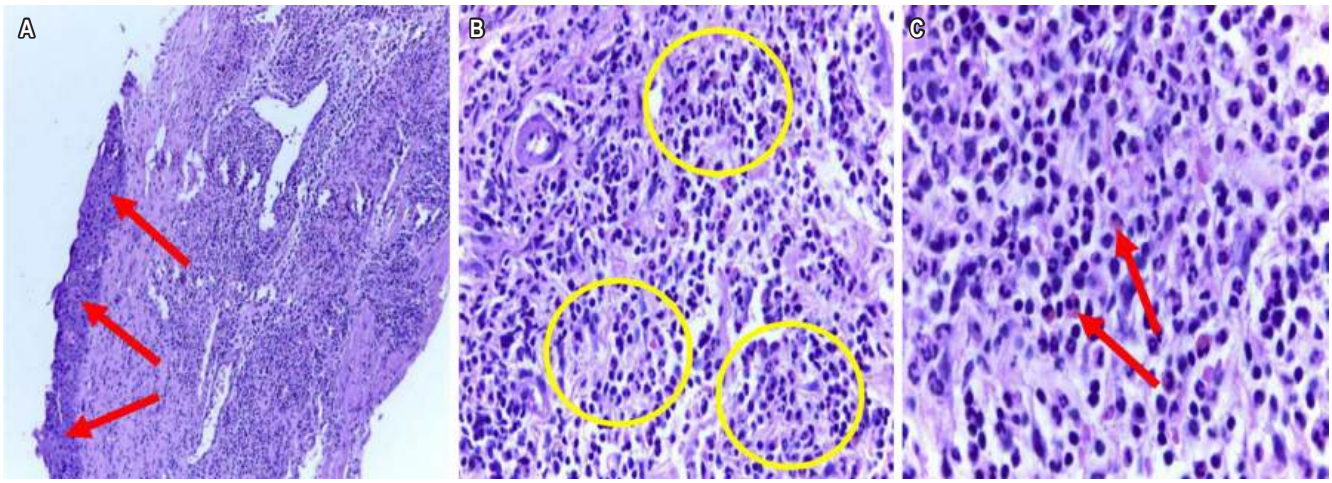


Figura 2. A. Red arrows: panoramic view showing involvement of the esophageal epithelium and mucosa by a severe eosinophilic infiltrate. **B.** Yellow circles: involvement of the stroma and submucosa by eosinophilic infiltration. **C.** Red arrows: close-up view of eosinophils with their granules. Author's file.

nical entities, it is essential to differentiate them accurately through a detailed epidemiologic history and a thorough clinical interview, as was done in the patient we present.

Currently, there are no studies that demonstrate the exact pathophysiology of this exaggerated eosinophilic infiltrate in certain patients with drug-induced esophagitis; however, this finding may be explained by a marked atopic component, mediated by hypersensitivity reactions to certain medications[14–18]. For this reason, it is important to evaluate specific factors in this group of patients, such as immunoallergic characteristics or inadequate fluid intake at the time of drug ingestion, as both may contribute to triggering new events in the medium and long term. Our patient had a history of allergic rhinitis, peripheral eosinophilia, and elevated serum IgE levels as markers of an underlying allergic component.

CONCLUSION

Drug-induced esophagitis is a clinical entity that should be considered among the etiologies capable of generating severe eosinophilic infiltration, which may even produce an endoscopic-histologic profile similar to that traditionally described in other conditions such as eosinophilic esophagitis. Likewise, it is necessary to evaluate the immunoallergic component and accurately identify the responsible drug in order to appropriately counsel this group of patients and prevent new events in the medium to long term.

Informed Consent

The authors declare that informed consent was obtained from the patient in this case.

Conflict of Interest

The authors declare no conflict of interest.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

Author Contributions

Study conception and design: all authors; data and information acquisition: all authors; article planning: all authors; critical revision of important intellectual content: all authors; final approval of the version to be published: all authors.

Acknowledgments

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REFERENCES

1. Dellon ES, Muir AB, Katzka DA, Shah SC, Sauer BG, Aceves SS, et al. ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis. Am J Gastroenterol. 2025;120(1):31-59. https://doi.org/10.14309/ajg.0000000000003194
2. Hirano I, Chan ES, Rank MA, Sharaf RN, Stollman NH, Stukus DR, et al. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. Ann Allergy Asthma Immunol. 2020;124(5):416-23. https://doi.org/10.1016/j.anai.2020.03.020
3. Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: Proceedings of the AGREE conference. Gastroenterology. 2018;155(4):1022-33. https://doi.org/10.1053/j.gastro.2018.07.009
4. Juliao-Baños F, Lúquez-Mindiola A. Esofagitis eosinofílica: estado del arte en 2024. Rev Colomb Gastroenterol. 2024;39(4):435-46. https://doi.org/10.22516/25007440.1276
5. Castaño R, Rivera J, Diazgranados L, Baena JD, Puerta Botero JE, Cadavid I, et al. Esofagitis eosinofílica y las diferencias clínicas, endoscópicas y terapéuticas entre adolescentes y adultos. Rev Colomb Gastroenterol. 2024;39(4):376-85. https://doi.org/10.22516/25007440.1137
6. Yoshikawa T , Hara T, Araki H, Tsurumi H, Oyama M, Moriwaki H. First report of drug-induced esophagitis by deferasirox. Int J Hematol. 2012;95(6):689-91. https://doi.org/10.1007/s12185-012-1060-7
7. Apostolov R, Tan N, Vasudevan A. A difficult pill to swallow: drug-induced oesophagitis. Lancet 2019;394(10210):1764. https://doi.org/10.1016/S0140-6736(19)32565-6
8. Kim SH, Jeong JB, Kim JW, Koh SJ, Kim BG, Lee KL, et al. Clinical and endoscopic characteristics of drug-induced esophagitis. World J Gastroenterol. 2014;20(31):10994-9. https://doi.org/10.3748/wjg.v20.i31.10994
9. Arhinful JS, Arhinful B, Akins TA, Hossain S. Caffeine-Induced Severe Erosive Esophagitis. Cureus 2021;13(7):1-3. https://doi.org/10.7759/cureus.16253
10. Rivero-Borrell de la Parra P, González-Cruz M, Ferreiro-Marin A, Casaubón-Garcín PR. L-arginine-induced esophagitis, report of six cases. Bol Med Hosp Infant Mex. 2020;77(1):38-41. https://doi.org/10.24875/BMHIM.19000109
11. Bestari MB, Agustanti N, Abdurachman SA. Clindamycin-Induced Esophageal Injury: Is It an Underdiagnosed Entity? Clin Med Insights Case Rep. 2019;12:1-4. https://doi.org/10.1177/1179547619884055
12. Zezos P, Harel Z, Saibil F. Cloxacillin: A New Cause of Pill-Induced Esophagitis. Can J Gastroenterol Hepatol 2016;2016:1-2. https://doi.org/10.1155/2016/2904256
13. Toya Y, Nakamura S, Tomita K, Matsuda N, Abe K, Abiko Y, et al. Dabigatran-induced esophagitis: The prevalence and endoscopic characteristics. J Gastroenterol Hepatol 2016; 31(3):610-4. https://doi.org/10.1111/jgh.13024
14. Kim JW, Kim BG, Kim SH, Kim W, Lee KL, Byeon SJ, et al. Histomorphological and Immunophenotypic Features of Pill-Induced Esophagitis. PLoS One. 2015;10(6):1-12. https://doi.org/10.1371/journal.pone.0128110
15. Kuramoto T, Umegaki E, Nouda S, Narabayashi K, Kojima Y, Yoda Y, et al. Preventive effect of irsogladine or omeprazole on non-steroidal anti-inflammatory drug-induced esophagitis, peptic ulcers, and small intestinal lesions in humans, a prospective randomized controlled study. BMC Gastroenterol. 2013;13:1-8. https://doi.org/10.1186/1471-230X-13-85
16. Dağ MS, Öztürk ZA, Akın I, Tutar E, Çıkman Ö, Gülşen MT. Drug-induced esophageal ulcers: Case series and the review of the literature. Turk J Gastroenterol. 2014;;25(2):180-4. https://doi.org/10.5152/tjg.2014.5415
17. Zhang Y, Tong Y, Wang W, Xu L. Chest pain from pill-induced esophagitis: A rare side effect of ascorbic acid. SAGE Open Med Case Rep. 2018;6:1-3. https://doi.org/10.1177/2050313X18775004
18. Hu SW, Chen AC, Wu SF. Drug-Induced Esophageal Ulcer in Adolescent Population: Experience at a Single Medical Center in Central Taiwan. Medicine 2021;57(12):1-7. https://doi.org/10.3390/medicina57121286

https://doi.org/10.22516/25007440.1304

Case report

Advanced Hepatocellular Carcinoma: Benefits of Atezolizumab and Bevacizumab in Clinical Practice. Case Report

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Citation:
Cantor-Rizo EA, Bejarano-Ramírez AF, Gómez-Giraldo ZF, Murillo-Silva JA, Vargas-Díaz HA, Tapias-Mantilla ML. Advanced Hepatocellular Carcinoma: Benefits of Atezolizumab and Bevacizumab in Clinical Practice. Case Report. Revista. colomb. Gastroenterol. 2025;40(4):497-501.
https://doi.org/10.22516/25007440.1304

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Received: 22/11/2024
Accepted: 30/05/2025

Abstract

Background: Hepatocellular carcinoma (HCC), originating from hepatocytes, ranks as the sixth most common cancer worldwide and the fourth leading cause of cancer-related mortality. Treatment options include surgical resection, locoregional therapies, systemic therapy, and liver transplantation, depending on disease stage. **Case report:** We describe a 78-year-old male with multiple comorbidities diagnosed with stage IIIB hepatocellular carcinoma according to the BCLC B classification. He was treated with atezolizumab and bevacizumab, achieving a favorable response with tumor marker negativization and stable disease. **Discussion:** Since 2008, HCC treatment has undergone substantial progress. Earlier systemic therapies such as sorafenib and lenvatinib offered response rates around 24% and overall survival of up to 13 months. Current therapies have demonstrated significantly improved outcomes. Notably, the phase III IMbrave150 trial (2020) showed the advantages of combining immunotherapy with antiangiogenic agents over sorafenib in patients with advanced HCC, with overall survival reaching up to 89%.

Keywords

Hepatocellular carcinoma, immunotherapy, tyrosine kinase inhibitors.

INTRODUCTION

Hepatocellular carcinoma is the fourth most common cause of cancer-related death worldwide and is among the five most frequent malignant neoplasms globally. More than 80% of primary liver cancers are caused by hepatocellular carcinoma, which arises from the parenchymal cells of the liver (hepatocytes)[1,2].

It is estimated that in Colombia there are two cases per 100,000 people. Alcohol consumption, cirrhosis, and hepatitis (B-C) are the main risk factors. With a ratio of 2.8:1, men are more likely than women to develop this disease. The five-year survival rate is approximately 18%[1,3].

Initial treatment focuses on a variety of options, including liver transplantation, surgical resection, and local ablation. Patients in the intermediate stage are treated with chemoembolization and other locoregional therapies[3–5]. Tyrosine kinase inhibitors have historically been used in advanced stages, with only modest improvements in overall survival and objective response rates[1]. The benefits of immunotherapy over management with tyrosine kinase inhibitors have been demonstrated; consequently, monotherapy and combination regimens including these agents are becoming increasingly prevalent[1]. We present the case of a patient with stage IIIB hepatocellular carcinoma treated with atezolizumab and bevacizumab.

CASE PRESENTATION

A 78-year-old male patient with a medical history of obesity, type 2 diabetes *mellitus*, hypertension, hypothyroidism, dyslipidemia, vitiligo, and autoimmune gastritis. A routine abdominal ultrasound performed on September 25, 2021, revealed a heterogeneous hyperechoic mass with lobulated, well-defined contours involving segments VI and VII of the right hepatic lobe, with peripheral flow. Color Doppler examination showed an image suggestive of a central scar, exerting significant local compressive effect by medially and superiorly displacing the suprahepatic veins, portal vein, and hepatic artery without compressing it.

Following these findings, an abdominal magnetic resonance imaging (MRI) study was performed on October 7, 2021, confirming the presence of a solid mass with heterogeneous content in segments VII and VIII of the right hepatic lobe, measuring 17 × 11 cm in axial diameter, located in a morphologically normal liver, without signs of cirrhosis, steatosis, or stigmata of chronic liver disease. The lesion exhibited a heterogeneous enhancement pattern after contrast administration. Increased focal uptake was observed in the right hepatic lobe, corresponding to segment 6/7, with no evidence of other hypermetabolic foci (**Figure 1**).

A percutaneous liver biopsy was performed on October 14, 2021, confirming the diagnosis of well-differentiated hepatocellular carcinoma, with a nuclear grade of 1–2, classified as stage B (intermediate) according to the Barcelona Clinic Liver Cancer (BCLC) system. A Child-Pugh score of A5 and a MELD score of 8 were reported; these were used as tools to assess liver function rather than as indicators of cirrhosis, since imaging showed no signs of chronic liver disease. At that time, the patient had an optimal functional status, with ECOG 0, a Karnofsky performance status of 100%, and an alpha-fetoprotein (AFP) level of 4.22 ng/mL.

A multidisciplinary evaluation, in collaboration with the hepatobiliary surgery service, determined that although the patient had a single lesion and was classified as BCLC stage B, his clinical condition of multimorbidity, together with the inherent risks of any locoregional intervention, meant that the procedural risk could potentially outweigh the expected benefits. In this context, and despite not meeting criteria for tumor progression (BCLC C), a systemic approach was chosen based on the patient's individual characteristics, prioritizing clinical safety. In accordance with the findings of the IMbrave150 study[6], systemic treatment with intravenous atezolizumab 1,200 mg plus intravenous bevacizumab 400 mg every three weeks was initiated. Treatment began on November 9, 2021.

Two follow-up abdominal computed tomography scans performed in January and April 2022 showed no radiological progression of the hepatic lesion, with no evidence of tumor size increase or the appearance of associated complications such as vascular thrombosis or new lesions. This allowed continuation of the same treatment under criteria of clinical and radiological stability, until toxicity or intole-

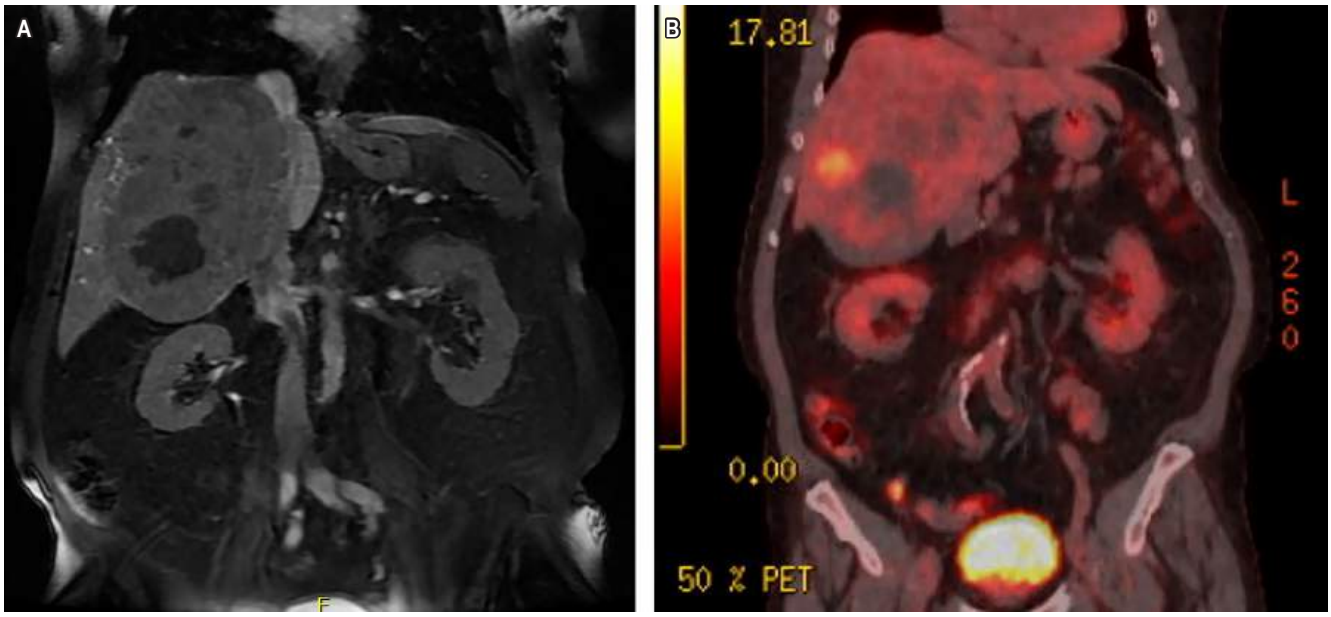


Figure 1. A. Magnetic resonance imaging (MRI): presence of a solid mass with heterogeneous content in segments VII and VIII of the right hepatic lobe. **B.** Positron emission tomography (PET): increased focal uptake observed in the right hepatic lobe, corresponding to segment 6/7. Author's file.

rance developed (**Figure 2**). Additionally, follow-up AFP levels measured in June and December 2022 showed fluctuations within the normal range, with a downward trend compared with the initial value. Although this was not considered normalization (as AFP was already normal in early phases of follow-up), it was interpreted as an indirect marker of favorable evolution under systemic therapy, supporting the decision to maintain the established regimen.

In November 2022, after the 18th treatment cycle, a follow-up positron emission tomography (PET) scan was performed, revealing a stable hypermetabolic malignant lesion, with no evidence of progression (**Figure 3**).

The patient remained clinically stable in February and March 2023. A new MRI performed during this period (**Figure 4**) demonstrated stability in the size of the hepatic lesion, with no evidence of progression or the development of complications such as thrombosis or new lesions, supporting continuation of treatment. Routine laboratory tests also revealed AFP levels persistently within the normal range, which, together with radiological stability, was interpreted as a positive response to the current treatment.

The patient continued to receive therapy at Fundación Santa Fe de Bogotá in August 2023, after completing 31 treatment cycles and 21 months of therapy. No immunotherapy-related adverse effects were reported that required dose reduction or modification. Since February 2023, the disease has remained stable, and immune response and tumor markers have shown negative results.

DISCUSSION

Previously, treatment options for patients diagnosed with advanced or incurable hepatocellular carcinoma were limited. Palliative systemic chemotherapy did not provide sufficient benefit to outweigh the associated toxicity and subsequent complications, particularly given the chemoresistance of these tumors. Sorafenib and lenvatinib, two of the first treatments to demonstrate some improvement in overall survival and objective responses since 2008, have yielded overall response rates of 24% and survivals ranging from 12 to 13 months[7,8]. Since then, the management of hepatocellular carcinoma has advanced, with encouraging results. These include the use of monotherapies and combination regimens such as tyrosine kinase inhibitors, antiangiogenic agents, and immunotherapy.

The randomized phase III IMbrave-150 clinical trial demonstrated the advantages of immunotherapy plus antiangiogenic agents over sorafenib as systemic treatment for individuals with advanced hepatocellular carcinoma in 2020. With a median follow-up of 6.8 months, the combination of atezolizumab plus bevacizumab showed overall survival at 6 and 12 months of 84.8% (95% CI: 80.9–88.7) and 67.2% (95% CI: 61.3–73.1), respectively, compared with 72.2% (95% CI: 65.1–79.4) and 54.6% (95% CI: 45.2–64.0) in the sorafenib group. Compared with the sorafenib group (37.2%), the atezolizumab plus bevacizumab group (54.3%) had significantly longer progression-

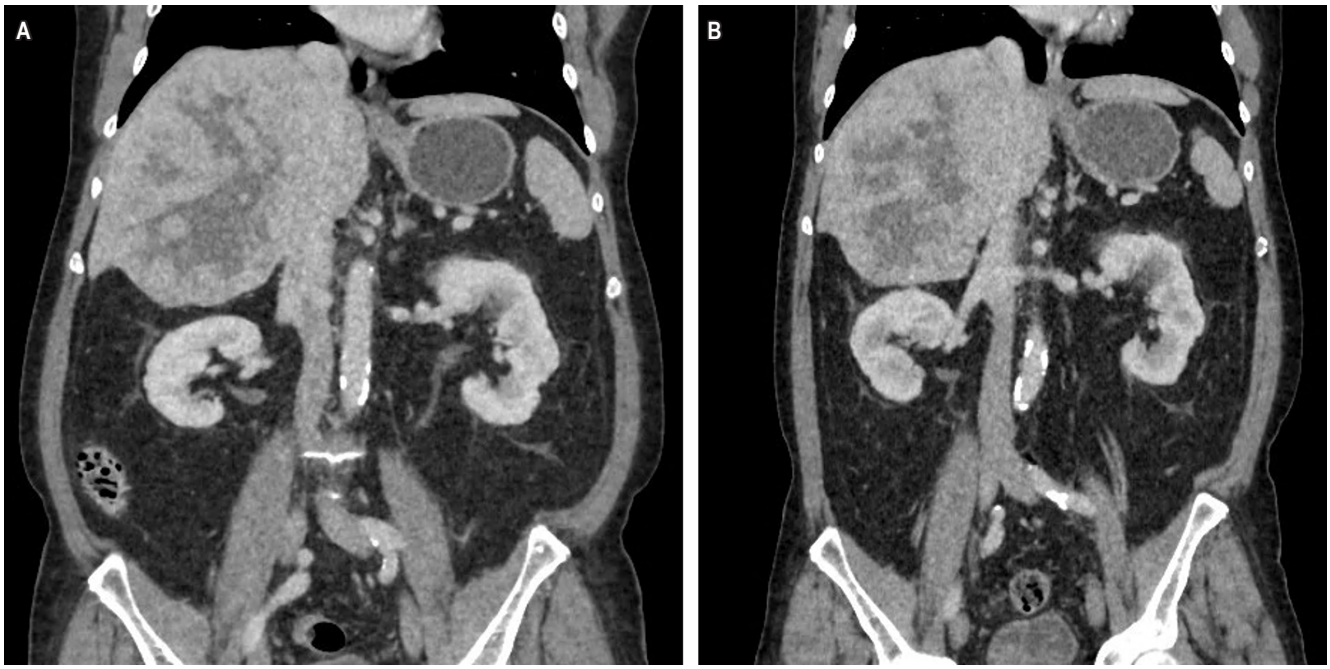


Figure 2. Coronal-section computed tomography in January 2022 (**A**) and April 2022 (**B**). Author's file.

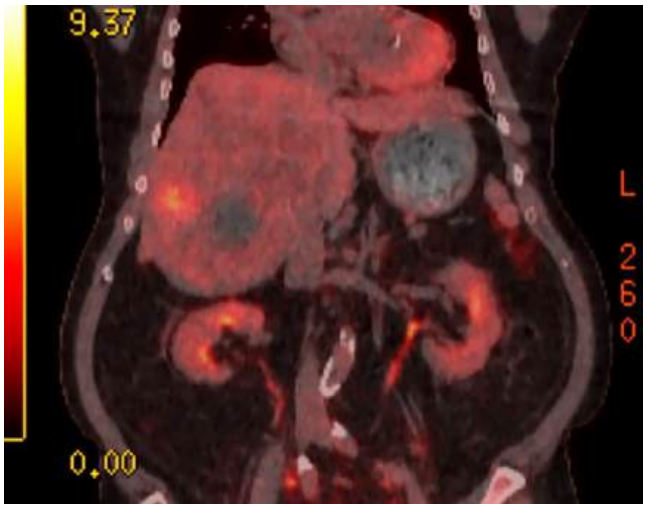


Figure 3. Positron emission tomography (PET) performed in November 2022 as part of follow-up, showing a stable hypermetabolic malignant lesion, with no signs of progression. Author's file.

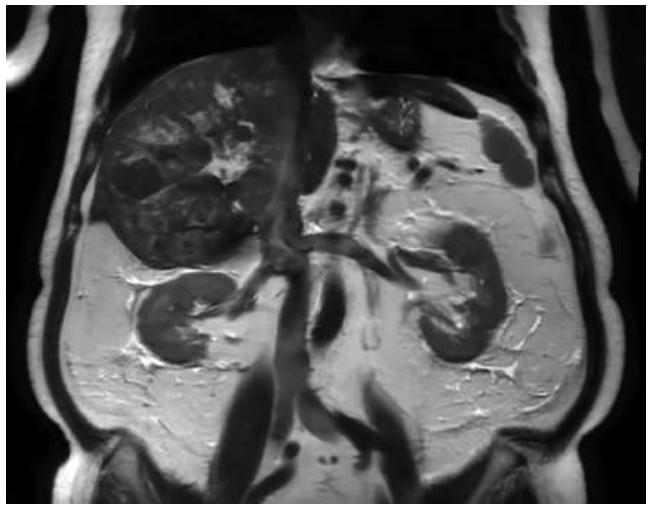


Figure 4. March 2023: magnetic resonance imaging showing no evidence of tumor growth or the development of complications. Author's file.

free survival at six months. In addition, objective response rates showed a marked advantage with the IMbrave-150 combination compared with sorafenib (89% vs. 19%)[6]. Moreover, the updated follow-up reported in 2022 in the Journal of Hepatology showed a median overall survival of 19.2 months, with a 95% CI of 17–23.7 months[9].

In our case, at the time of diagnosis the patient presented with a single lesion. However, his clinical condition, characterized by multimorbidity, together with the inherent risks of any intervention, meant that the procedural risk outweighed the expected benefits. For this reason, surgical management and locoregional therapy were not feasible. After a risk-benefit assessment, the most appropriate first-line treatment was considered to be the regimen with bevacizumab and atezolizumab. In addition to demonstrating good treatment tolerance, with no need for dose adjustments or treatment discontinuations due to toxicity, the patient showed a partial response, with a significant reduction in lesion size, improvement in systemic symptoms, and persistently negative tumor marker levels during follow-up.

At present, the patient continues under regular follow-up and, based on medical history and physical examination, remains asymptomatic, with adequate nutritional status, weight recovery, good quality of life, and maintenance of the response achieved for more than 18 months since treatment initiation, reinforcing the benefit of combined immunotherapy and antiangiogenic therapy.

Conflict of Interest

The authors declare no conflicts of interest.

Funding Sources

The authors received no funding for the research and preparation of this article.

Consent for Publication

Written informed consent for the publication of this manuscript was obtained from the patient.

REFERENCES

1. Chidambaranathan-Reghupaty S, Fisher PB, Sarkar D. Hepatocellular carcinoma (HCC): Epidemiology, etiology and molecular classification. Adv Cancer Res. 2021;149:1-61. https://doi.org/10.1016/bs.acr.2020.10.001
2. Yang JD, Hainaut P, Gores GJ, Amadou A, Plymoth A, Roberts LR. A global view of hepatocellular carcinoma: trends, risk, prevention and management. Nat Rev Gastroenterol Hepatol. 2019;16(10):589-604. https://doi.org/10.1038/s41575-019-0186-y

3. Vogel A, Meyer T, Sapisochin G, Salem R, Saborowski A. Hepatocellular carcinoma. Lancet (London). 2022;400(10360):1345-62. https://doi.org/10.1016/S0140-6736(22)01200-4
4. Ganesan P, Kulik LM. Hepatocellular Carcinoma: New Developments. Clin Liver Dis. 2023;27(1):85-102. https://doi.org/10.1016/j.cld.2022.08.004
5. Sim HW, Knox J. Hepatocellular carcinoma in the era of immunotherapy. Curr Probl Cancer. 2018;42(1):40-8. https://doi.org/10.1016/j.currproblcancer.2017.10.007
6. Finn RS, Ducreux M, Qin S, Galle PR, Zhu AX, Ikeda M, et al. IMbrave150: A randomized phase III study of 1L atezolizumab plus bevacizumab vs sorafenib in locally advanced or metastatic hepatocellular carcinoma. J Clin Oncol 2018;36(15_suppl):TPS4141-TPS4141. https://doi.org/10.1200/JCO.2018.36.15_suppl.TPS4141
7. Vogel A, Qin S, Kudo M, Su Y, Hudgens S, Yamashita T, et al. Lenvatinib versus sorafenib for first-line treatment of unresectable hepatocellular carcinoma: Patient-reported outcomes from a randomised, open-label, non-inferiority, phase 3 trial. Lancet Gastroenterol Hepatol. 2021;6(8):649-58.
8. Yamashita T, Kudo M, Ikeda K, Izumi N, Tateishi R, Ikeda M, et al. REFLECT-a phase 3 trial comparing efficacy and safety of lenvatinib to sorafenib for the treatment of unresectable hepatocellular carcinoma: an analysis of Japanese subset. J Gastroenterol. 2020;55(1):113-22. https://doi.org/10.1007/s00535-019-01642-1
9. Cheng AL, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY. Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. J Hepatol. 2022;76(4):862-73. https://doi.org/10.1016/j.jhep.2021.11.030

https://doi.org/10.22516/25007440.1311

Case report

Pancreatic Cystic Lymphangioma: Case Report

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OPEN ACCESS

Citation:
Medina-Ortega MA, Duarte-Misol DR, Coronado-Arévalo D, Pérez-Orozco JM. Pancreatic Cystic Lymphangioma: Case Report. Revista. colomb. Gastroenterol. 2025;40(4):502-505. https://doi.org/10.22516/25007440.1311

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Received: 23/12/2024
Accepted: 24/02/2025

Abstract

Lymphangiomas are benign hamartomatous malformations composed of lymphatic fluid and are exceedingly rare lesions. While they may occur in various anatomical sites, only 5% are found in the abdomen, and pancreatic lymphangiomas represent approximately 0.2% of all pancreatic neoplasms. Their diagnosis is challenging using conventional imaging modalities, making endoscopic ultrasound (EUS) a key tool for both diagnosis and drainage. We report the case of a man in his fifth decade of life who was undergoing evaluation for abdominal pain secondary to renal lithiasis. During diagnostic workup, an incidental mass was identified in the pancreatic head, which could not be characterized by conventional radiologic imaging. Endoscopic ultrasound facilitated diagnostic clarification and enabled cyst drainage, with fluid analysis confirming a pancreatic cystic lymphangioma.

Keywords

Cystic lymphangioma, pancreatic lymphangioma, abdominal lymphangioma, endoscopic ultrasound, EUS-guided drainage

INTRODUCTION

Lymphangiomas are benign hamartomatous malformations with lymphatic differentiation, in which cysts filled with lymph form due to a disorder in the communication between lymphatic channels and vessels. They primarily affect children and are very rarely found in adults (less than 10% of cases)[1,2]. Most are located in the neck and axillary region, and only 5% occur in the mediastinum and abdomen[3]. Pancreatic lymphangiomas are exceedingly rare (less than 1% of abdominal lymphangiomas) and account for less than 0.2% of pancreatic neoplasms[4].

Cyst size correlates with clinical manifestations; however, most symptoms are nonspecific, and imaging diagnosis is also uncertain because it is not easy to distinguish among serous cystadenomas, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms, and pseudocysts[5,6].

CASE DESCRIPTION

A 41-year-old male patient with no relevant medical history presented with a two-day history of pain in the right lumbar region radiating to the ipsilateral inguinoscrotal region, accompanied by episodes of vomiting. On physical examination, bilateral costovertebral angle tenderness was observed, predominantly on the right.

Based on the presenting symptoms, physical examination findings, and laboratory results, a probable diagnosis

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of renoureteral colic was considered. A urinary tract ultrasound was requested, which identified mild right hydronephrosis associated with lithiasis in the proximal third of the ureter, measuring 34.2 mm in diameter. The patient was evaluated by the urology service, which requested a contrast-enhanced CT urography. The results confirmed the presence of a 6-mm proximal right ureterolithiasis; however, an image suggestive of a space-occupying lesion in the head of the pancreas, located in the uncinate process, was also observed. This lesion was described as a cystic lesion measuring 45 × 34 mm (**Figure 1**), which drew attention during the evaluation.

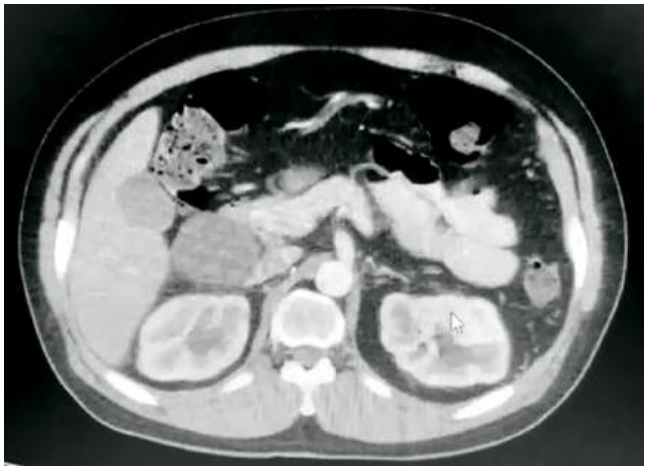


Figure 1. Contrast-enhanced abdominal computed tomography showing a cystic lesion measuring 45 × 34 mm in the head and uncinate process of the pancreas. Author's file.

Admission laboratory tests showed mild leukocytosis without neutrophilia, with no anemia or thrombocytopenia. Coagulation parameters were within normal limits. Elevations in liver enzymes were observed, including alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and lactate dehydrogenase (LDH).

Given this pancreatic finding, biliopancreatic endoscopic ultrasound was performed. It revealed a unilocular but multilobulated cystic lesion located in the uncinate process of the pancreas. The lesion measured 48 × 36 mm and demonstrated an adequate cleavage plane with the organ and adjacent vascular structures (**Figure 2**). The remainder of the pancreas showed normal echogenicity without lesions, and the duct of Wirsung was of normal caliber. The common bile duct had a normal diameter. No signs of ascites or lymphadenopathy were identified in the celiac trunk. Blood flow in the evaluated vessels was adequate on Doppler assessment.

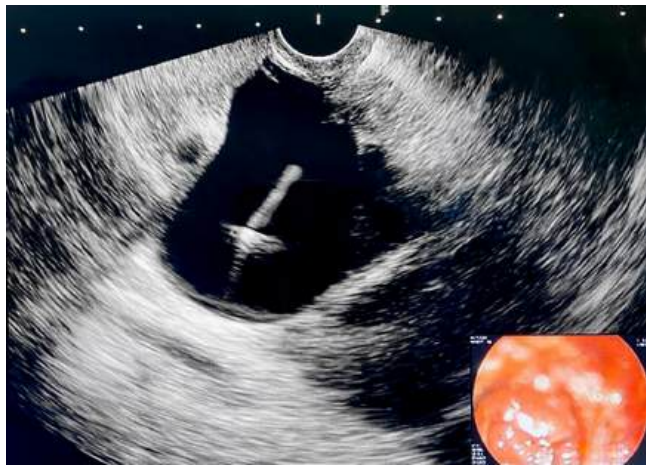


Figure 2. Biliopancreatic endoscopic ultrasound showing a unilocular but multilobulated cystic lesion located in the uncinate process of the pancreas. The lesion measures 48 × 36 mm and has an adequate cleavage plane with the organ and adjacent vascular structures. Author's file.

Fine-needle puncture and drainage of the cystic lesion were performed in three passes using a 22-gauge needle. A milky, thick, non-mucinous fluid was obtained and drained, yielding 10 mL for cytological and additional analyses (**Figure 3**).



Figure 3. Drainage of a pancreatic head cyst visualized on endoscopic ultrasound with the outflow of milky fluid. Author's file.

Cytochemical analysis revealed elevated triglyceride levels (2,405 mg/dL) and cholesterol levels (140 mg/dL). Cytology of the submitted sample was negative for malignancy, showing a proteinaceous and hemorrhagic background within the cyst contents, with the presence of histiocytes, lymphocytes, and some native cells.

DISCUSSION

Pancreatic lymphangiomas are rare, benign lesions of lymphatic origin that most often present as incidental findings[1], as occurred in this case, in which a pancreatic lymphangioma was identified during the evaluation of renoureteral colic. The patient, a 41-year-old man with no relevant medical history, was initially evaluated for right lumbar pain radiating to the inguinoscrotal region, associated with episodes of vomiting.

Initial evaluation with ultrasound and CT urography revealed proximal right ureterolithiasis, accompanied by the unexpected finding of a cystic lesion in the uncinate process of the pancreas. It should be noted that, according to the medical literature, the most frequent location is typically the pancreatic tail, followed by the pancreatic head.

On both computed tomography and magnetic resonance imaging, the most common finding is a multiloculated lesion in 74% of cases and a uniloculated lesion in 19%[6]. In this patient, the observed lesion measured 45 × 34 mm and showed a unilocular but multilobulated pattern, without invasion of vascular structures or pancreatic ducts. These features, together with the absence of related symptoms, were suggestive of a benign lesion.

Definitive diagnosis was established by endoscopic ultrasound with fine-needle puncture and drainage, which allowed the acquisition of a milky fluid with significantly elevated triglyceride and cholesterol levels, considering that values greater than 110 mg/dL are suggestive of lymphangioma.

Cytological analysis showed no evidence of malignancy, which further supported the benign nature of the lesion. This diagnostic approach is relevant, as lymphangiomas lack pathognomonic features on imaging studies, and their diagnosis requires histological or biochemical confirmation

It is important to note that pancreatic lymphangiomas are extremely rare, with fewer than 100 cases reported in the literature[7]. Although they are more frequently diagnosed in women, this case contributes to broadening the understanding of their presentation in men and underscores the need to consider this entity in the evaluation of nonspecific abdominal pain. In most cases, lymphangiomas are asymptomatic, and management does not require surgical intervention in the absence of associated symptoms[8].

The use of endoscopic ultrasound with fine-needle puncture and drainage proved to be a safe and effective technique for diagnosing this lesion. In this case, the procedure was performed without complications, yielding sufficient material for biochemical and cytological studies. This approach minimized the need for more invasive interventions and allowed for appropriate conservative management. Given the benign nature of the lesion, periodic follow-up could be continued to avoid complex and morbid surgical procedures such as pancreaticoduodenectomy, particularly since the patient's lesion is located between the head and the uncinate process of the pancreas.

CONCLUSIONS

Lymphangioma is a very rare pancreatic lesion with nonspecific clinical and imaging characteristics. This case highlights the importance of careful evaluation of incidental findings on imaging studies. Although pancreatic lymphangiomas are benign lesions, early and accurate diagnosis is essential to avoid unnecessary interventions and to ensure appropriate management. Complete surgical resection of the lesion is the definitive treatment; however, given its benign nature and considering surgical risks, endoscopic ultrasound with image-guided puncture constitutes a valuable tool in the management of this entity, especially in cases in which the diagnosis is not initially clear. In the absence of symptoms attributable to this condition, clinical and tomographic follow-up may be performed.

Ethical Considerations

We declare that this article does not contain personal information that could identify the patient, and that anonymity has been preserved in accordance with institutional protocols. Clinical history data were accessed and managed solely by the researchers. This publication complies with current regulations in bioethical research, and no experiments were conducted in animals or humans. In accordance with Resolution 8430 of 1993 of the Colombian Ministry of Health, Title II: Research in Human Beings, Chapter 1: Ethical Aspects of Research in Human Beings, Article 11, this study is considered to involve no ethical risk. Authorization for publication of this case report was obtained from the institutional ethics committee of IPS Endomedical, Barranquilla, Colombia.

Conflict of Interests

The authors declare no conflicts of interest.

Funding Sources

This research did not receive any specific grants from public sector agencies, commercial entities, or non-profit organizations.

REFERENCES

1. Gupta S, Phatak S, Onkar P, Ambhore AN, Mitra K. A Case of Lymphangioma of the Calf Region: Imaging Spectrum With Histopathological Correlation. Cureus. 2023;15(11):e48818. https://doi.org/10.7759/cureus.48818
2. Bellido Luque JA, García Reyes A, Nogales Muñoz Á. Giant pancreatic cystic lymphangioma. Rev Esp Enferm Dig. 2021;113(1):75-6. https://doi.org/10.17235/reed.2020.7003/2020
3. Chen D, Feng X, Lv Z, Xu X, Ding C, Wu J. Cystic lymphangioma of pancreas. A rare case report and review of the literature. Medicine (Baltimore). 2018;97(28):e11238. https://doi.org/10.1097/MD.0000000000011238
4. Tasis N, Mpalampou E, Sarafi A, Skafida E, Tsouknidas I, Fradelos E, et al. Large cystic lymphangioma of the pancreas: unusual finding with differential diagnosis and therapeutic considerations. J Surg Case Rep. 2023;2023(12):rjad676. https://doi.org/10.1093/jscr/rjad676
5. Ray R, Baruah TD, Mahobia HS, Borkar A. Pancreatic Lymphangioma: An Unusual Cause of Abdominal Lump. Cureus. 2021;13(11):e19452. https://doi.org/10.7759/cureus.19452
6. Karajgikar J, Deshmukh S. Pancreatic Lymphangioma: A Case Report and Literature Review. J Comput Assist Tomogr. 2019;43(2):242-4. https://doi.org/10.1097/RCT.0000000000000818
7. Jiménez-Gutiérrez JM, Alonso-Lárraga JO, Villegas-González LF, Ortega-Caballero AY. Linfangioma de páncreas diagnosticado mediante biopsia con aguja fina guiada por ultrasonido endoscópico: Reporte de caso. Rev Gastroenterol México. 2024;89(4):539-41. https://doi.org/10.1016/j.rgmx.2024.05.003
8. Santes O, Chan C. Cystic Lymphangioma of the Pancreas: a Rare Entity. J Gastrointest Surg. 2016;20(12):2100-1. https://doi.org/10.1007/s11605-016-3191-2

https://doi.org/10.22516/25007440.1326

Case report

Endoscopic Ultrasound–Guided Gastroenterostomy in Malignant Gastric Outlet and Biliary Obstruction

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OPEN ACCESS

Citation:
Peralta-Vera MJ, Acevedo-Toro L, Ricaurte-Ciro JC, Gutierrez AA. Endoscopic Ultrasound–Guided Gastroenterostomy in Malignant Gastric Outlet and Biliary Obstruction. Revista. colomb. Gastroenterol. 2025;40(4):506-511. https://doi.org/10.22516/25007440.1326

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Received: 23/12/2024
Accepted: 19/02/2025

Abstract

Endoscopic ultrasound–guided gastroenterostomy (EUS-GE) has emerged as an innovative, minimally invasive technique and a palliative management option for patients with malignant gastric outlet obstruction, particularly those with locally advanced gastric or pancreatic cancers. Additionally, endoscopic ultrasound–guided biliary drainage (EUS-BD), performed using a transmural gastric or duodenal approach, has become an alternative for malignant biliary obstruction, especially in cases where duodenal papilla access is limited due to local disease, anatomic variation, or failed endoscopic retrograde cholangiopancreatography (ERCP).

This article presents the case of a patient with concurrent malignant gastric outlet obstruction and biliary obstruction secondary to recurrence of infiltrating ductal adenocarcinoma of the pancreas. The patient had previously undergone proximal pancreatoduodenectomy, biliary reconstruction, lymphadenectomy, and adjuvant chemotherapy, and was successfully managed with EUS-guided gastroenterostomy.

Keywords

Gastric outlet obstruction, extrahepatic bile duct obstruction, endoscopic ultrasound, gastroenterostomy.

INTRODUCTION

One of the leading causes of gastric outlet obstruction is locally advanced gastric and pancreatic carcinomas. In patients with advanced, unresectable disease, management is oriented toward a palliative approach aimed at symptom relief and improvement of quality of life[(1)]. Available therapeutic options include placement of metallic stents—performed under fluoroscopic guidance or using a combination of fluoroscopic and endoscopic techniques—[(2)], surgical gastrojejunostomy, and more recently, endoscopic gastroenteroanastomosis with stent (EUS-GE). This latter technique has proven to be highly effective, with excellent technical and clinical success rates and a low incidence of complications, making it a valuable alternative in the management of this complex condition.

Herein, we present a successful case of EUS-GE in a patient with malignant gastric outlet obstruction and malignant biliary obstruction secondary to recurrence of an infiltrating ductal adenocarcinoma of the pancreas, which had initially been managed with proximal pancreaticoduodenectomy, biliary reconstruction, lymphadenectomy, and adjuvant chemotherapy.

CLINICAL CASE

A 78-year-old male patient with an ECOG performance status of 1, diagnosed with adenocarcinoma of the pancrea-

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tic head, underwent proximal pancreaticoduodenectomy along with biliary reconstruction and lymphadenectomy. Histopathological analysis revealed a 3 cm tumor with perineural invasion (PNI+), no lymphovascular invasion (LVI–), R0 resection, and 0/10 lymph nodes negative for disease; the final classification was stage IB (pT2pN0cM0R0G2). Accordingly, the patient was considered a candidate for adjuvant chemotherapy with curative intent. He received six cycles of single-agent gemcitabine due to mild frailty (vulnerability) and age.

Seven months after completing the sixth cycle of chemotherapy, the patient presented with chills, fever, abdominal pain in the mesogastrium, and episodes of vomiting. Abdominal computed tomography demonstrated a 40 × 40 × 28 mm mass with central necrosis and peripheral enhancement with irregular contours, located anterior to the abdominal aorta and associated with peritoneal and perihepatic implants. This mass infiltrated the mesenteric artery and caused occlusion of the inferior mesenteric vein, as well as severe obliteration of the splenomesenteric or portal confluence. In addition, tumoral involvement of the bilioenteric diversion intestinal loop was observed, resulting in luminal occlusion and subsequent retrograde dilation (**Figure 1**).

Given these findings, magnetic resonance cholangiopancreatography was requested, confirming tumor recurrence manifested by an infiltrative mass at the root of the mesentery and the presence of peritoneal implants. In addition, a tumoral "closed-loop" obstruction of the bilioenteric diversion jejunum was described, with biliary duct dilation due to reflux and ascending hepatobiliary cholangitis (**Figure 2**). During hospitalization, the patient developed fever. *Escherichia coli* bacteremia secondary to cholangitis was documented, and he received antibiotic therapy for seven days, initially with meropenem and subsequently with ciprofloxacin.

Therefore, the condition was considered to be malignant gastric outlet obstruction and malignant biliary obstruction with associated cholangitis secondary to an unresectable locoregional recurrence. The patient was evaluated by the Gastroenterology service and deemed a candidate for EUS-GE.

A linear endoscopic ultrasound with a disposable balloon was performed, revealing a distended biliary loop measuring up to 3 cm in diameter in contact with the gastric wall. A 20 mm × 10 mm HOT AXIOS lumen-apposing metal stent was introduced; the loop was punctured from the gastric body, a Jagwire metal guidewire was advanced into the intestine, and the stent was deployed under combined ultrasound and endoscopic visualization. Copious drainage of retained bile was observed (**Figure 3**).

After the procedure, the patient was transferred to the general ward. He was discharged two days later following a non-contrast abdominal computed tomography that demonstrated a patent gastroenteroanastomosis without signs of complications, intestinal loop dilation, or obstruction (**Figure 4**). Subsequently, he was evaluated in the outpatient setting by clinical oncology, where systemic chemotherapy with gemcitabine and nab-paclitaxel was indicated with palliative intent.

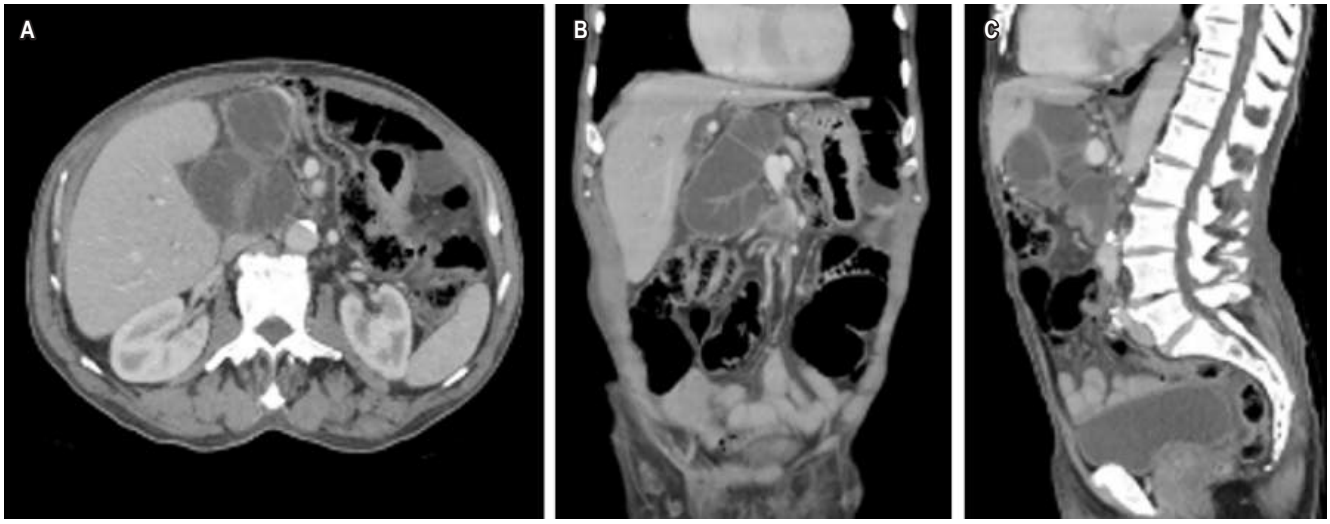


Figure 1. Contrast-enhanced abdominal computed tomography showing tumoral involvement of the bilioenteric diversion intestinal loop, occluding its lumen and causing retrograde dilation. **A.** Axial view. **B.** Coronal view. **C.** Sagittal view. Author's file.

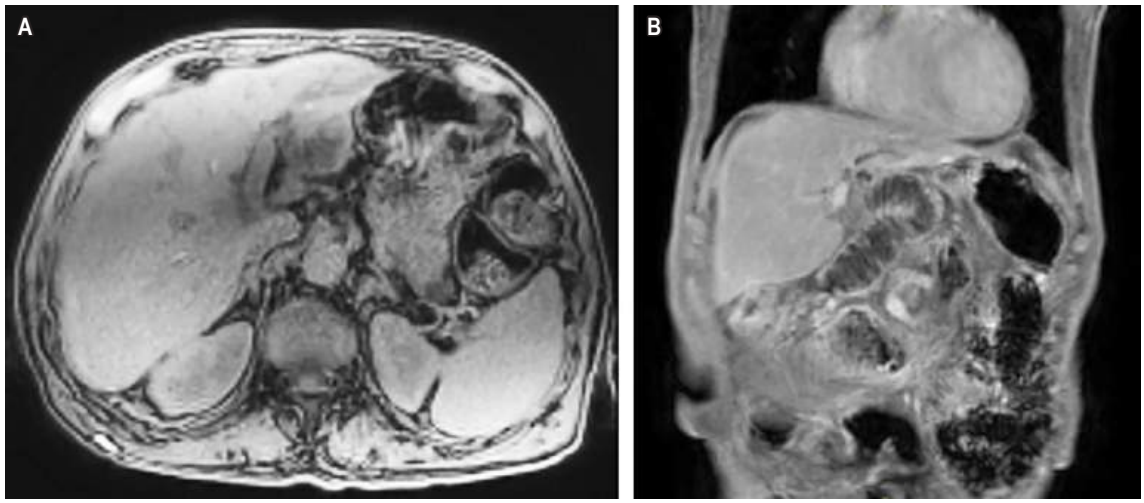


Figure 2. Magnetic resonance cholangiopancreatography showing: **A.** Infiltrative mass at the root of the mesentery and **B.** Tumoral "closed-loop" obstruction of the bilioenteric diversion jejunum. Author's file.

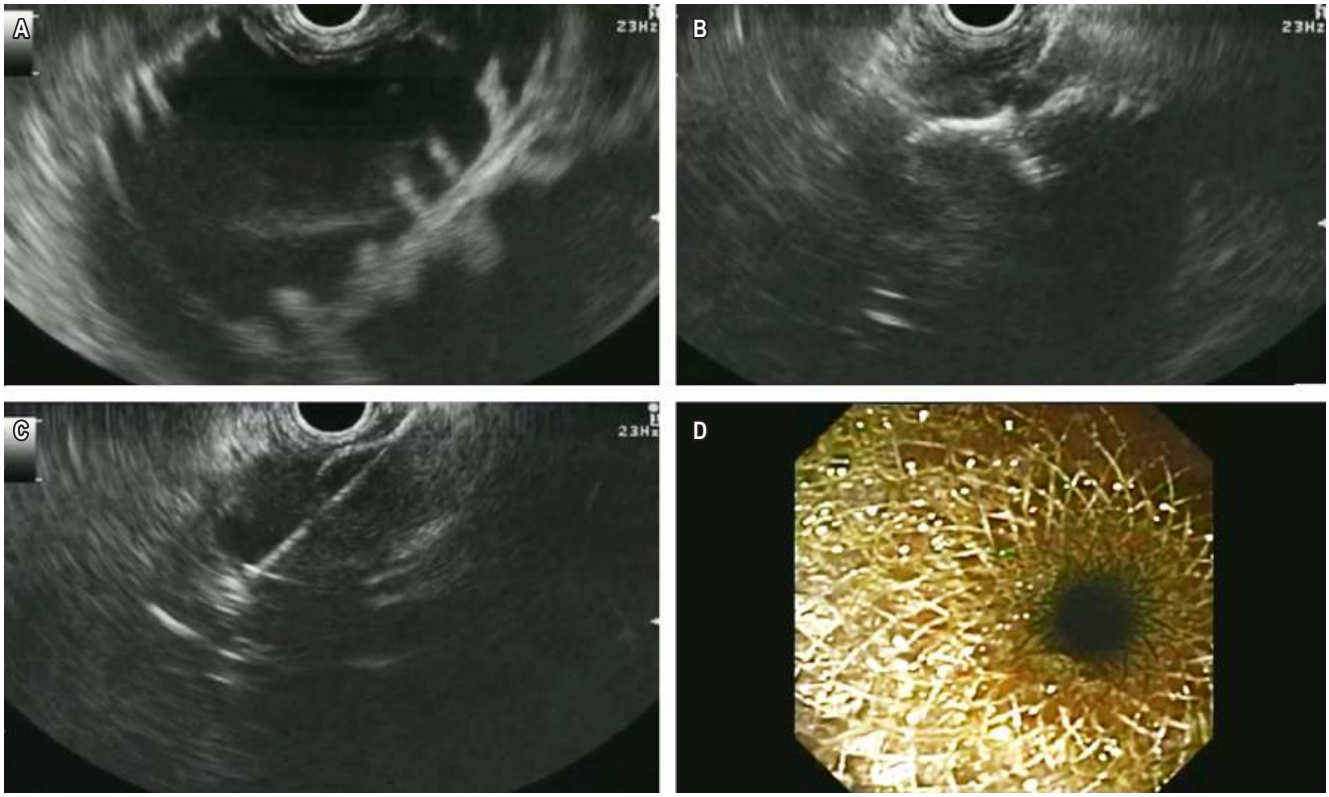


Figure 3. A. Endoscopic ultrasound showing a distended biliary loop up to 3 cm. **B and C.** Puncture of the loop from the gastric body and stent deployment. **D.** Stent under endoscopic view with evidence of bile drainage. Author's file.



Figure 4. Non-contrast abdominal computed tomography showing a patent gastroenteroanastomosis. Author's file.

DISCUSSION

Gastric outlet obstruction may be caused by motility disorders or by mechanical obstruction resulting from benign or malignant conditions. Malignant neoplasms are the most frequent cause, accounting for 50%–80% of cases. Among these, locally advanced gastric and pancreatic carcinomas are the most common, particularly when there is infiltration of the stomach and duodenum[1,3–5].

In patients with advanced, unresectable disease, palliative management focuses on symptom control. Options include endoscopic placement of self-expanding metal stents, surgical gastrojejunostomy, and, more recently, endoscopic ultrasound-guided gastroenteroanastomosis (EUS-GE). This technique involves deployment of a lumen-apposing metal stent (LAMS) to create a transmural tract between the stomach and the small intestine, thereby bypassing the site of obstruction. The stent used in this clinical case was the AXIOS, a device designed to facilitate transluminal flow and fully covered with silicone. Its name combines the terms axial and ostomy, reflecting two fundamental characteristics of LAMS: axial deployment and creation of a transluminal anastomosis. This stent is available in a range of luminal diameters, from 6 mm to 20 mm. Selection of the optimal diameter depends on multiple anatomical factors, including the size and location of the target lumen and the intestinal lumen, as well as the therapeutic intent[6].

Use of the largest feasible diameter is recommended to optimize drainage of retained contents. In cases of concomitant biliary obstruction, a diameter of 10 mm has been shown to be effective for drainage. In addition, it is essential to assess the transverse diameter of the site where the distal anchoring flange will be positioned, as a 20 mm stent requires a minimum transverse diameter of 29 mm, corresponding to the size of the flange.

In most cases, fluoroscopy is used to confirm stent insertion into the appropriate loop, guiding the passage of contrast medium through catheters across the stenotic site or via ultrasound-guided puncture with a 19 G needle. However, in the setting of closed-loop obstruction, sonographic identification of the dilated loop is sufficient to define the puncture site; therefore, fluoroscopy is not indispensable in these cases.

EUS-GE has demonstrated technical and clinical success rates comparable to those of surgical gastrojejunostomy and conventional stent placement, with lower rates of reintervention, adverse events, and costs. Acquisition of the skills required to perform the technique is estimated to require approximately 25 procedures, while full mastery is achieved after about 40 cases[7]. As operator experience increases, technical and clinical success rates tend to improve, reaching 92,9% and 90,1%, respectively. In high-volume centers, optimization of the learning curve also contributes to a reduction in adverse events, which in multicenter studies have been reported at 10,6% overall and 5,6% for severe adverse events[4,8,9].

Similarly, endoscopic ultrasound-guided biliary drainage (EUS-BD) has been described as a modality for primary decompression in patients with malignant biliary obstruction, particularly in cases of altered anatomy, ampullary distortion, periampullary diverticulum, gastric outlet obstruction, presence of *in situ* duodenal stents, or after failed attempts at endoscopic retrograde cholangiopancreatography (ERCP)[10]. This is because EUS-BD can provide direct biliary drainage through a transmural gastric or duodenal approach, as well as via a transpapillary route[11–13].

This report documents the first recorded case of successful endoscopic gastroenteroanastomosis in a patient with a history of proximal pancreaticoduodenectomy for oncologic disease at Hospital San Vicente Fundación in Medellín. A PubMed search was performed using the terms ((“endosonography”[MeSH Terms] OR endosonography [Text Word]) AND (gastroenteric)) AND (“anastomosis, surgical”[MeSH Terms]), limited to human cases, adults older than 19 years, over the past 33 years. As a result, only a small number of case reports were identified in the global medical literature[14]. This underscores the uniqueness of the case and highlights the importance of the procedure as an innovative alternative for managing gastric outlet obstruction of both benign and malignant origin. Endoscopic

gastroenteroanastomosis avoids complications associated with major surgery, such as high morbidity and prolonged recovery times—factors that are particularly relevant in frail patients and those with advanced oncologic disease. This report opens new possibilities in the palliative treatment of these complex conditions, improving patient prognosis and quality of life.

However, the procedure faces certain limitations, including the lack of prospective studies with larger cohorts to confirm its effectiveness and safety compared with conventional management[15,16]. In addition, the limited availability of personnel trained in endoscopic gastroenteroanastomosis reduces its widespread applicability, restricting implementation to highly specialized centers.

CONCLUSION

EUS-GE is a valuable and innovative technique for the treatment of malignant gastric outlet obstruction and malignant biliary obstruction. It has proven to be particularly beneficial in patients with advanced, unresectable pancreatic cancer, as in the case presented, with technical and clinical success rates close to 90%. These outcomes are comparable to those of surgical gastrojejunostomy, but with significantly lower morbidity and need for reintervention. In the present case, EUS-GE successfully restored intestinal transit, relieving obstructive symptoms, and resolved biliary obstruction, thereby positively impacting the patient's quality of life.

REFERENCES

1. Cominardi A, Tamanini G, Brighi N, Fusaroli P, Lisotti A. Conservative management of malignant gastric outlet obstruction syndrome-evidence based evaluation of endoscopic ultrasound-guided gastroentero-anastomosis. World J Gastrointest Oncol. 2021;13(9):1086-1098. https://doi.org/10.4251/wjgo.v13.i9.1086
2. Lopera JE, Brazzini A, Gonzales A, Castaneda-Zuniga WR. Gastroduodenal Stent Placement: Current Status. RadioGraphics. 2004;24(6):1561-1573. https://doi.org/10.1148/rg.246045033
3. Bishay K, Boyne D, Yaghoobi M, Khashab MA, Shorr R, Ichkhanian Y, et al. Endoscopic ultrasound-guided transmural approach versus ERCP-guided transpapillary approach for primary decompression of malignant biliary obstruction: a meta-analysis. Endoscopy. 2019;51(10):950-960. https://doi.org/10.1055/a-0901-7343
4. Rizzo GEM, Carrozza L, Quintini D, Ligresti D, Traina M, Tarantino I. A Systematic Review of Endoscopic Treatments for Concomitant Malignant Biliary Obstruction and Malignant Gastric Outlet Obstruction and the Outstanding Role of Endoscopic Ultrasound-Guided Therapies. Cancers. 2023;15(9):2585. https://doi.org/10.3390/cancers15092585
5. Canakis A, Irani SS. Endoscopic Treatment of Gastric Outlet Obstruction. Gastrointest Endosc Clin N Am. 2024;34(1):111-125. https://doi.org/10.1016/j.giec.2023.08.005
6. Binmoeller KF, DeSimio T, Donovan R. Design considerations of the AXIOS stent and electrocautery enhanced delivery system. Tech Innov Gastrointest Endosc. 2020;22(1):3-8. https://doi.org/10.1016/j.tgie.2019.150653
7. Jovani M, Ichkhanian Y, Parsa N, Singh S, Brewer Gutierrez OI, Keane MG, et al. Assessment of the learning curve for EUS-guided gastroenterostomy for a single operator. Gastrointest Endosc. 2021;93(5):1088-1093. https://doi.org/10.1016/j.gie.2020.09.041
8. Fugazza A, Andreozzi M, Asadzadeh Aghdaei H, Insausti A, Spadaccini M, Colombo M, et al. Management of Malignant Gastric Outlet Obstruction: A Comprehensive Review on the Old, the Classic and the Innovative Approaches. Medicina (Mex). 2024;60(4):638. https://doi.org/10.3390/medicina60040638
9. van Wanrooij RLJ, Vanella G, Bronswijk M, de Gooyer P, Laleman W, van Malenstein H, et al. Endoscopic ultrasound-guided gastroenterostomy versus duodenal stenting for malignant gastric outlet obstruction: an international, multicenter, propensity score-matched comparison. Endoscopy. 2022;54(11):1023-1031. https://doi.org/10.1055/a-1782-7568
10. Dietrich CF, Braden B, Burmeister S, Aabakken L, Arciadacono PG, Bhutani MS, et al. How to perform EUS-guided biliary drainage. Endosc Ultrasound. 2022;11(5):342-354. https://doi.org/10.4103/EUS-D-21-00188
11. Baars J, Kaffes A, Saxena P. EUS-guided biliary drainage: A comprehensive review of the literature. Endosc Ultrasound. 2018;7(1):4. https://doi.org/10.4103/eus.eus_105_17
12. Brewer Gutierrez OI, Nieto J, Irani S, James T, Pieratti Bueno R, Chen YI, et al. Double endoscopic bypass for gastric outlet obstruction and biliary obstruction. Endosc Int Open. 2017;05(09):E893-E899. https://doi.org/10.1055/s-0043-115386
13. van der Merwe SW, van Wanrooij RLJ, Bronswijk M, Everett S, Lakhtakia S, Rimbas M, et al. Therapeutic endoscopic ultrasound: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2022;54(02):185-205. https://doi.org/10.1055/a-1717-1391

14. Rodrigues-Pinto E, Grimm IS, Baron TH. Efficacy of Endoscopically Created Bypass Anastomosis in Treatment of Afferent Limb Syndrome: A Single-Center Study. Clin Gastroenterol Hepatol. 2016;14(4):633-637. https://doi.org/10.1016/j.cgh.2015.11.010
15. Vanella G, Bronswijk M, van Wanrooij RL, Dell'Anna G, Laleman W, van Malenstein H, et al. Combined endoscopic mAnagement of BiliaRy and gastrIc OutLET obstruction (CABRIOLET Study): A multicenter retrospective analysis. DEN Open. 2023;3(1):e132. https://doi.org/10.1002/deo2.132
16. Paik WH, Lee TH, Park DH, Choi JH, Kim SO, Jang S, et al. EUS-Guided Biliary Drainage Versus ERCP for the Primary Palliation of Malignant Biliary Obstruction: A Multicenter Randomized Clinical Trial. Am J Gastroenterol. 2018;113(7):987-997. https://doi.org/10.1038/s41395-018-0122-8

https://doi.org/10.22516/25007440.1329

Case report

Gastric Adenosquamous Carcinoma. A Rare Tumor With Aggressive Behavior: Case Report

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Citation:
Portilla-Arenas F, Basuri-Guzman FC, Lima MA, Arcos-Ramírez M, Bastidas M, Portillo-Miño JD. Gastric Adenosquamous Carcinoma. A Rare Tumor With Aggressive Behavior: Case Report. Revista. colomb. Gastroenterol. 2025;40(4):512-516. https://doi.org/10.22516/25007440.1329

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Received: 15/01/2025
Accepted: 31/03/2025

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Abstract

Gastric cancer ranks as the fifth leading cause of cancer-related mortality worldwide. According to the Global Cancer Observatory (GLOBOCAN), approximately one million new cases and 768,000 deaths were reported in 2020. Gastric adenosquamous carcinoma is exceptionally uncommon, accounting for only 0.2% of cases, with roughly 164 cases described in the literature. We report the case of a 62-year-old man who presented to the emergency department with a one-month history of burning epigastric pain, unintentional weight loss, and hematochezia. Upper gastrointestinal endoscopy revealed a Borrmann type II lesion in the gastric body. Histopathological analysis showed diffuse gastric adenocarcinoma involving both the body and the antrum. Subsequent histology and immunohistochemistry confirmed gastric adenosquamous carcinoma, with positive staining for AE1/AE3 pan-cytokeratin, CK7, and p63, supporting the diagnosis.

Keywords

Gastric cancer, *Helicobacter*, survival, carcinoma, adenosquamous, neoplasms.

INTRODUCTION

Gastric cancer (GC) is the fifth most lethal cancer worldwide. According to the Global Cancer Observatory (GLOBOCAN), approximately 1,000,000 new cases were reported, with an estimated mortality of 768,000 individuals in 2020[(1)]. In Colombia, 7,419 cases of GC were reported, of which 5,505 patients died, making it the leading cause of cancer-related mortality in 2018[(2)]. According to the Lauren classification, adenocarcinoma is divided into intestinal and diffuse types and accounts for approximately 90% of GC cases[(3)]. According to the classifications of the World Health Organization (WHO) and the Japanese Gastric Cancer Association (JGCA), several GC subtypes are recognized based on microscopic morphology and topography, including gastric adenosquamous carcinoma (GASC), squamous cell carcinoma, undifferentiated carcinoma, carcinoma with lymphoid stroma, hepatoid carci-

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noma, adenocarcinoma with enteroblastic differentiation, fundic gland-type adenocarcinoma, micropapillary adenocarcinoma, and other rare histologic variants. Among these uncommon subtypes, GASC represents 0.2%, with approximately 164 cases reported in the literature[3].

Regarding demographic, environmental, and host-related conditions, together with other risk factors that influence disease onset and progression, a family history of GC is present in 10% of cases[4]. In diffuse-type GC, familial factors are related to mutations in the CDH1 gene, which encodes E-cadherin; in addition, mutations may occur in germline genes (CTNNA1)[5]. This type of GC is more frequently observed in hereditary conditions such as familial adenomatous polyposis or Lynch syndrome[6]. Conversely, in intestinal-type GC, associated risk factors include age, male sex, smoking, high salt intake, iron deficiency, and obesity[5]. *Helicobacter pylori* infection is a risk factor associated with both diffuse and intestinal types, including proximal GC and a subset of adenocarcinomas of the gastroesophageal junction[7,8]. The role of the different classical risk factors (diffuse and intestinal) and the *H. pylori*-mediated carcinogenesis model in GASC has not been fully elucidated, which in itself contributes to the development and progression of this tumor type.

In this context, we present a rare clinical case of a patient with GASC, highlighting the associated diagnostic and therapeutic challenges, and we explore the different hypotheses regarding GASC carcinogenesis.

CLINICAL CASE

A 62-year-old male patient presented to the emergency department with burning epigastric abdominal pain, accompanied by weight loss and bloody stools for one month. He reported no significant past medical history. Physical examination revealed a patient with mucocutaneous pallor; the abdomen was soft, compressible, non-distended, with pain on deep palpation in the epigastrium, and no other clinical findings. Laboratory tests showed a hemoglobin level within the range of grade I anemia (10.5 g/dL), with no requirement for transfusion. Upper gastrointestinal endoscopy (UGE) was performed and revealed a Borrmann type II lesion in the gastric body. Colonoscopy showed no relevant findings. According to the histopathological report of the biopsy, the lesion was compatible with diffuse gastric adenocarcinoma involving the gastric body and antrum.

Tumor markers were obtained (carcinoembryonic antigen [CEA] 3.3, CA 19-9: 74.7, CA-125: 22.4). Imaging studies, including computed tomography (CT) of the abdomen and chest, revealed no metastatic foci. Staging laparoscopy demonstrated a tumor at the incisura angularis and along the lesser curvature, with no free fluid in the abdominal cavity. The disease was staged as IIIB (T4N2M0) according to the American Joint Committee on Cancer (AJCC).

Neoadjuvant chemotherapy was initiated using the FLOT regimen, of which the patient received two cycles, followed by ten sessions of radiotherapy as a hemostatic boost due to the finding of tumor bleeding. Subsequently, a laparoscopic total gastrectomy with esophagojejunostomy and Roux-en-Y jejunojejunostomy was performed. Intraoperatively, a lesion involving the body and fundus along the greater curvature and posterior wall of the stomach was identified, firmly adherent to the pancreatic body, measuring 7 × 6 cm. No hepatic metastases, ascites, or omental involvement were found.

Histopathological examination of the resected specimen revealed a Borrmann type IV tumor, a high-grade malignant epithelial tumor measuring 8 × 5 cm, composed of cells with large, bizarre nuclei, glandular chromatin, and prominent micronuclei—some bilobulated—with polygonal, clear, and eosinophilic cytoplasm. The cells formed solid masses and tended to form glands involving the mucosa through the serosa (**Figure 1**). Negative resection margins were obtained.

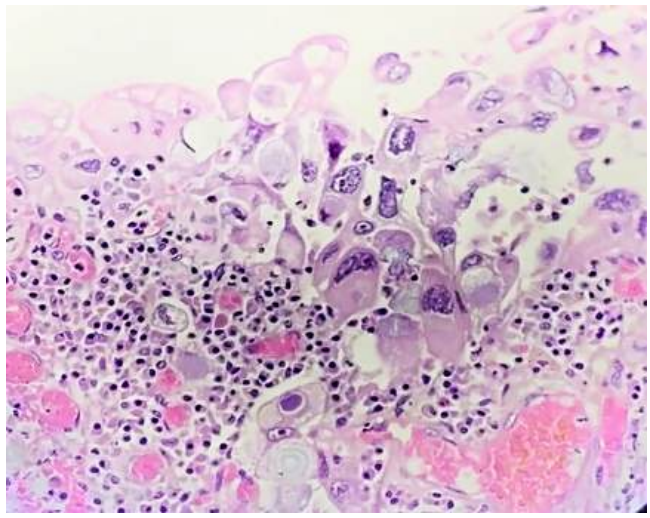


Figure 1. Tumor histopathology. Author's file.

The pathological evaluation was completed with tumor immunohistochemistry, which confirmed gastric adenosquamous carcinoma, with positivity for pancytokeratin AE1–AE3, CK7, and p63; CDX2 expression was observed in the neoplastic cells, with negativity for CK20 and preserved nuclear expression of MSH2, MSH6, MLH1, and PMS2 (**Figures 2–5**). Adjuvant chemotherapy was initiated using the XELOX regimen. The patient remains under follow-up by the Clinical Oncology service.

DISCUSSION

Gastric adenosquamous carcinoma (GASC) is an uncommon type of adenocarcinoma and is therefore rarely reported in the literature, with an incidence rate of approximately 0.2%. GASC is characterized by the formation of keratin pearls, accompanied by intercellular and glandular bridges, with a neoplastic squamous component occupying more than 25% of the tumor[9].

The etiopathogenic process involved in the development of GASC remains unknown. Several hypotheses have been proposed to explain its development and biological behavior; however, to date, there is insufficient evidence to establish a definitive mechanism. In this regard, proposed hypotheses to explain the etiopathogenesis of GASC include the emergence of squamous metaplasia from a pre-existing adenocarcinoma; carcinomatous transformation of non-neoplastic metaplastic squamous cells; malignant

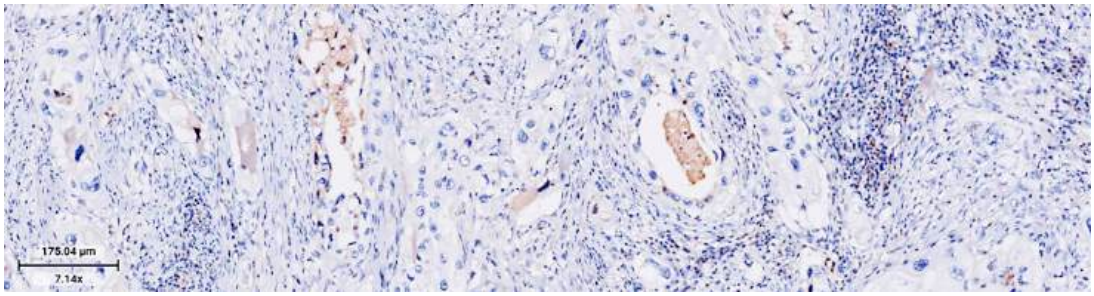


Figure 2.
Immunohistochemistry positive for CDX2.
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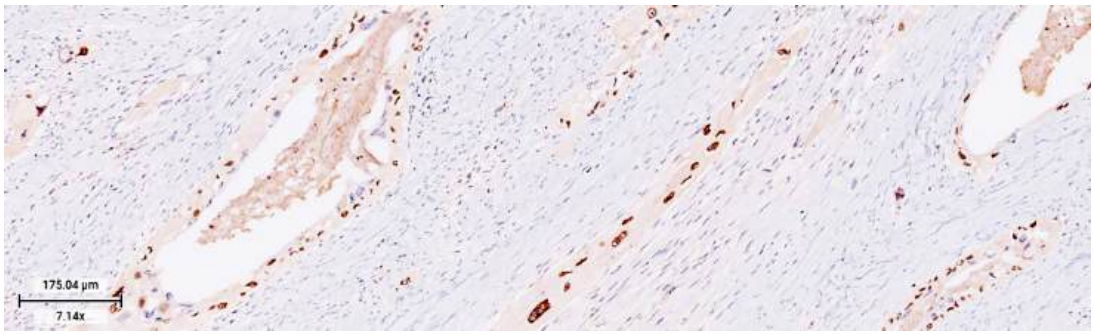


Figure 3.
Immunohistochemistry positive for p63.
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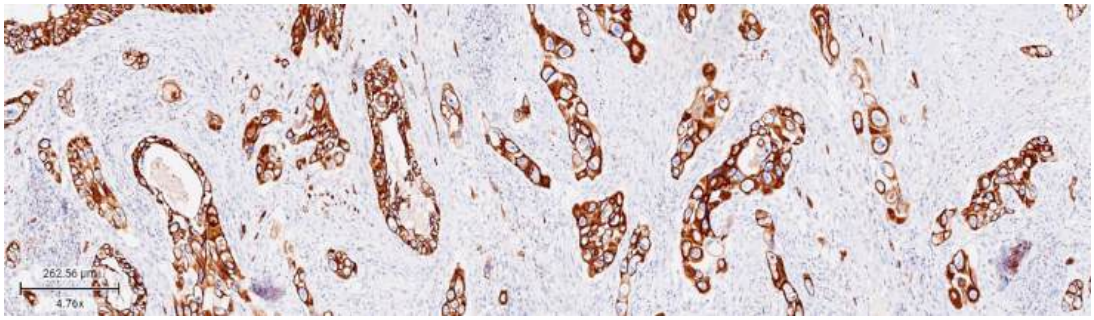


Figure 4.
Immunohistochemistry positive for CK7.
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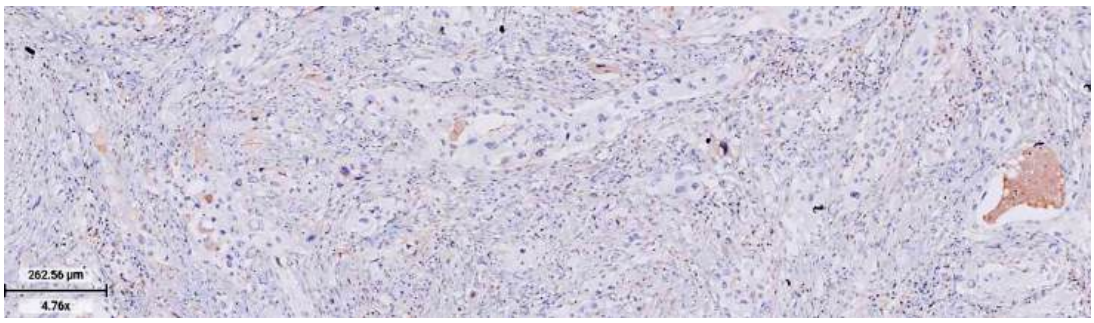


Figure 5.
Immunohistochemistry positive for CK20.
Author's file.

transformation of ectopic squamous tissue; differentiation of squamous and glandular cells from the same stem cell; and collision tumors composed of concurrent adenocarcinoma and GASC[10]. It should also be noted that the appearance of squamous cells may occur from the same stem cell together with cells consistent with adenocarcinoma. In addition, squamous differentiation of preexisting metaplastic cells has been proposed[11]; however, the cellular and molecular mechanisms by which this process culminates in GASC remain unknown. Finally, these theories are supported by reported cases in the literature; nevertheless, discrepancies exist among the findings. Some authors have ruled out squamous metaplasia arising from a preexisting adenocarcinoma, as histologically it represents tissue without a mucin-secreting component[12]. Based on the above, further research is required to elucidate a more precise mechanism underlying the development of this rare type of GC[13–15].

With respect to the immunohistochemical profile identified in the patient, the findings were consistent with gastric cancer with a squamous component, PD-L1 positive with a combined positive score (CPS) of 29, and negative expression of HER2, p63, CK7, and CK2. In the study conducted by Du and colleagues[16], immunohistochemistry showed that 31 patients were positive for p63, CK5, and CK6 in squamous cells, and positive for CK7, CK20, and CK8/18 in adenocarcinoma cells[16]. Owing to its low frequency, very little has been described in the literature regarding the immunohistochemical profile of patients with GASC[17].

Furthermore, due to the limited understanding of this disease, its treatment has yet to be defined in clinical practice guidelines. Surgical resection is widely used; however, given the low incidence of this tumor, approximately half of patients present with metastases at the time of diagnosis. Moreover, there is no consensus regarding the management of GASC, and few studies have described the use of radiotherapy, chemotherapy, and their respective treatment regimens[3,16]. Therefore, as this tumor exhibits aggressive biological behavior and there is no expert consensus on its management, with limited therapeutic options, a poor survival rate has been reported, with a median survival of approximately 17 months[16].

CONCLUSIONS

In conclusion, GASC is an unusual tumor with aggressive behavior and poor survival. Further research is urgently needed to improve understanding of its etiopathogenesis, enabling the identification of new therapeutic targets and the development of standardized, targeted therapies to improve clinical outcomes for affected patients.

Acknowledgments

None.

Conflict of Interest

None.

Funding Sources

None.

Author Contributions

All authors contributed equally to this manuscript.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49. https://doi.org/10.3322/caac.21660
2. Oliveros R, Pinilla Morales RE, Facundo Navia H, Sánchez Pedraza R. Cáncer gástrico: una enfermedad prevenible. Estrategias para intervención en la historia natural. Rev Colomb Gastroenterol. 2019;34(2):177-89. https://doi.org/10.22516/25007440.394
3. Akce M, Jiang R, Alese OB, Shaib WL, Wu C, Behera M, et al. Gastric squamous cell carcinoma and gastric adenosquamous carcinoma, clinical features and outcomes of rare clinical entities: a National Cancer Database (NCDB) analysis. J Gastrointest Oncol. 2019;10(1):85-94. https://doi.org/10.21037/jgo.2018.10.06
4. Machlowska J, Baj J, Sitarz M, Maciejewski R, Sitarz R. Gastric Cancer: Epidemiology, Risk Factors, Classification, Genomic Characteristics and Treatment Strategies. Int J Mol Sci. 2020;21(11):4012. https://doi.org/10.3390/ijms21114012
5. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. Cancer Epidemiol Biomarkers Prev. 2014;23(5):700-13. https://doi.org/10.1158/1055-9965.EPI-13-1057
6. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. Lancet. 2020;396(10251):635-48. https://doi.org/10.1016/S0140-6736(20)31288-5

7. Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, et al. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. Gut. 2022;gutjnl-2022-327745. https://doi.org/10.1136/gutjnl-2022-327745
8. Leja M. Where are we with gastric cancer screening in Europe in 2024? Gut. 2024;73(12):2074-82. https://doi.org/10.1136/gutjnl-2024-332705
9. Mori M, Iwashita A, Enjoji M. Adenosquamous carcinoma of the stomach. A clinicopathologic analysis of 28 cases. Cancer. 1986;57(2):333-9. https://doi.org/10.1002/1097-0142(19860115)57:2<333::AID-CNCR2820570224>3.0.CO;2-U
10. Chen YY, Li AF, Huang KH, Lan YT, Chen MH, Chao Y, et al. Adenosquamous carcinoma of the stomach and review of the literature. Pathol Oncol Res. 2015;21(3):547-51. https://doi.org/10.1007/s12253-014-9890-7
11. Cao F, Yan Y, Niu D, Huang X, Jia L, Diao X, et al. Epstein-Barr virus-associated gastric adenosquamous carcinoma with concurrent gastric carcinoma with lymphoid stroma: a case report and review of the literature. BMC Gastroenterol. 2022;22(1):346. https://doi.org/10.1186/s12876-022-02417-4
12. Boswell JT, Helwig EB. Squamous Cell Carcinoma and Adenoacanthoma of the Stomach. A Clinicopathologic Study. Cancer. 1965;18:181-92. https://doi.org/10.1002/1097-0142(196502)18:2<181::AID-CNCR2820180209>3.0.CO;2-3
13. Correa P. Gastric Cancer: Overview. Gastroenterol Clin North Am. 2013;42(2):211-7. https://doi.org/10.1016/j.gtc.2013.01.002
14. Meyer AR, Goldenring JR. Injury, repair, inflammation, and metaplasia in the stomach. J Physiol. 2018;596(17):3861-7. https://doi.org/10.1113/JP275512
15. Goldenring JR, Mills JC. Cellular Plasticity, Reprogramming, and Regeneration: Metaplasia in the Stomach and Beyond. Gastroenterology. 2022;162(2):415-30. https://doi.org/10.1053/j.gastro.2021.10.036
16. Du Y, Tian H, Chen Z, Mao G, Shen Q, Jiang Q, et al. Analysis of clinicopathological characteristics and prognosis on primary gastric adenosquamous carcinoma. Sci Rep. 2024;14(1):16198. https://doi.org/10.1038/s41598-024-66701-x
17. Wu CH, Lai CL, Teng CJ, Fang WL, Huang KH, Fen-Yau Li A, et al. Immunoprofile of adenosquamous carcinoma in gastric cancer. J Chin Med Assoc. 2023;86(6):542-8. https://doi.org/10.1097/JCMA.0000000000000922

https://doi.org/10.22516/25007440.1335

Case report

Atypical Presentation of Gurvits Syndrome as an Uncommon Cause of Gastrointestinal Bleeding: Case Report

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OPEN ACCESS

Citation:
Quiroz-Álvarez JE, Muñoz-Ríos M. Atypical Presentation of Gurvits Syndrome as an Uncommon Cause of Gastrointestinal Bleeding: Case Report. Revista. colomb. Gastroenterol. 2025;40(4):517-520.
https://doi.org/10.22516/25007440.1335

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Received: 11/02/2025
Accepted: 25/03/2025

Abstract

Introduction: Gurvits syndrome, also referred to as *acute esophageal necrosis*, is characterized by circumferential black discoloration of the esophageal mucosa. It is a rare entity, with an estimated incidence ranging from 0.01% to 0.28% in autopsy studies and endoscopic series. Its pathophysiology is multifactorial, the clinical presentation nonspecific, and diagnosis requires esophagogastroduodenoscopy. No standardized therapeutic approach has been established; however, management focuses on addressing the underlying cause and preventing complications. **Case report:** We present the case of a 71-year-old woman with a history of controlled hypertension who was initially hospitalized for lumbar pain. She later developed sudden epigastric pain and a single episode of hematemesis. Esophagogastroduodenoscopy confirmed acute esophageal necrosis. A conservative management strategy—established jointly with the general surgery and gastroenterology teams—resulted in favorable clinical outcomes. **Conclusion:** Recognizing Gurvits syndrome as an uncommon cause of gastrointestinal bleeding is essential to ensure timely diagnostic and therapeutic intervention, ultimately improving patient outcomes.

Keywords

Necrosis, esophagus, endoscopy, gastrointestinal bleeding.

INTRODUCTION

Gurvits syndrome, also known as acute esophageal necrosis or black esophagus, is a rare entity characterized by circumferential black discoloration of the esophageal mucosa, with an estimated incidence ranging from 0.01% to 0.28% in autopsy series and endoscopic studies[1].

Its etiology is not fully understood; however, its pathophysiology is considered multifactorial, involving noxious factors such as ischemic events, corrosive injury from gastric acid, and intrinsic alterations of the esophageal mucosal barrier[2].

Clinical presentation is nonspecific, and esophagogastroduodenoscopy (EGD) is required for diagnostic confirmation, in which variable involvement of the esophagus is observed. Most commonly, the distal portion is affected due to its lower degree of vascularization compared with the proximal and middle segments[3].

Currently, there is no specific treatment. Initial measures aim to restore hemodynamic stability, correct the underlying cause, and prevent the development of complications[4].

We report the case of a patient with sudden epigastric abdominal pain and an episode of hematemesis, in whom EGD revealed acute necrotizing esophagitis. The patient was managed conservatively, with favorable clinical outcomes and no development of complications. The objective is to highlight the diagnostic and therapeutic approach to an unusual entity such as Gurvits syndrome.

CLINICAL CASE

A 71-year-old female patient with a single medical history of controlled arterial hypertension presented with a two-day history of nonradiating low back pain associated with nausea, without other symptoms such as fever, angina, dyspnea, or vomiting.

Upon admission to the emergency department, blood pressure was 140/80 millimeters of mercury (mm Hg), heart rate (HR) was 92 beats per minute (bpm), oxygen saturation (SpO_2) was 94% on room air, and temperature was 37 degrees Celsius.

Laboratory tests were obtained and showed evidence of acute kidney injury. The remaining studies revealed no electrolyte abnormalities, anemia, leukocytosis, thrombocytopenia, or prolonged coagulation times, and urinalysis showed no evidence of infection. Given the characteristics of the pain, thoracoabdominal aortic computed tomography angiography was performed, which ruled out aortic emergency and other differential diagnoses.

The neurosurgery team considered the pain to be nonspecific low back pain without signs suggesting a clear etiology and therefore decided on symptomatic management.

During the following 24 hours, the patient developed sudden epigastric abdominal pain and a single episode of non-coffee-ground hematemesis. She was evaluated by the general surgery service, which noted marked abdominal pain but no hemodynamic instability or signs of peritoneal irritation. Consequently, an urgent non-contrast abdominal computed tomography (CT) scan was requested, which ruled out pneumoperitoneum, hollow viscus perforation, and showed no causal findings explaining the patient's pain. Immediate EGD was therefore considered, which revealed acute necrotizing esophagitis without complications (**Figure 1**).

Conservative management was chosen. Parenteral nutrition (PN) was initiated, and additional extension studies were completed by internal medicine without identifying an underlying etiology. The patient was evaluated by gastroenterology, which concluded that, after ruling out differential diagnoses and given the clinical presentation, the extensive esophageal involvement was secondary to gastroesophageal reflux disease.

At 72 hours, with favorable clinical evolution and without abdominal pain, sepsis, or signs of perforation or mediastinitis, PN was discontinued and the diet was advanced until full tolerance of oral intake was achieved. The following day, after reassessment by gastroenterology, the patient was discharged with dual-dose proton pump inhibitor therapy for 12 weeks and a follow-up endoscopic evaluation scheduled in four weeks. The patient ultimately decided not to continue follow-up.

DISCUSSION

Gurvits syndrome is an uncommon clinical condition characterized by circumferential black discoloration of the esophageal mucosa[3,4]. The first case was described in 1990 by Goldenberg and colleagues, and it was subsequently classified as a syndrome by Gurvits and colleagues[5].

Acute esophageal necrosis is four times more common in men than in women and occurs more frequently in the sixth decade of life, with a mean age at presentation of 71 years. The most common risk factors include arterial hypertension, diabetes *mellitus*, dyslipidemia, chronic kidney disease, peripheral arterial disease, coronary artery disease, heart failure, cancer, and cardiovascular disease[5].

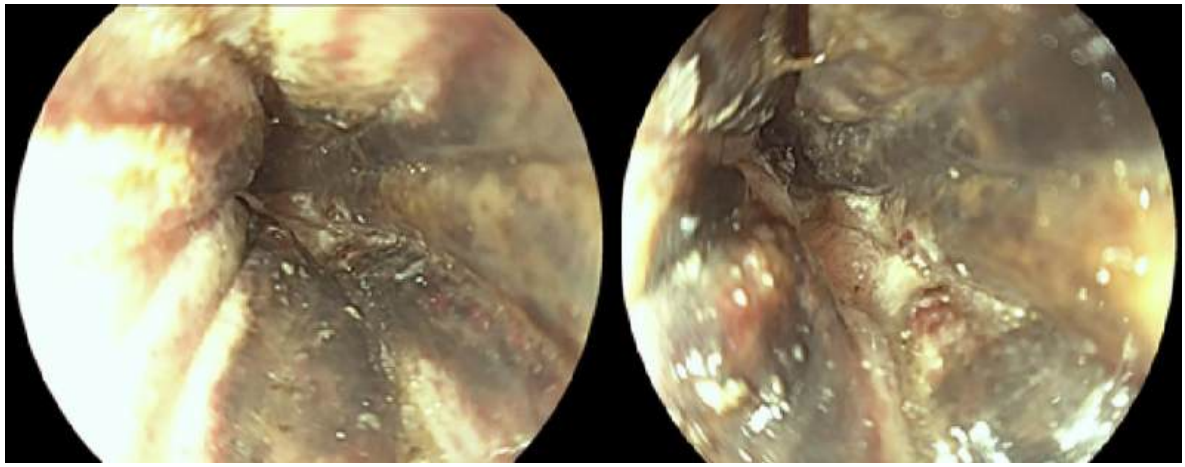


Figure 1. Esophagogastroduodenoscopy showing extensive esophageal necrosis. Author's file.

As mentioned previously, its etiology is often multifactorial, resulting from the combination of factors such as vascular compromise due to ischemic alterations, corrosive injury from massive secretions in the setting of gastroesophageal reflux, and reduced effectiveness of the protective barriers of the mucosa[6].

Clinical presentation is nonspecific, which makes diagnostic suspicion difficult. Onset may occur with symptoms related to complications associated with the underlying condition (diabetic ketoacidosis, anemia, pharyngitis, sepsis of urinary or gastrointestinal origin) and, in some cases, with upper gastrointestinal bleeding (UGIB). Given the rarity of this entity and the heterogeneity of its clinical spectrum, the true frequency of UGIB as the initial manifestation of acute esophageal necrosis remains unknown[7,8].

UGIB is, in turn, a common cause of consultation and hospitalization worldwide, with an incidence of 40 to 150 cases per 100,000 inhabitants. Pinto and colleagues performed a statistical analysis of the main causes of UGIB in a series of 249 patients and found that 72% were due to nonvariceal bleeding. Of these, 44% corresponded to peptic ulcer disease, 11% to erosive gastropathy or duodenopathy, 10% to esophageal ulcer, 5% to gastrointestinal neoplasia, 4% to Mallory-Weiss syndrome, 4% to Dieulafoy's lesion, 2% to angiodysplasia, 2% to gastric antral vascular ectasia, and another 2% to Cameron ulcer; Gurvits syndrome was not mentioned among the causes of UGIB in this study[9]. Notably, in the literature review conducted, Gurvits syndrome is considered an unusual cause of bleeding, and no records were found regarding the incidence of this entity as an etiology of UGIB.

A particular feature of our case is that the patient had controlled arterial hypertension as her only medical history, in contrast to most reported cases, which describe patients with a high burden of comorbidities and multiple risk factors, such as hemodynamic shock, advanced cardiovascular disease, metabolic dysfunction, and gastric outlet obstruction secondary to malignancy or gastroduodenal ulcer disease[6].

Esophagogastroduodenoscopy is the diagnostic method of choice, in which multiple findings may be observed, including active bleeding, clots, and esophageal, duodenal, or gastric ulcerations. It is characterized by predominant involvement of the distal esophagus due to its lower degree of vascularization[5,10]. Computed tomography has been described as a useful modality to rule out complications[4,11].

Treatment is usually conservative. A systematic review by Bayati and colleagues reported that most cases were managed conservatively with favorable outcomes and that the rate of endoscopic intervention with stent placement increased from 9.7% to 30%[12].

Conservative measures include withholding oral intake, initiating intravenous fluid resuscitation, transfusion of blood products when necessary, treatment of the underlying cause or coexisting clinical conditions, use of proton pump inhibitors, and administration of antibiotics in cases of concomitant infection or esophageal perforation. Surgical interventions are indicated in the presence of hemodynamic instability, signs of peritoneal irritation, failure of medical management, or complications[8,13,14].

Regarding complications, none exceed an incidence of 10% of all cases, with esophageal perforation being the most severe. This complication should be suspected in the presence of rapid clinical or hemodynamic deterioration. Other complications include mediastinitis, pneumomediastinum, abscess formation, superinfection, and stricture development[15].

Overall, prognosis is poor and largely depends on the presence and decompensation of underlying comorbidities, the patient's hemodynamic status, critical illness, or the development of complications. Exact mortality data for the different clinical scenarios are not available; however, disease-specific mortality is estimated to be approximately 6%[15].

CONCLUSION

Considering Gurvits syndrome as an unusual cause of gastrointestinal bleeding allows for a timely diagnostic and therapeutic approach and, consequently, a favorable impact on patient clinical outcomes.

Conflict of Interests

The authors declare no conflicts of interest.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

Ethical Considerations

This research complies with current regulations in bioethical research. Authorization was requested and obtained from the Research and Research Ethics Committee of Hospital Pablo Tobón Uribe to proceed with publication. The images used do not disclose personal information that would allow patient identification, and complete anonymity has been preserved.

REFERENCES

1. Monteiro JMC, Castelo LF, Fischer WGG, Felipe-Silva A. Black esophagus. Autops Case Rep. 2019;9(1):e2018077. https://doi.org/10.4322/acr.2018.077
2. Bong HSS, Soh YSA, Shabbir A, So JBY. Gastrointestinal: Black esophagus. J Gastroenterol Hepatol. 2022;37(1):46. https://doi.org/10.1111/jgh.15542
3. Thomas M, Sostre Santiago V, Suhail FK, Polanco Serra G, Manocha D. The Black Esophagus. Cureus. 2021;13(10):e18655. https://doi.org/10.7759/cureus.18655
4. Uyar S, Duman A, Tan A, Akbay Harmandar F, İnal G, Köker G, et al. Black esophagus. Turk J Gastroenterol. 2019;30(11):986-7. https://doi.org/10.5152/tjg.2019.181019
5. Dias E, Santos-Antunes J, Macedo G. Diagnosis and management of acute esophageal necrosis. Ann Gastroenterol. 2019;32(6):529-40. https://doi.org/10.20524/aog.2019.0418
6. Chugh P, Tzimas D, Gurvits GE. A rare cause of upper gastrointestinal bleeding. Gastroenterology. 2013;145(6):e11-2. https://doi.org/10.1053/j.gastro.2013.07.045
7. González Díaz I, Moreno-Sánchez M, Zarauza Soto Y, Burgos Garcia A. Black esophagus. Rev Esp Enferm Dig. 2023;115(11):646-7. https://doi.org/10.17235/reed.2022.9217/2022
8. Rehman O, Jaferi U, Padda I, Khehra N, Atwal H, Parmar M. Epidemiology, Pathogenesis, and Clinical Manifestations of Acute Esophageal Necrosis in Adults. Cureus. 2021;13(7):e16618. https://doi.org/10.7759/cureus.16618
9. Pinto C, Parra P, Magna J, Gajardo A, Berger Z, Montenegro C, et al. Hemorragia digestiva alta variceal y no variceal: mortalidad intrahospitalaria y características clínicas en un hospital universitario (2015-2017). Rev Med Chil. 2020;148(3):288-94. https://doi.org/10.4067/S0034-98872020000300288
10. Chinta S, Jyala A, Ghazanfar H, Makker J. Black Esophagus: A Rare Case of Acute Esophageal Necrosis. Cureus. 2024;16(1):e52660. https://doi.org/10.7759/cureus.52660
11. Grigore M, Enache I, Chirvase M, Popescu AL, Lonita-Radu F, Jinga M, et al. Acute Esophageal Necrosis in Acute Pancreatitis-Report of a Case and Endoscopic and Clinical Perspective. Diagnostics (Basel). 2023;13(3):562. https://doi.org/10.3390/diagnostics13030562
12. Al Bayati I, Badhiwala V, Al Obaidi S, Didia C, Zuckerman MJ, Elhanafi S. Endoscopic Treatment of Black Esophagus With Fully Covered Metallic Stent. J Investig Med High Impact Case Rep. 2022;10:23247096221084540. https://doi.org/10.1177/23247096221084540
13. Kitawaki D, Nishida A, Sakai K, Owaki Y, Nishino K, Noda Y, et al. Gurvits syndrome: a case of acute esophageal necrosis associated with diabetic ketoacidosis. BMC Gastroenterol. 2022;22(1):277. https://doi.org/10.1186/s12876-022-02349-z
14. Jaber F, Alsakarneh S, Sripada S, Gaur R, Rajab R, Mohamed I, et al. "Black Esophagus" or Gurvits Syndrome: A Rare Cause of Upper Gastrointestinal Bleeding in Diabetic Ketoacidosis. Cureus. 2023;15(2):e34989. https://doi.org/10.7759/cureus.34989
15. Gurvits GE. Black esophagus: acute esophageal necrosis syndrome. World J Gastroenterol. 2010;16(26):3219-25. https://doi.org/10.3748/wjg.v16.i26.3219

https://doi.org/10.22516/25007440.1338

Case report

Delayed Diagnosis and Uneventful Recovery: Unusual 20-Month Case of an Esophageal Foreign Body

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OPEN ACCESS

Citation:
Santamaría-Losada PA, Pedroza-Sabogal SE. Delayed Diagnosis and Uneventful Recovery: Unusual 20-Month Case of an Esophageal Foreign Body. Revista. colomb. Gastroenterol. 2025;40(4):521-527.
https://doi.org/10.22516/25007440.1338

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Received: 17/02/2025
Accepted: 25/03/2025

Abstract

Background: Prolonged retention of foreign bodies in the esophagus is rare and often delays diagnosis. Most patients seek medical attention within the first 72 hours after ingestion, preventing severe complications. **Case presentation:** We describe a 46-year-old man with an 18-month history of progressive dysphagia. After extensive diagnostic evaluation, a foreign body was identified in the upper esophagus—a dental prosthesis accidentally ingested 20 months earlier during an episode of alcohol intoxication. Given the degree of structural esophageal compromise, surgical extraction via cervicotomy and esophagotomy was performed. Postoperative recovery was favorable, with no major complications. **Conclusion:** This case underscores the importance of considering prolonged foreign body retention in patients with chronic, unexplained dysphagia. A detailed clinical history, appropriate imaging and endoscopic studies, and timely surgical intervention were critical to achieving a successful outcome. The absence of postoperative complications highlights the value of early recognition and proper management.

Keywords

Foreign body, esophagus, delayed diagnosis.

INTRODUCTION

Accidental or intentional ingestion of a foreign body is a relatively common situation in clinical practice[1]. Seventy-five percent of cases occur in children[2], primarily between three months and six years of age[3], and 25% in adults[2], in whom the main risk factors are intellectual disability, psychiatric disorders, alcohol abuse, and edentulism[4]. In the pediatric population, foreign bodies include objects such as coins, small toys, or even partially chewed food[2], whereas in adults the most frequent foreign bodies are fish bones and other bones[5]. In Colombia, González M. and colleagues conducted an observational study that included 110 patients aged 1 to 79 years, in which the esophageal foreign body was a fish bone in 33% of cases, a bone in 30%, coins in 13%, impacted meat in 11%, dentures in 3.3%, and another object in 8.4%[6]. Similarly, Aponte-Marín D. and colleagues carried out a 14-year retrospective descriptive study including patients aged 18 to 95 years, which determined that the most common location was the esophagus in 12.53% of cases, followed by the cricopharynx in 11.18% and the hypopharynx in 10%[7].

Although 80% to 90% of foreign bodies pass spontaneously through the gastrointestinal tract[1–3,8], the remaining 10% to 20% require intervention for removal. Endoscopy is usually the procedure of choice[6,9], and fewer than 1% of cases require surgical intervention[3]. An impacted foreign body carries a risk of serious complications such

as perforation, acute mediastinitis, and hemorrhage[10]. For this reason, patients with a history of ingestion and a sensation of foreign body impaction typically seek medical care an average of 1 to 72 hours after the event[6]. However, very few cases have been reported in which an esophageal foreign body persists for months, such as the case of a 57-year-old patient who remained asymptomatic until seven months after ingestion[11], or that of a six-month-old infant who presented with respiratory symptoms, including a three-month history of chronic cough secondary to a pistachio shell lodged in the esophagus[12]. There are even dramatic clinical presentations, such as the presence of an inflammatory mass in the posterior mediastinum after 26 months due to an aluminum cap in the esophagus[10].

We present the clinical case of a patient who developed gradually progressive dysphagia over 18 months, in whom multiple differential diagnoses were considered prior to the identification of an esophageal foreign body secondary to ingestion of his dental prosthesis during a state of intoxication 20 months earlier. The patient provided and signed informed consent authorizing the scientific publication of this report.

CASE REPORT

We describe a 46-year-old male patient from Apulo, Cundinamarca, a construction worker with a high-school level education, who presented to the medical center with an 18-month history of progressive dysphagia. Due to worsening symptoms and the endoscopic finding of a solid esophageal lesion with severe stenosis, he was referred to the emergency department.

Prior to admission to our institution, the patient had initially sought outpatient medical care after six months of progressive dysphagia and odynophagia and was referred to the otorhinolaryngology service, where he was first evaluated nine months after symptom onset. Nasofibrolaryngoscopy was performed under the diagnostic suspicion of chronic pharyngitis and revealed left septal deviation, bilateral inferior turbinate hypertrophy, oral moniliasis, and laryngeal manifestations of gastroesophageal reflux disease. Based on these findings, he was referred to gastroenterology.

The gastroenterology service indicated an upper gastrointestinal endoscopy to evaluate chronic dysphagia of 13 months' duration at that time. The procedure was performed four months prior to admission and reported chronic antral gastritis and a mass in the cervical esophagus. A biopsy was obtained, and the pathology report described a fibrin mesh, mucohemorrhagic material with severe acute inflammation, occasional bacterial colonies, scattered epithelial cells, and reactive changes, concluding moderate lymphoid aggregate activity with the presence of foveolar hyperplasia.

Additionally, a barium esophagogram was ordered two months prior to hospital admission at our institution. The radiology report described adequate coordination of the soft palate, opacification of an esophagus of normal caliber throughout its entire length, no intrinsic lesions or extrinsic compression, adequate passage of contrast into the stomach, and no evidence of gastroesophageal reflux (**Figure 1**). Based on these results, gastroenterology recommended follow-up with endoscopic ultrasound, which was performed two days prior to admission to our institution and reported upper esophageal stenosis due to a space-occupying lesion with whitish, submucosal, solid characteristics. Ultrasonographic scanning at 12 MHz demonstrated an irregular hyperechoic component causing stenosis that impeded distal advancement of the endoscopic equipment.

The diagnosis was a solid lesion of the upper esophagus; an embedded foreign body within the esophageal wall and secondary severe stenosis were ruled out. Therefore, the patient was referred to the emergency department for evaluation by gastroenterology and general surgery.

During hospitalization, given the high suspicion of a neoplastic lesion on the right anterolateral proximal esophageal wall, involving 50% of the lumen, a contrast-enhanced computed tomography (CT) scan of the chest and neck was indicated. This study reported an image suggestive of a hyperdense foreign body in the proximal esophagus at the level of the T1–T2 vertebral bodies, associated with thickening of the esophageal walls at this location. Correlation with a complementary endoscopic study was recommended for adequate characterization (**Figures 2** and **3**). In light of these imaging findings, the patient was reinterviewed and reported that 20 months earlier, during an episode of intoxication, he had lost his dental prosthesis. He stated that he had not attributed his symptoms to that episode, as he remained asymptomatic until two months later and assumed that the prosthesis had been lost rather than swallowed.

Given the new findings, gastroenterology performed a third endoscopy, which reported a five-centimeter foreign body embedded immediately below the cricopharyngeal muscle, with a high suspicion of contained perforation. However, the patient showed no signs suggestive of mediastinitis, was hemodynamically stable, had no signs of systemic inflammatory response or ventilatory failure, and laboratory tests showed no leukocytosis or neutrophilia, with normal nitrogenous waste levels. Therefore, a scheduled surgical procedure was indicated.

A left cervicotomy with esophagotomy was performed, revealing severe tissue edema, marked fibrosis in the tra-



Figure 1. Esophagogram prior to hospital admission. Author's file.

cheoesophageal groove that completely distorted the anatomy, and a foreign body (dental prosthesis) (**Figure 4**) embedded in the esophageal mucosa. The foreign body was removed, esophagorrhaphy was performed, and a sternocleidomastoid muscle patch was fashioned. Finally, layered closure was completed, a Jackson-Pratt drain was placed, and inpatient monitoring was indicated with antibiotic therapy using cefuroxime and metronidazole, in addition to parenteral nutrition.

A methylene blue test was performed on postoperative day five and was negative for leaks. An esophagogram was performed on postoperative day six, which reported parameters within normal limits, with no leaks or stenosis (**Figure 5**). Progressive oral intake was then initiated and was tolerated without complications. The patient was ultimately discharged on postoperative day eight after removal of the drain, with no need for further interventions. The patient returned for follow-up one month after hospital



Figure 2. Axial chest CT. The green arrow indicates a foreign body at the T2 level. Author's file.

discharge, at which time satisfactory clinical evolution was observed, the surgical wound was in good condition, swallowing was adequate, and there was no dysphagia, respiratory symptoms, or signs suggestive of fistulization, nor chest pain or limitations in daily activities.

DISCUSSION

Prolonged retention of a foreign body in the esophagus is an uncommon phenomenon and represents a considerable diagnostic challenge. In most cases, patients with esophageal foreign bodies seek medical attention within the first 72 hours after ingestion, allowing for early identification and removal with minimal complications. However, the case presented highlights the possibility of a prolonged course with nonspecific and progressive symptoms, which can lead to significant diagnostic delay.

The patient described in this report required approximately 18 months to develop significant dysphagia and 20 months to receive a definitive diagnosis. The absence of acute initial symptoms and the lack of a clear history of foreign body ingestion during the clinical interview contributed to the diagnostic difficulty. This phenomenon has been previously documented in the literature, with reports of foreign bodies retained for months or even years before detection[10–12]; however, this is a novel case given the favorable outcome, as the patient did not develop serious complications such as esophageal perforation, mediastinitis, or postoperative stenosis, which are common adverse events in these scenarios. Despite severe fibrosis and the prolonged duration of foreign body retention, postoperative recovery was successful, with no need for additional interventions or long-term complications.

From a clinical standpoint, this case underscores the importance of maintaining a high index of suspicion in patients with chronic dysphagia of undetermined cause, particularly in those with a history of foreign body ingestion, episodes of intoxication, or daily use of dental

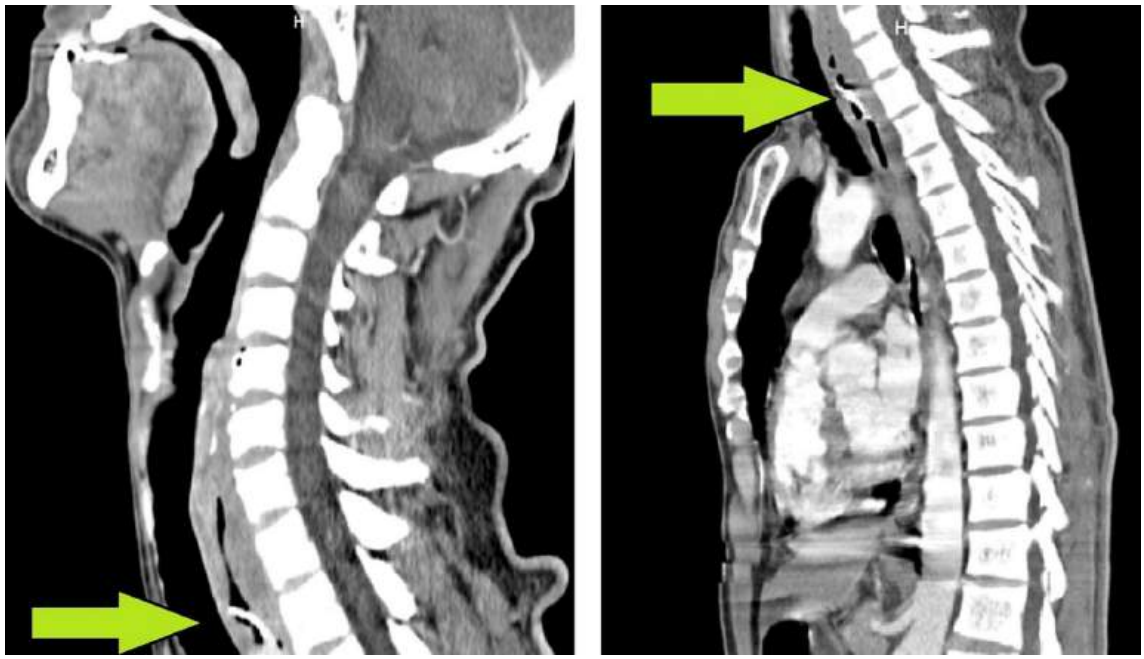


Figure 3. Sagittal CT of the chest and neck. The green arrow indicates a foreign body at the T2 level and significant edema causing esophageal stenosis. Author's file.

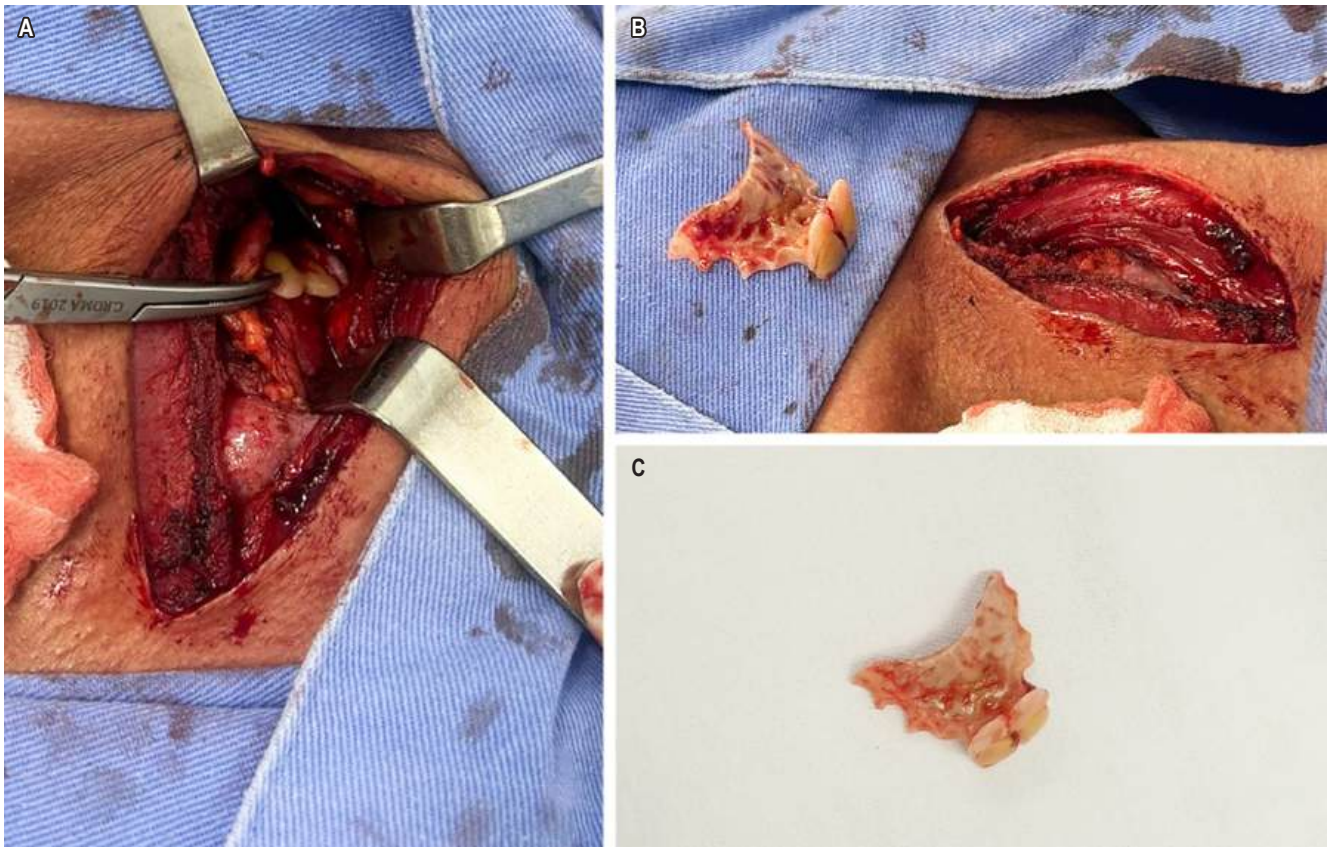


Figure 4. A. Intraoperative view of left cervicotomy and esophagotomy with a foreign body embedded in the esophageal wall. **B** and **C.** Extracted foreign body (dental prosthesis). Author's file.

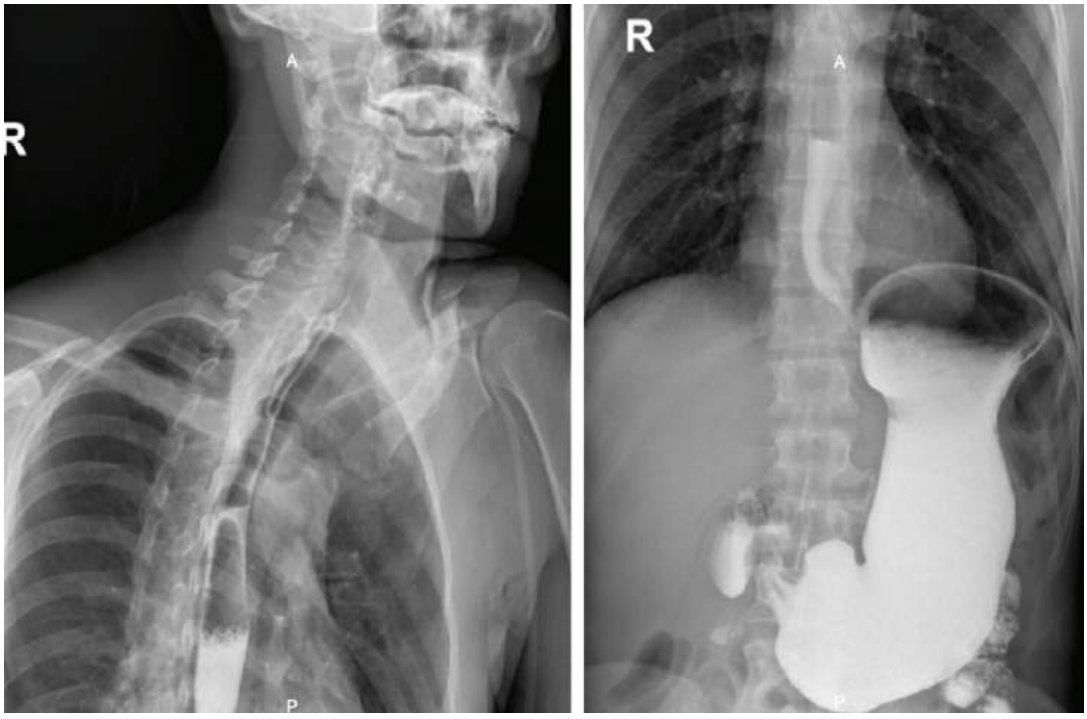


Figure 5. Postoperative esophagogram. Author's file.

prostheses. In this case, imaging studies were essential for establishing the diagnosis, as the prolonged symptomatic course and the unclear history of foreign body ingestion led to multiple delays in reaching a definitive diagnosis. In addition, nonspecific findings on the initial endoscopic examinations were interpreted as nonspecific inflammatory activity and neoplastic masses.

The surgical approach via left cervicotomy and esophagotomy was required due to the location of the foreign body and the severe fibrosis of the surrounding tissue. Although most esophageal foreign bodies can be removed endoscopically[9], this case illustrates the importance of surgical intervention in scenarios where there is suspicion of contained perforation, severe fibrosis, or structural compromise of the esophagus.

CONCLUSION

This case highlights the importance of considering retained foreign bodies in the differential diagnosis of patients with progressive chronic dysphagia. A thorough clinical history, appropriate use of endoscopic and imaging studies, and a multidisciplinary approach are key to early detection and selection of the most appropriate treatment. Although endoscopy remains the method of choice for foreign body removal, surgical intervention continues to be an indispensable alternative in complex cases with structural esophageal involvement. Finally, this case underscores the need to educate patients with risk factors about the importance of seeking early medical attention when foreign body ingestion is suspected, in order to prevent complications and optimize prognosis. It also highlights the relevance of appropriate follow-up to assess postoperative evolution and ensure recovery without sequelae.

Declaration of Conflicts of Interest

The authors declare no conflicts of interest.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

Use of Artificial Intelligence

The ChatGPT tool was used as an aid in drafting the discussion section of the article.

REFERENCES

1. Boumarah DN, Binkhamis LS, AlDuhileb M. Foreign body ingestion: Is intervention always a necessity? Ann Med Surg (Lond). 2022;84:104944. https://doi.org/10.1016/j.amsu.2022.104944
2. Totadri VM, Mohanty SK, Tudu HC, Praharaj D, Giri S, Gupta S. Sharp-pointed foreign body ingestion in a child: a unique case report and literature review. J Integr Med Res. 2024;2(4):265-8. https://doi.org/10.4103/jimr.jimr_25_24
3. Salman H, Gürsoy Koca T, Dereci S, Akçam M. Foreign body ingestion and management in children. Pediatr Emerg Care. 2022;38(11):617-20. https://doi.org/10.1097/PEC.0000000000002856
4. Jims DAD, Soundrarajan S, RanjithKumar M, Senthilnathan M. Superior thyroid artery injury following foreign body ingestion in an intellectually disabled patient: A case report. Saudi J Anaesth. 2024;18(4):576-9. https://doi.org/10.4103/sja.sja_234_24
5. Boo SJ, Kim HU. Esophageal foreign body: treatment and complications. Korean J Gastroenterol. 2018;72(1):1-5. https://doi.org/10.4166/kjg.2018.72.1.1
6. González M, Gómez M, Otero W. Cuerpos extraños en esófago. Rev Colomb Gastroenterol. 2006;21(3):150-61.
7. Aponte-Martín DM, Nuñez-Renza JE, Córdoba-Guzmán AC, Parra-Parra V, Huertas-Quintero MM, Acero F, et al. Cuerpos extraños del tracto digestivo: experiencia de 14 años en una clínica universitaria. Rev Colomb Gastroenterol. 2024;38(4):472-8. https://doi.org/10.22516/25007440.1086
8. Veerapthiran K, Tudu HC, Mohanty SK, Totadri VM, Debata PK. Impacted metallic foreign body in esophagus: our experience with a turbulent case and a review of management protocols. J Indian Assoc Pediatr Surg. 2025;30(2):241-3. https://doi.org/10.4103/jiaps.jiaps_218_24
9. Ahmed Z, Arif SF, Ong SL, Badal J, Lee-Smith W, Renno A, et al. Cap-assisted endoscopic esophageal foreign body removal is safe and efficacious compared to conventional methods. Dig Dis Sci. 2023;68(5):1411-25. https://doi.org/10.1007/s10620-022-07741-z
10. Tashtush NA, Bataineh ZA, Yusef DH, Quran TM, Rousan LA, Khasawneh R, et al. Ingested sharp foreign body presented as chronic esophageal stricture and inflammatory mediastinal mass for 113 weeks: case report. Ann Med Surg (Lond). 2019;45:91-4. https://doi.org/10.1016/j.amsu.2019.07.028
11. Mohajeri G, Fakhari S, Ghaffarzadeh Z, Piri-Ardakani M. A case of the long-time presence of a large foreign body in esophagus without complication. Adv Biomed Res.

2016;5:205.
https://doi.org/10.4103/2277-9175.191001
12. Yahyaoui S, Jahaouat I, Brini I, Sammoud A. Delayed diagnosis of esophageal foreign body: A case report. Int J Surg Case Rep. 2017;36:179-81.
https://doi.org/10.1016/j.ijscr.2017.05.028

https://doi.org/10.22516/25007440.1341

Case report

Primary Lymphoma of the Distal Ileum: Case Presentation and Literature Review

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OPEN ACCESS

Citation:
Melo-Peñaloza M. Primary Lymphoma of the Distal Ileum: Case Presentation and Literature Review. Revista. colomb. Gastroenterol. 2025;40(4):528-533.
https://doi.org/10.22516/25007440.1341

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Received: 25/02/2025
Accepted: 01/04/2025

Abstract

Introduction: Primary lymphoma of the small intestine is an uncommon neoplasm representing a small subset of extranodal non-Hodgkin lymphomas. Diagnosis is often challenging due to nonspecific symptoms, including abdominal pain, weight loss, and anemia, and may present as intestinal obstruction in advanced cases. Endoscopy with biopsy and computed tomography are key diagnostic tools, though surgical exploration is required in some instances. **Case report:** We describe a patient diagnosed with marginal zone B-cell lymphoma (MALT type) in the distal ileum, detected incidentally during colonoscopy. The patient underwent treatment with R-bendamustine/rituximab, achieving complete remission, with clinical and endoscopic follow-up over 8 years showing no recurrence. **Conclusions:** This review summarizes current evidence on anatomical distribution, clinical manifestations, radiologic and endoscopic findings, prognosis, and treatment strategies for intestinal lymphomas. Recent studies show that B-cell lymphomas carry a better prognosis than T-cell types, and that combining surgery with chemotherapy improves survival in localized disease. The findings underscore the importance of evaluating the distal ileum during routine colonoscopy, as thorough assessment may facilitate earlier diagnosis and improve patient outcomes.

Keywords

Lymphoma, intestine, B-cell lymphoma, diagnosis, endoscopy, MALT lymphoma, prognosis.

INTRODUCTION

In the intestine, lymphoid tissue is distributed under the designation GALT (gut-associated lymphoid tissue), which constitutes an essential component of the immune system and is designed to address the constant exposure to a high antigenic load derived from the diet and the commensal microbiota. This system is divided into two main compartments: organized GALT, which includes Peyer's patches and mesenteric lymph nodes, and diffuse GALT, composed of intraepithelial lymphocytes (IELs) and lamina propria lymphocytes (LPLs). Organized GALT acts as a key inducer of the intestinal immune response, whereas diffuse GALT functions as a direct effector of specific immune and tolerance responses. This structure allows discrimination between invasive antigens and innocuous components, thereby promoting intestinal protection and homeostasis[(1)].

The GALT of the ileum is characterized by a greater abundance of Peyer's patches, appearing as prominent organized lymphoid follicles. These patches are located primarily on the antimesenteric surface of the intestinal mucosa. Being more exposed to a higher antigenic load from intestinal contents (diet and microbiota), the ileum plays a more active role in the generation of adaptive immune responses. Peyer's patches in the ileum are key to capturing luminal antigens through specialized M cells[(1,2)].

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Interactions among T and B lymphocytes, dendritic cells, and factors such as transforming growth factor beta (TGF-β), a proliferation-inducing ligand (APRIL), and B-cell activating factor (BAFF) are critical for the differentiation and proliferation of B cells in the small intestine. APRIL and BAFF are cytokines of the tumor necrosis factor (TNF) family that play a crucial role in regulating the immune system, particularly in B-cell survival, activation, and differentiation. Both molecules are essential for mucosal immunity and the production of immunoglobulin A (IgA), which is key in Peyer's patches and other areas of the GALT[3].

Hematologic neoplasms include leukemias, lymphomas, myeloproliferative neoplasms, plasma cell dyscrasias, histiocytic tumors, and dendritic cell neoplasms. The classification currently in force is that of the World Health Organization (WHO) 2022[4]. Lymphomas are a heterogeneous group of neoplasms arising from lymphohematopoietic tissues and originating from B cells, T cells, or NK/T cells. They are divided into two main groups: Hodgkin disease and non-Hodgkin lymphoma. Hodgkin lymphoma is composed of B cells known as Reed-Sternberg cells; these very large cells are multinucleated or have a bilobed nucleus with prominent inclusion-like nucleoli. Reed-Sternberg cells tend to be CD30- and CD15-positive and are usually CD20- and CD45-negative[5].

Although most lymphomas are located in lymphoid organs (lymph nodes, spleen, thymus, Waldeyer's ring), up to 15%–48% of lymphomas arise in extralymphoid tissues or organs. Most of these belong to the non-Hodgkin lymphoma group, as extranodal presentation of Hodgkin disease accounts for less than 1% of cases. The extranodal sites most frequently affected by lymphoma are the gastrointestinal tract, skin, and bone. Gastrointestinal lymphomas represent approximately 30%–44% of extranodal lymphomas[6].

The stomach is the most frequently involved site within the gastrointestinal tract, followed by the small intestine and, lastly, the colon. These account for 1%–7% of malignant tumors of the stomach, 20% of those of the small intestine, and 0.4% of those of the large intestine. Most are non-Hodgkin lymphomas, with B cells predominating over T cells[7]. Primary lymphoma of the small intestine is an infrequent entity within non-Hodgkin lymphomas (NHL), representing only a small fraction of these tumors and an even smaller proportion within the spectrum of gastrointestinal tract lymphomas, where most involve the stomach. Its low incidence, combined with nonspecific clinical presentation and the difficulty of accessing the small intestine with conventional endoscopic methods, makes early diagnosis challenging. Advances in colonoscopy and distal ileal exploration in recent years have allowed better characterization of these neoplasms; however, systematic evaluation of the distal ileum is neither mandatory nor routine in endoscopic practice, which may hinder diagnosis[8].

Due to its low worldwide frequency, treatment—whether surgery plus chemotherapy or chemotherapy alone—remains controversial. Clinical follow-up, whether conventional endoscopic surveillance or using other techniques, is still evolving. These considerations underscore the clinical and academic interest of the present case.

CLINICAL CASE

This is a 49-year-old female patient first evaluated on November 4, 2015, during a colonoscopy requested for the assessment of nonspecific abdominal pain. Colonoscopy findings were normal; however, in the distal ileum, approximately 3 cm from the valve, nodular-appearing lesions were identified over an extension of approximately 6 cm, from which biopsies were difficult to obtain (**Figure 1**).

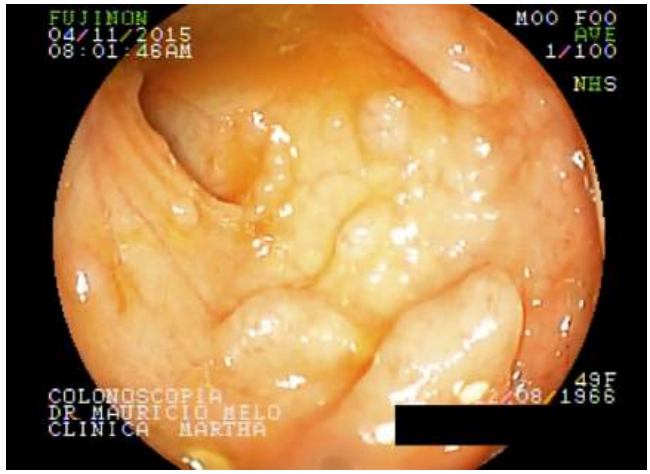


Figure 1. Year 2015. Appearance of the distal ileum with multiple nodular-appearing lesions. Pre-treatment image without histologic diagnosis. Author's File.

Biopsy showed reactive lymphoid hyperplasia. Given the nonspecific biopsy findings, a repeat ileocolonoscopy was suggested; however, the patient did not attend follow-up until April 26, 2017, when a new ileocolonoscopy was performed. In the distal ileum, approximately 3 cm from the ileocecal valve and extending for about 4 cm, irregular polypoid-appearing tissue with a rubbery consistency was found, making biopsy difficult; therefore, ten biopsies were obtained (**Figure 2**).

Pathology reported nodular ileitis, extranodal marginal zone B-cell lymphoma (MALT), with Ki-67: 1%, and positivity for CD20, CD5, CD43, and CD23. The hematologist staged the disease as stage IV (the classification system used was not specified), with involvement of the

ileum and bone marrow. The patient received the first cycle of chemotherapy with R-bendamustine/rituximab on July 7, 2017, followed by four similar cycles, which were completed on October 17, 2017. In May 2017, an abdominal computed tomography (CT) scan was normal, and a chest CT was also normal.

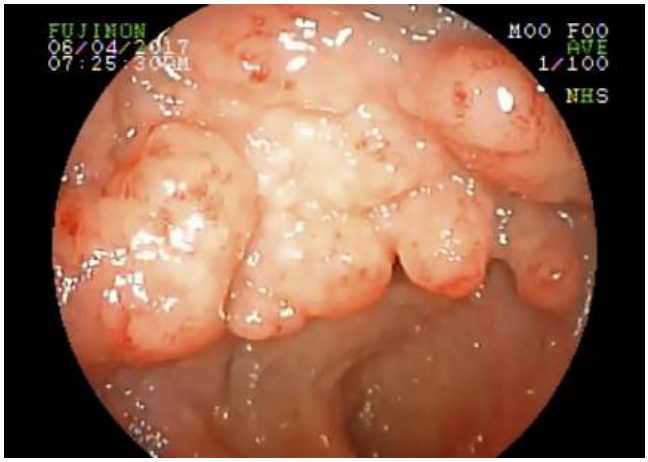


Figure 2. Year 2017. Distal ileum with irregular polypoid-appearing tissue, several with superficial erosions. Pre-treatment and diagnostic image. Author's File.

On follow-up colonoscopy on September 22, 2017, the ileal description revealed ileal mucosa in the process of healing. Biopsies were negative for malignancy, while ileal mucosal fragments showed reactive and cicatricial changes. In February 2018, ileocolonoscopy showed that the ileum appeared morphologically normal, and the previously described lesions now appeared as normal Peyer's patches (**Figure 3**). Biopsies demonstrated an infiltrate of lymphocytes with variable morphology that did not suggest monoclonality, and no evident lymphoepithelial lesion was identified. The hematologist noted that there was no evidence of a hematolymphoid lesion.

On September 9, 2018, the following complete blood count was reported: hemoglobin (Hb) 12.7; leukocytes 4,070; neutrophils 2,380; platelets 280,000. Ultrasound revealed cholelithiasis without cholecystitis, and lactate dehydrogenase (LDH) was 178.8 (normal value [NV]: 214 IU/L). On March 3, 2019, chest and abdominal CT scans showed cholelithiasis, with otherwise normal findings. On August 18, 2019, upper gastrointestinal endoscopy (EGD) showed nodular antral gastritis, while biopsy revealed the formation of lymphoid aggregates with scant forms of *Helicobacter pylori*. Eradication therapy was prescribed with esomeprazole 20 mg (two daily), amoxicillin 500 mg (four daily), and clarithromycin 500 mg (two daily) for 14 days. Ileocolonoscopy was normal, while ileal biopsies indicated nonspecific chronic ileitis and were negative for granulomas or malignancy (**Figure 4**).

At endoscopic follow-up on October 22, 2020, gastric biopsies showed chronic gastritis with mild acute activity, multifocal atrophy, and complete-type intestinal metaplasia, with *H. pylori* negativity. Ileocolonoscopy in October 2020 showed a normal appearance of the distal ileum. Three biopsies were obtained (**Figure 5**). Ileal biopsies revealed edema, increased interstitial infiltrate, and the presence of lymphoid aggregates, some with reactive centers. The interpretation was chronic ileitis. At endoscopic follow-up in February 2025, the ileum was found to be normal (**Figure 6**).



Figure 3. Year 2018. Distal ileum with normal appearance. Post-treatment image No. 1, normal. Author's File.



Figure 4. Year 2019. Distal ileum with Peyer's patches of normal appearance. Post-treatment image No. 2. Author's File.

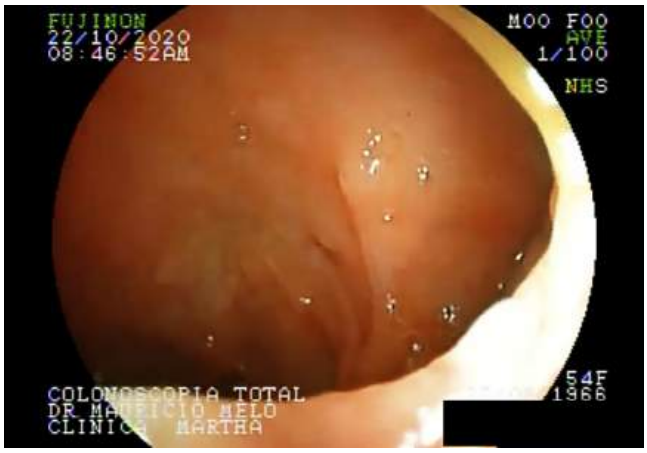


Figure 5. Year 2020. Panoramic view of the distal ileum at the edge of the ileocecal valve. Post-treatment image No. 3. Author's File.

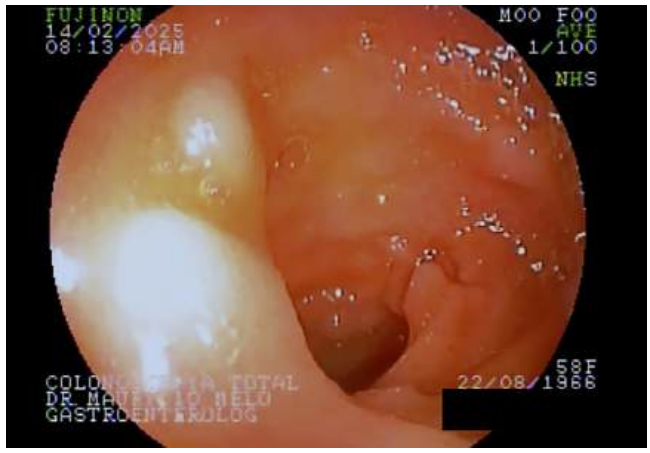


Figure 6. Year 2025. Distal ileum with normal appearance. Post-treatment image. Author's File.

DISCUSSION

Clinical diagnosis is not straightforward, as in uncomplicated cases of intestinal lymphoma the symptoms include persistent abdominal discomfort, fatigue and progressive weight loss, diarrhea or changes in bowel habits, and mild to moderate anemia with chronic subclinical bleeding. In cases with severe complications, patients present with obstructive symptoms such as abdominal distension, absence of bowel movements, and vomiting. When presentation includes perforation, fever and signs of septic shock are added to the aforementioned symptoms[9].

Facundo Navia and Manrique emphasize that primary lymphoma of the small intestine accounts for only 1%–4% of malignant tumors of the digestive tract. The lymphoma described in their publication was diagnosed after multiple medical consultations and imaging studies, which is consistent with the diagnostic challenge described in the literature[10]. In the series by Ge Z, the anatomic distribution of intestinal lymphomas (87 cases) showed a predominance in the distal ileum: 70.3% (within the 100 meters proximal to the ileocecal valve), followed by the jejunum: 16.2%, with multiple involvement of the small intestine in 5.4%. The greater involvement of the ileum is likely due to the higher concentration of lymphoid tissue in this region[11].

The endoscopic presentation of intestinal lymphoma is variable and may mimic other conditions such as Crohn's disease, intestinal tuberculosis, or even adenocarcinoma[12]. In up to 51.4% of cases, plaques or flat lesions predominate; elevated lesions occur in 20.7%, exophytic masses in 12.9%, and elevated lesions with ulceration in 9.3%. More aggressive lymphomas, such as diffuse large B-cell lymphoma (DLBCL), usually present with fungating or protruding lesions with ulcers[13].

According to a retrospective study, the distal ileum is the most frequent location of intestinal lymphomas, probably due to the abundance of lymphoid tissue in this region[11]. The most common histologic type is diffuse large B-cell lymphoma of the small intestine, characterized by large, pleomorphic cells with high proliferative activity (high Ki-67). It may arise from transformation of a pre-existing MALT lymphoma. It is characterized by CD20 positivity, Bcl-6 positivity, CD10 positivity or negativity, and a high proliferation rate (Ki-67 >50%)[14,15].

Diagnosis requires histopathology and immunophenotyping to differentiate B-cell from T-cell lymphomas, which determines treatment. In the case of MALT lymphomas associated with *H. pylori*, eradication with antibiotics may induce remission, whereas high-grade B-cell lymphomas usually require rituximab-based chemotherapy (R-CHOP)[15,16].

Treatment of primary intestinal lymphoma remains controversial. Retrospective studies have shown that the combination of surgery and chemotherapy improves survival in localized disease[17]. A comparative study reported higher survival rates and lower relapse rates in patients with intestinal DLBCL treated with surgery plus chemotherapy compared with those who received chemotherapy alone[18]. Nevertheless, management should be individualized according to stage, histologic type, and the presence of complications[19].

Gou retrospectively analyzed 116 patients to determine factors related to survival and treatment outcomes and found that unfavorable prognostic indicators included male sex, T-cell lymphoma, age over 60 years (associated

with worse outcomes compared with DLBCL), hypoalbuminemia, diagnosis at the time of intestinal perforation, stages III and IV, and not receiving chemotherapy[19].

In a retrospective study by Kim including 581 cases of primary intestinal lymphoma, favorable outcomes were associated with DLBCL or MALT histology, lymphoma localized to the ileocecal area, low LDH levels, Lugano classification I to III, and absence of fever or weight loss at presentation[20].

The clinical case presented here has several favorable response factors, including female sex, age under 50 years, LDH less than 200 IU, and B-cell MALT-type lymphoma. Endoscopy revealed pseudopolypoid lesions without a mass effect.

With respect to treatment, the case described received chemotherapy alone and showed a favorable outcome after 8 years of follow-up when compared with prior series in which both chemotherapy and surgery were administered. It should be noted that these are retrospective studies and that surgery was used in many cases in the presence of perforation or obstruction. Therefore, only prospective studies with random case selection—such as ours, which was detected at an early stage—could resolve this controversy. However, given the small number of cases and the heterogeneity of diagnostic scenarios, treatment decisions still largely depend on clinical judgment. In the present case, chemotherapy with endoscopic follow-up has proven effective, and in the era of monoclonal antibody-based chemotherapy (rituximab), this approach could potentially contribute to increasing case series in our setting and support chemotherapy-based treatment without surgery.

CONCLUSION

We reviewed a case of primary small intestinal lymphoma located in the distal ileum, detected during colonoscopy and ileoscopy performed for nonspecific abdominal symptoms. The patient was treated by the hematologist with a combination of R-bendamustine/rituximab for four cycles, resulting in clinical, endoscopic, and histopathologic improvement, and she has remained recurrence-free after eight years of follow-up. Based on the review, favorable factors included age, sex, location, and early-stage diagnosis.

In addition, this case highlights that all colonoscopies should, whenever possible, report intubation of the ileocecal valve and evaluation of the distal ileum. As discussed, early symptoms of these lymphomas are nonspecific, and as demonstrated in the reviewed studies, most primary lymphomas are located in the ileocecal region. Similar diagnoses may be missed if the ileocecal valve is not intubated and the greatest possible length of ileum is not explored during the procedure.

REFERENCES

1. Ramiro-Puig E, Pérez Cano F, Castellote C. El intestino: pieza clave del sistema inmunitario. Revista Española de Enfermedades digestivas. 2008;100(1):29-34. https://doi.org/10.4321/S1130-01082008000100006
2. Santaella ML. Components of the Immune System. En: Mak TW, Saunders ME, Jett BD (editores). Primer to the Immune Response. 2.ª edición. Elsevier; 2014. p. 21-54. https://doi.org/10.1016/B978-0-12-385245-8.00002-9
3. Park JI, Cho SW, Kang JH, Park TE. Intestinal Peyer's Patches: Structure, Function, and In Vitro Modeling. Tissue Eng Regen Med. 2023;20(3):341-353. https://doi.org/10.1007/s13770-023-00543-y
4. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IB de O, Berti E, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022;36(7):1720-1748. https://doi.org/10.1038/s41375-022-01620-2
5. Watanabe M, Hatsuse H, Nagao K, Nakashima M, Uchimaru K, Otsu M, et al. CD30 induces Reed-Sternberg cell-like morphology and chromosomal instability in classic Hodgkin lymphoma cell lines. Cancer Sci. 2023;114(8):3433-45. https://doi.org/10.1111/cas.15874
6. Rojas AC, Monterroso V, Luis J, Regocez Z. Linfomas del tracto gastrointestinal: reporte de 19 casos. Rev Cost de Cienc Méd. 1994;15(1,2):3-14.
7. Shirsat HS, Vaiphei K. Primary gastrointestinal lymphomas-A study of 81 Cases from a Tertiary Healthcare Centre. Indian J Cancer. 2014;51(3):290-2. https://doi.org/10.4103/0019-509X.146777
8. Hierro González A, Hano García OM, Jiménez G. Estudio endoscópico del íleon terminal. Rev Cubana Med. 2002;41(3):141-145. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75232002000300003&lng=es.
9. Liu XH, Chen G, Cao DD, Liu H, Ke XK, Hu YG, et al. Comparison of clinical features of patients with or without severe gastrointestinal complications in aggressive gastrointestinal lymphomas. World J Gastrointest Oncol. 2024;16(11):4409-23. https://doi.org/10.4251/wjgo.v16.i11.4409
10. Facundo Navia H, Manrique Acevedo ME. Linfoma primario del intestino delgado: reporte de un caso y revisión de la

literatura. Rev Colomb Gastroenterol. 2017;32(1):65-71. https://doi.org/10.22516/25007440.132
11. Ge Z, Liu Z, Hu X. Anatomic distribution, clinical features, and survival data of 87 cases primary gastrointestinal lymphoma. World J Surg Oncol. 2016;14:85. https://doi.org/10.1186/s12957-016-0821-9
12. Thomas AS, Schwartz M, Quigley E. Gastrointestinal lymphoma: the new mimic. BMJ Open Gastroenterol. 2019;6(1):e000320. https://doi.org/10.1136/bmjgast-2019-000320
13. Vetro C, Romano A, Amico I, Conticello C, Motta G, Figuera A, et al. Endoscopic features of gastro-intestinal lymphomas: from diagnosis to follow-up. World J Gastroenterol. 2014;20(36):12993-3005. https://doi.org/10.3748/wjg.v20.i36.12993
14. Hwang HS, Yoon DH, Suh C, Park CS, Huh J. Intestinal diffuse large B-cell lymphoma: an evaluation of different staging systems. J Korean Med Sci. 2014;29(1):53-60. https://doi.org/10.3346/jkms.2014.29.1.53
15. Tran QT, Nguyen Duy T, Nguyen-Tran BS, Nguyen-Thanh T, Ngo QT, Tran Thi NP, et al. Endoscopic and Histopathological Characteristics of Gastrointestinal Lymphoma: A Multicentric Study. Diagnostics (Basel). 2023;13(17):2767. https://doi.org/10.3390/diagnostics13172767
16. Bautista-Quach MA, Ake CD, Chen M, Wang J. Gastrointestinal lymphomas: Morphology, immunophenotype and molecular features. J Gastrointest Oncol. 2012;3(3):209-25. https://doi.org/10.3978/j.issn.2078-6891.2012.024
17. Hong YW, Kuo IM, Liu YY, Yeh TS. The role of surgical management in primary small bowel lymphoma: A single-center experience. Eur J Surg Oncol. 2017;43(10):1886-93. https://doi.org/10.1016/j.ejso.2017.06.016
18. Lee HS, Park LC, Lee EM, Shin SH, Ye BJ, Yong S, et al. Comparison of therapeutic outcomes between surgical resection followed by R-CHOP and R-CHOP alone for localized primary intestinal diffuse large B-cell lymphoma. American Journal of Clinical Oncology: Cancer Clinical Trials. 2014;37(2):182-7. https://doi.org/10.1097/COC.0b013e318271b125
19. Gou HF, Zang J, Jiang M, Yang Y, Cao D, Chen XC. Clinical prognostic analysis of 116 patients with primary intestinal non-Hodgkin lymphoma. Medical Oncology. 2012;29(1):227-34. https://doi.org/10.1007/s12032-010-9783-x
20. Kim SJ, Choi CW, Mun YC, Oh SY, Kang HJ, Lee SI, et al. Multicenter retrospective analysis of 581 patients with primary intestinal non-hodgkin lymphoma from the Consortium for Improving Survival of Lymphoma (CISL). BMC Cancer. 2011;11:321. https://doi.org/10.1186/1471-2407-11-321

https://doi.org/10.22516/25007440.1464

Commentary on the methodology of the article "Comorbidities of Irritable Bowel Syndrome in Colombia: Analysis of Data from the Ministry of Health"

Gerardo Andrés Puentes-Leal.[1*]

OPEN ACCESS

Citation:
Puentes-Leal GA. Commentary on the methodology of the article "Comorbidities of Irritable Bowel Syndrome in Colombia: Analysis of Data from the Ministry of Health. Revista. colomb. Gastroenterol. 2025;40(4):534-536.
https://doi.org/10.22516/25007440.1464

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Received: 09/10/2025
Accepted: 13/11/2025

Dear Editor,

The article by Saade and Rosselli[1], published in volume 40, issue 2 of 2025, highlights the importance of having national registries of health diagnoses that make it possible to strengthen epidemiological surveillance, optimize resource allocation, assess the impact of health interventions, and serve as a basis for prevalence studies, provided that the recorded information is valid, sensitive, and specific[2,3].

In Colombia, the Individual Health Services Delivery Records (Registros Individuales de Prestación de Servicios de Salud, RIPS), established by Resolution 3374 of 2000 of the Ministry of Health[4], require health service providers (IPS) and health insurers (EPS) to report the ICD-10 diagnoses generated during patient care. However, the use of RIPS as a primary data source for estimating prevalence presents important methodological limitations. These records serve an administrative and billing purpose, not a clinical one; therefore, it is not possible to verify compliance with diagnostic criteria or the use of ancillary diagnostic tests[5–7]. In addition, they lack traceability regarding patient follow-up and changes in diagnoses over time, which compromises their validity for prevalence estimation[8,9].

Furthermore, RIPS are susceptible to ICD-10 coding errors, overdiagnosis in emergency or primary care settings, and underreporting in patients with multiple comorbidities[10,11]. They also fail to adequately represent decentralized regions of the country that, due to coverage limitations, do not report information[12]. In rare or high-cost diseases that require specialized diagnostic confirmation, administrative records may constitute reliable sources. However, for conditions whose diagnosis depends on clinical criteria based on symptoms and time frames (such as irritable bowel syndrome [IBS]), these records introduce classification biases that compromise the internal validity of analyses[13,14].

IBS belongs to the group of disorders of gut-brain interaction, chronic conditions that produce varying degrees of severity, disability, and impairment in quality of life. Since 2016, diagnosis should be established using the Rome IV criteria, which are mandatory for research use and recommended as inclusion criteria in clinical practice[15–17]. Historically, variability in the approach to these symptoms led to the creation of The Rome Foundation in 1996, composed of leading expert gastroenterology researchers worldwide. This organization has developed and updated diagnostic criteria based on evidence in order to standardize diagnosis and research. The most recent update (Rome IV, 2016) incorporated pathophysiological mechanisms, promoted transcultural adaptation of the criteria, and strengthened the biopsychosocial approach[17,18]. The next

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version, Rome V, is expected in 2026. In Colombia, clinical practice guidelines officially recognize the Rome criteria as the diagnostic reference[16].

The transition from Rome III (2006) to Rome IV (2016) reduced the estimated prevalence of IBS by applying more specific criteria and excluding cases of symptom overlap, such as functional dyspepsia[17,18]. Therefore, studies that do not specify which version of the criteria was applied may overestimate or underestimate true prevalence. Likewise, underdiagnosis occurs in patients with mild symptoms who do not seek care, whereas overdiagnosis occurs when physicians do not apply the Rome IV criteria and label patients with nonspecific symptoms as having IBS without assessing symptom severity or persistence. Not all abdominal pain or episodes of constipation or diarrhea correspond to IBS[19–21].

At present, it is not recommended to use as a global reference the IBS prevalence figures reported by Canavan and colleagues, as cited by Saade and Rosselli[22], because that review included studies from different decades and with heterogeneous diagnostic criteria. More recently, the global epidemiological study by The Rome Foundation estimated an IBS prevalence of 4.3% in Colombia using strict application of the Rome IV criteria, thereby minimizing measurement and information biases[23].

One limitation of the study by Saade and Rosselli[1] is that the diagnostic instrument used to identify IBS cases is not specified. It is unclear whether the records were based on Rome III criteria, Rome IV criteria, or nonspecific clinical diagnoses. For this reason, prevalence results should be interpreted with caution: RIPS do not constitute a valid clinical instrument that guarantees a true diagnosis of IBS, but rather an administrative data source whose usefulness is primarily descriptive and subject to registration biases.

Consequently, the calculation of prevalence ratios or the quantification of increased risks of comorbidities in this population should be considered affected by measurement and classification biases, which distort both the magnitude and direction of the estimated associations. Although the coexistence of certain clinical conditions with IBS has been documented, others should be analyzed with caution, as in the case of the risk of schizophrenia. To increase the validity of the findings, it is advisable to complement analyses with clinical data sources, medical record review, or diagnostic validation using the Rome IV criteria.

The study by Saade and Rosselli[1] underscores the need to optimize national health information systems by strengthening the quality and traceability of clinical data. Only then can the potential of administrative records be harnessed as complementary tools in epidemiological research, provided their limitations are acknowledged and methods to mitigate measurement biases are employed.

RESPONSE TO THE LETTER TO THE EDITOR

We appreciate the comments made on our article and agree that the observation raised is valid. We acknowledge that the reported prevalences may be affected by underreporting and underdiagnosis, an issue we noted in the manuscript, particularly in the discussion and conclusion sections. This applies both to irritable bowel syndrome (IBS) and, to a lesser extent, to the other conditions evaluated. For this reason, prevalence values and prevalence ratios should not be interpreted as absolute estimates, but rather as approximations based on the available data.

The primary objective of the article was to demonstrate, using the methodology of prevalence ratios, that these conditions tend to coexist. The findings presented, derived from real-world data, make it possible to demonstrate such coexistence, in line with what has been described by other authors. Nevertheless, the manuscript also adequately discusses the study's limitations, allowing the results to be appropriately contextualized.

Sincerely,

Natalia Saade Cleves, MD
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REFERENCES

1. Saade-Cleves N, Rosselli D. Comorbilidades del síndrome de intestino irritable en Colombia: análisis de datos del Ministerio de Salud. Rev Colomb Gastroenterol. 2025;40(2):145-152. https://doi.org/10.22516/25007440.1289
2. Organización Mundial de la Salud (OMS). Global Health Observatory: Health data and statistics [Internet]. Ginebra: WHO; 2023 [consultado el 7 de octubre de 2025]. Disponible en: https://www.who.int/data/gh
3. Centers for Disease Control and Prevention (CDC). National Notifiable Diseases Surveillance System (NNDSS) [Internet]. Atlanta: CDC; 2024 [consultado el 7 de octubre de 2025]. Disponible en: https://www.cdc.gov/nndss

4. Ministerio de Salud y Protección Social. Resolución 3374 de 2000. Diario Oficial No. 44 184 [Internet]. Colombia: Ministerio de Salud y Protección Social; 2000 [consultado el 7 de octubre de 2025]. Disponible en: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/DE/DIJ/Resoluci%C3%B3n_3374_de_2000.pdf
5. Rosselli D, Pantoja-Ruiz C. SISPRO: la base de datos administrativa del sistema de salud colombiano. Acta Neurol Colomb. 2022;38(4):187-190. https://doi.org/10.22379/24224022426
6. Garcia-Subirats I, Vargas Lorenzo I, Mogollón-Pérez AS, De Paepe P, Ferreira da Silva MR, Unger JP, et al. Determinantes del uso de distintos niveles asistenciales en el Sistema General de Seguridad Social en Salud y Sistema Único de Salud en Colombia y Brasil. Gac Sanit. 2014;28(6):480-488. https://doi.org/10.1016/j.gaceta.2014.05.010
7. Murillo R, Bonilla S, Patiño D, Buitrago G. Validación del diagnóstico de cáncer gástrico en las bases de datos administrativas del sistema de salud colombiano. Rev Col Cancerol. 2024;28(4):139-148. https://doi.org/10.35509/01239015.1048
8. Ministerio de Salud y Protección Social. Lineamiento Técnico para el Registro y envío de los datos del Registro Individual de Prestaciones de Salud – RIPS, desde las Instituciones Prestadoras de Servicios de Salud a las EAPB. Oficina de Tecnología de la Información y la Comunicación – OTIC. Bogotá: Minsalud; 2019. Disponible en: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/DE/OT/Lineamientos-tecnicos-para-IPS.pdf
9. Ministerio de Salud y Protección Social. Lineamientos para el uso de información en salud en Colombia [Internet]. Bogotá: Minsalud; 2020 [consultado el 7 de octubre de 2025]. Disponible en: https://www.minsalud.gov.co/Lineamientos/Lineamientos%20t%C3%A9cnicos%20IPS.pdf
10. Fandiño-Losada A, Idrovo AJ, Téllez-Rozo N. Calidad de la información del sistema de salud colombiano: desafíos y oportunidades. Rev Salud Pública (Bogotá). 2019;21(3):357-366.
11. Gómez-Garcia LC. Comparación de las fuentes de información sobre cuatro eventos de interés en salud pública de gran demanda en los servicios de salud, Neiva, 2013. Biomédica. 2015;35(Supl.3):154. Disponible en: https://revistabiomedica.org/index.php/biomedica/issue/view/143
12. Ministerio de Salud y Protección Social. Informe de Gestión 2023 [Internet]. Bogotá: Minsalud; 2023 [consultado el 7 de octubre de 2025]. Disponible en: https://www.minsalud.gov.co/Ministerio/RCuentas/Documents/Informe-de-gestion-290124.pdf
13. Park JS, Lee CH. Clinical study using healthcare claims database. J Rheum Dis. 2021;28(3):119-125. https://doi.org/10.4078/jrd.2021.28.3.119
14. Gil Rojas Y, Torres Duque CA, Figueredo M del C, Hernández F, Castañeda Cardona C, Lasalvia P, et al. Estimación de la prevalencia de EPOC en Colombia a partir del Registro Individual de Prestaciones de Servicios de Salud (RIPS). Rev Colomb Neumol. 2019;31(1):5-15. https://doi.org/10.30789/rcneumologia.v31.n1.2019.325
15. Alvarado J, Otero W, Jaramillo Santos MA, Roa PA, Puentes GA, Jiménez AM, et al. Guía de práctica clínica para el diagnóstico y tratamiento del síndrome de intestino irritable en población adulta. Rev Colomb Gastroenterol. 2015;30:43-56.
16. Concha A, García del Risco F, Meisel Chinchilla E, Rincón Sánchez R, Leguizamo AM, Pulgar G, et al. Guía de práctica clínica en el diagnóstico y tratamiento del síndrome de intestino irritable en la población adulta: actualización y recomendaciones. Versión corta [Internet]. Asociación Colombiana de Gastroenterología, Universidad Nacional de Colombia; 2021 [consultado el 7 de octubre de 2025]. Disponible en: https://www.gastrocol.com/wp-content/uploads/2022/05/GUIA-PRACTICA-CLINICA-SII-VERSION-CORTA-2021.pdf
17. Drossman DA, Hasler WL. Rome IV - Functional GI Disorders: Disorders of Gut-Brain Interaction. Gastroenterology. 2016;150(6):1257-1261. https://doi.org/10.1053/j.gastro.2016.03.035
18. Schmulson MJ, Drossman DA. What Is New in Rome IV. J Neurogastroenterol Motil. 2017;23(2):151-163. https://doi.org/10.5056/jnm16214
19. Tariq T, Sieloff M, Irfan F. 488 National Trends and Outcomes of Irritable Bowel Syndrome Presenting to Emergency Departments: Results From the Nationwide Emergency Department Sample (NEDS) Database. ACG. 2019;114:S282-S283. https://doi.org/10.14309/01.ajg.0000591484.81819.37
20. Hayat M, Ali IA, Nusrat S. Emergency Department Visits and Inpatient Admissions - Trends in IBS Over a Decade: 439. ACG. 2018;113:S256. https://doi.org/10.14309/00000434-201810001-00439
21. Longstreth GF, Wong C, Chen Q. Misdiagnosis of diverticulitis after a prior diagnosis of irritable bowel syndrome (IBS). J Am Board Fam Med. 2020;33(4):549-560. https://doi.org/10.3122/jabfm.2020.04.190328
22. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. Clin Epidemiol. 2014;6:71-80. https://doi.org/10.2147/CLEP.S40245
23. Schmulson MJ, Puentes-Leal GA, Bustos-Fernández L, Francisconi C, Hani A, López-Colombo A, et al. Comparison of the epidemiology of disorders of gut-brain interaction in four Latin American countries: Results of The Rome Foundation Global Epidemiology Study. Neurogastroenterol Motil. 2023;35(6):e14569. https://doi.org/10.1111/nmo.14569