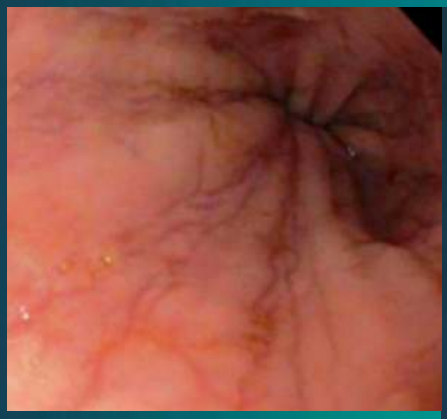
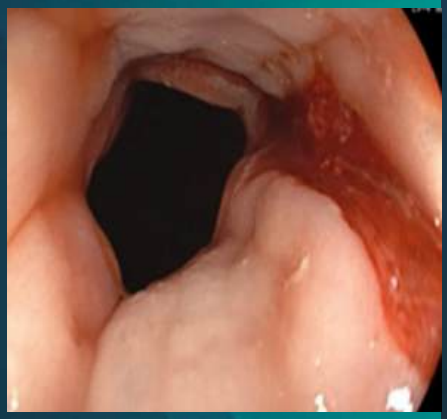
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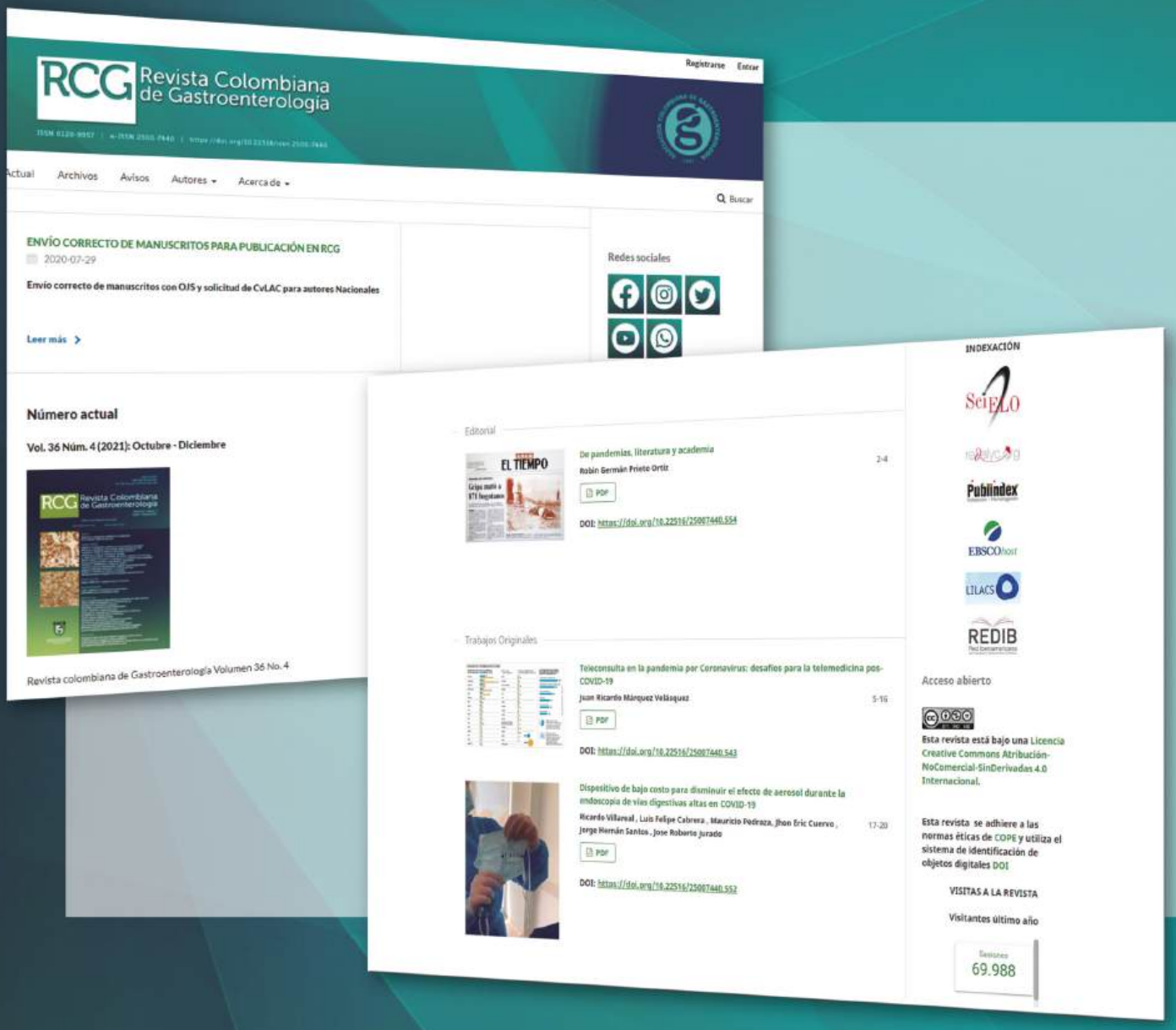
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Article: Esofagitis eosinofílica: estado del arte en 2024
Courtesy by the authors: Fabián Juliao-Baños, Adán Lúquez-Mindiola

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Editorial

Eosinophilic Esophagitis

Víctor Arbeláez.[1*]

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This issue of the Revista Colombiana de Gastroenterología features two articles related to eosinophilic esophagitis (EoE). The first, by Drs. Castaño, Álvarez, and colleagues[(1)], examines a cohort of 330 patients retrospectively collected from esophageal biopsy pathology results at four centers in Medellín. The study compares demographic characteristics, endoscopic findings, eosinophil counts in esophageal mucosa, concomitant atopic diseases, treatments received, diagnostic delays, and disease phenotypes between adolescents aged 12–17 and adults over 18. Undoubtedly, this is a noteworthy contribution, deserving of recognition and congratulations, as it helps the medical community in Colombia to more frequently and promptly identify and diagnose patients with this relatively new disease, whose global incidence has been increasing over the past few decades.

In addition, two leaders in the field of gastroenterology, Drs. Juliao and Lúquez[(2)], provide an enlightening state-of-the-art review on EoE. Their extensive, engaging, and up-to-date review covers the most relevant information on the epidemiology, pathophysiology, diagnosis, and treatment of the condition. Without doubt, this represents a significant contribution to the knowledge and education surrounding this disease in Colombia.

Dr. Castaño and colleagues' study highlights that 80% of patients with EoE are adults, with the remaining 20% being adolescents, most of whom are male. The study identified an average diagnostic delay of two years in adults, significantly longer than the 12-month delay observed in adolescents. This finding underscores the need to increase awareness of the disease among general practitioners, family physicians, and internists, among others. Differences were also observed in the frequency of stenotic/mixed and inflammatory phenotypes, which were more common in adults—likely due to the disease's longer duration and differences in treatment approaches between adolescents and adults[(3)]. However, the study was unable to determine whether clinical presentation differed significantly between the two age groups, possibly because the adolescents studied had an average age of 14. As noted in the publication by Drs. Juliao and Lúquez, the presentation in children is primarily characterized by abdominal pain, vomiting, feeding difficulties, and growth delays[(2)], which are likely the predominant manifestations in younger children.

In summary, EoE is a chronic inflammatory disease driven by a type 2 immune response involving food allergens. It is histologically characterized by an increase in eosinophils (>15 per high-power field) in the esophageal mucosa, leading to esophageal dysfunction with defined clinical manifestations. Approximately 30% of cases may develop strictures or a narrow-caliber esophagus[(4,5)]. The condition has several treatment options with variable efficacy and differing profiles of adverse effects, convenience, costs, and availability, making its management a significant challenge.

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Treatment decisions should be made collaboratively with the patient and their family, particularly in pediatric cases. As highlighted in the review by Juliao and Lúquez, all proposed treatments have evidence of efficacy, which is further supported by a systematic review and meta-analysis of maintenance therapies presented at the American Digestive Disease Week 2024[6]. Empiric food elimination therapy is an effective treatment for patients of all ages. However, there is debate over whether to begin with a six-food elimination diet or to eliminate only cow's milk, which is an appealing option as it simplifies dietary restrictions. Arguments exist for both approaches[7,8], and overall adherence rates for long-term dietary maintenance are reported to be low, at approximately 20%. A recent study by Wang and colleagues found that 57% of patients who completed the six-food elimination diet entered the maintenance phase, with 100% maintaining remission at three years[4].

Proton pump inhibitors (PPIs) have demonstrated efficacy, are widely available, reasonably priced, and have a high tolerance and safety profile. Topical corticosteroids are effective medications; however, their prolonged use can lead to adverse effects, such as candidiasis (7%)[9]. There have been no significant changes in bone biomarkers with budesonide use[10,11], and the incidence of adrenal insufficiency is low[9]. Esophageal dilations performed using the appropriate technique are effective and carry a very low risk of complications[12].

Biological therapy with dupilumab may be considered a first-line treatment for patients with moderate-to-severe disease who also have asthma, atopic dermatitis, or nasal polyposis and who strongly prefer to avoid dietary restrictions or topical steroids. It may also be suitable for those with a low likelihood of responding to PPIs or topical steroids.

The development of a severity scale, available as an application, could significantly improve therapeutic decision-making in the near future. The goal of treatment is to achieve and maintain clinical, endoscopic, and histologic remission, whether through monotherapy or a combination of available therapies.

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Original article

Eosinophilic Esophagitis and Clinical, Endoscopic, and Therapeutic Differences Between Adolescents and Adults

Rodrigo Castaño,[1*] Jorge Rivera,[2] Lucy Diazgranados,[3] Juan Diego Baena,[4] Juan Esteban Puerta Botero,[5] Isabella Cadavid,[5] Óscar Álvarez.[6]

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Abstract

Background: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated esophageal condition triggered by exposure to food antigens. Its incidence is increasing, but the differences in its manifestations between adolescents and adults remain underexplored. **Objective:** This study aims to compare clinical characteristics, diagnostic delays, endoscopic and histological findings, allergic comorbidities, and therapeutic options in patients with EoE onset during adolescence (12–17 years) versus adulthood (≥18 years). **Materials and Methods:** A total of 334 patients diagnosed with EoE through esophageal biopsies across four institutions over five years were included. Data collected included variables such as sex, age, diagnostic delay, disease phenotype, presence of persistent allergic symptoms, endoscopic characteristics assessed using the EREFS score, and eosinophil counts in biopsies. Statistical analysis was performed to identify significant differences between the groups, with a significance threshold of $p < 0.05$. **Results:** Of the 334 patients, 272 were adults (81.4%) and 62 were adolescents (18.6%). No significant differences were found in sex distribution or allergic symptoms. However, adults experienced a longer diagnostic delay (22 months vs. 12 months, $p = 0.001$) and a higher prevalence of a stenotic phenotype (16.9% vs. 6.5%, $p = 0.02$). In contrast, adolescents exhibited a higher frequency of endoscopic findings indicative of EoE (EREFS: 95.2% vs. 90.1%; $p = 0.036$) and higher eosinophil counts (47 vs. 35 Eo/HPF [high power field], $p = 0.017$). Therapeutic approaches also differed: adolescents were predominantly treated with dietary restrictions and topical corticosteroids, while adults received proton pump inhibitors. **Conclusions:** EoE demonstrates differences in diagnosis, presentation, and treatment depending on the age of onset. These disparities highlight the need to develop age-specific management guidelines and to encourage further research into the factors driving these variations.

Keywords

Eosinophilic esophagitis, allergy, adults, adolescents, proton pump inhibitors.

INTRODUCTION

In the early 1990s, two case series described adult patients suffering from dysphagia histologically associated with esophageal infiltration by more than 15 eosinophils per high-power field (eos/HPF)[1,2], while control group patients with gastroesophageal reflux disease (GERD) had an average of 3.3 eos/HPF. This pattern was quickly recognized as a distinct entity from GERD and was described as primary or idiopathic eosinophilic esophagitis (EoE). The presentation of dysphagia and food impaction in atopic individuals, with endoscopic findings of esophageal rings and longitudinal furrows, was markedly different from the heartburn, regurgitation, and erosive esophagitis seen in GERD. A few months later, Kelly and colleagues[3] reported a series of allergic children presenting with GERD-like

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symptoms such as anorexia, vomiting, and failure to thrive, who were refractory to medical or surgical therapy. These pediatric patients demonstrated significant eosinophilic infiltration of the esophagus and responded to treatment with a hypoallergenic diet. In addition to coinciding with the increased use of endoscopy in children, it was recognized that esophageal biopsies could show inflammation even when the mucosa appeared normal endoscopically[4]. This observation led to the adoption of mucosal biopsies as a standard practice in children undergoing endoscopic evaluation for symptoms, a key difference from endoscopic practices in adults.

Additionally, Kelly's publication[3] laid the groundwork for a series of future studies examining the allergic diathesis and mechanisms of EoE. Therapeutic regimens were developed, including the elimination of the six most common food allergens and the implementation of a diet guided by food allergy testing[5,6]. Furthermore, the global concept emerged that EoE was a chronic disease, as patients experienced recurrence of symptoms when foods were reintroduced into their diet.

Due to the challenges of adhering to dietary restrictions and the impact of steroids on other eosinophilic diseases, researchers opted for two alternative therapies. In 1998, Faubion and colleagues[7] adapted a novel approach to deliver topical steroids to the esophageal mucosa. They utilized aerosolized steroids from an asthma inhaler, administered via ingestion to the esophageal mucosa, eliciting an anti-inflammatory response. In their series of four patients, they found this delivery method to be effective in alleviating symptoms and reducing esophageal eosinophilia upon examination. That same year, Liacouras and colleagues[8] demonstrated that patients with eosinophilic esophagitis (EoE) responded clinically and histologically to prednisone, although symptoms recurred when the medication was discontinued.

In the absence of secondary causes of esophageal eosinophilia, such as eosinophilic gastroenteritis, celiac disease, hypereosinophilic syndrome, or Crohn's disease, among others, EoE is a chronic, localized, and progressive disorder mediated by the type 2 T-helper immune response. It is characterized by symptoms of esophageal dysfunction and eosinophil-predominant inflammation. Over the past 20 years, the incidence and prevalence of EoE have increased significantly[9-11], including in our region[12,13], raising the question of whether the disease manifests similarly in children and adults. Children with EoE exhibit clinical and endoscopic features distinct from those seen in adults, which may explain some differences in symptom presentation.

Using esophageal biopsies from adult and adolescent patients diagnosed with eosinophilic esophagitis at three referral centers, the aim was to compare clinical characteristics, diagnostic delays (defined as the time elapsed between symptom onset and biopsy-confirmed diagnosis), endoscopic and histologic findings, allergenic comorbidities, and therapeutic options employed in adolescents (<18 years) versus adults (≥18 years) with EoE.

PATIENTS AND METHODS

This is a cross-sectional analysis based on the results of esophageal biopsies diagnosing EoE obtained over seven years (from January 2015 to December 2021) at four institutions in Medellín, Colombia. This diagnosis allowed for telephone or in-person contact with patients, and two age groups were considered in the evaluation: those under 18 years old (adolescents) and those 18 years or older (adults).

Analyzed Variables

The data collected include sex, date and age at diagnosis, endoscopic characteristics, the EoE phenotype (inflammatory, structuring, or mixed), the maximum eosinophil count at diagnosis, and the presence of concomitant atopic manifestations (persistent or seasonal), as determined at the time of EoE diagnosis. Additionally, the use of proton pump inhibitors (PPIs), dietary modifications, and therapies with swallowed topical steroids were considered, along with an evaluation of the response to therapy (both clinical and histological). Finally, the need for endoscopic dilation and the number of dilation sessions were assessed.

Definition of Terms

Based on the endoscopic report, EoE characteristics were recorded according to the EREFS classification system[14]. The total EREFS score (0–9) is calculated by summing the severity scores of five main individual components (edema: 0–1, rings: 0–3, exudates: 0–2, furrows: 0–1, and strictures: 0–1) and the minor finding of crepe paper esophagus (mucosal fragility or laceration upon endoscope passage: 0–1). Higher scores indicate more severe endoscopic findings. There are two phenotypic forms of the disease: an inflammatory form and a fibrostenotic form. A normal esophageal diameter, whitish exudates, edema, and linear furrows constitute the inflammatory form, while fixed rings, strictures, and esophageal narrowing characterize the fibrostenotic type. Given that ongoing eosinophilic inflammation tends to progress to fibrous remodeling with collagen deposition and stricture formation, a proportion of patients present with mixed endoscopic features of these two phenotypes.

Treatment response is independently evaluated based on clinical, endoscopic, and histological criteria. Symptomatic

improvement of >50% from baseline is considered a clinical response. Histological remission is defined as a maximum eosinophil count below the diagnostic threshold of 15 cells per high-power field (HPF) across all esophageal levels after treatment.

Treatment

The therapy evaluated reflects real-world experience in managing EoE. First-line anti-inflammatory therapies are selected based on patient characteristics and preferences. Endoscopic dilation is performed in cases of esophageal strictures (either at the time of disease diagnosis or in combination with effective anti-inflammatory treatment), narrow-caliber esophagus, or persistent symptoms despite histological and endoscopic remission.

Statistical Analysis

The mean, median, standard deviation (SD), and interquartile ranges (IQR) were calculated for continuous variables. The mean and SD were used for variables with a normal distribution, while the median and IQR were applied to those with a non-normal distribution. Normality was assessed using the Kolmogorov-Smirnov test. Comparisons were performed using the Student's T test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Percentages were calculated for categorical variables, which were compared between groups using the chi-square (χ^2) or Fisher's exact test. Statistical analyses were conducted using SPSS software version 26 (SPSS Inc., Chicago, USA). Statistical significance was defined as a p-value <0.05.

Ethical Considerations

The research involving human participants was conducted in compliance with fundamental human rights and ethical principles for biomedical research involving humans, in accordance with Article 11 (right to life) of the Political Constitution of Colombia and the agreement of the World Medical Association. Additionally, the study adhered to the principles of the Declaration of Helsinki, Law 23 of 1981, and Resolution 8430 of 1993. The study was carried out in conformity with the principles of the Declaration of Helsinki and the guidelines of the International Conference on Harmonization for Good Clinical Practice (ICH-GCP).

Institutional ethics committees from each participating entity approved the study protocol. In accordance with the ethical risk classification outlined in Colombia's Resolution 8430/93, this study was considered to be risk-free, as it involved the use of retrospective documentary research methods and techniques. There were no intentional interventions or modifications to the biological, physiological, psychological, or social variables of the individuals participating in the study. The research consisted of reviewing medical records, conducting interviews, completing questionnaires, and other methods where no sensitive aspects of participants' behavior were identified or addressed.

RESULTS

Demographic Characteristics

Patients were contacted following the histological confirmation of EoE, and data on birth dates and diagnosis dates were recorded. The adult cohort (≥18 years at diagnosis) consisted of 272 patients (81.4%), while the adolescent cohort (<18 years at diagnosis) included 62 patients (18.6%). No sex differences were observed between adults and adolescents, with males predominating in all age groups (75.8% in adolescents and 72.1% in adults; p = 0.659). The main demographic and clinical characteristics of these patient cohorts are detailed in **Table 1**.

Diagnosis Delay

The median diagnostic delay for EoE was 17.1 ± 5.5 months, significantly longer in adults compared to adolescents (22 ± 6.4 months versus 12 ± 2.9 months; p = 0.001).

Allergic Manifestations

Rhinitis, asthma, conjunctivitis, and dermatitis were the four main atopic conditions reported by patients. However, no significant differences were observed between the adolescent and adult populations (**Table 1**).

Endoscopic Evaluation

The EREFS scores for endoscopic activity are presented in **Figure 1** and **Table 2**. Pediatric patients predominantly exhibited higher mean scores for inflammatory features (edema, furrows, exudates, and friability) compared to the fibrotic components of the EREFS (rings or strictures), which were more prevalent among adults. This contributed to a significantly higher prevalence of stenotic phenotypes in adults (11.8% versus 4.8%) compared to adolescents at the time of EoE diagnosis (p < 0.048).

Eosinophil Count

Differences in peak eosinophil count per high-power field (HPF) were also assessed. Pediatric patients exhibited hig-

Table 1. Demographic and Clinical Characteristics, Atopic Comorbidities, Endoscopic Phenotype, Eosinophil Count at Diagnosis, and Therapies in Adult and Pediatric EoE Patients

		Adolescents n = 62 (%)	Adults n = 272 (%)	*p*-Value
Age (years): median ± SD		14 ± 1.6	33 ± 8.8	
Sex M:F		47:15	196:76	0.659
Diagnosis delay (months ± SD)		12 ± 2.9	22 ± 6.4	0.001
Allergies	No	33 (53.2)	169 (62.1)	0.195
	Rhinitis	8 (12.9)	32 (11.8)	0.572
	Conjunctivitis	5 (8.1)	21 (7.7)	0.709
	Dermatitis	7 (11.3)	17 (6.2)	0.119
	Asthma	9 (14.5)	33 (12.1)	0.426
Phenotype	Inflammatory	51 (82.2)	188 (69.1)	0.03
	Stenotic	4 (6.5)	46 (16.9)	0.02
	Mixed	7 (11.3)	38 (14.0)	0.33
Eosinophil count (median ± SD)		47 ± 15.7	35 ± 14.1	0.017
Treatment	Dietary	52 (83.8)	115 (42.3)	<0.01
	Oral steroids	48 (77.4)	137 (50.3)	<0.01
	Proton pump inhibitors	34 (54.8)	248 (91.2)	<0.01
	Dilations	1 (1.6)	26 (9.6)	0.038

SD: Standard Deviation. Author's own research.

her maximum eosinophil densities, with median counts in esophageal biopsies significantly exceeding those of adults (47 ± 15.7 versus 35 ± 14.1, $p = 0.017$). Correspondingly, the increased percentage of stenotic phenotypes with advancing patient age was inversely correlated with peak eosinophil counts in esophageal biopsies (Spearman's Rho = –0.161; $p < 0.003$).

Choice of First-Line Treatment and Efficacy in Inducing Remission

Differences were observed in the choice of first-line treatment for children and adults with EoE in real-world practice (**Table 1**). Dietary therapies (83.8% versus 42.3%) and oral steroids (77.4% versus 50.3%, $p < 0.01$) were used more frequently in children than in adults. A trend was noted where the use of dietary therapies as an initial intervention to induce EoE remission decreased with patient age at diagnosis, while the opposite was observed for proton pump inhibitor (PPI) therapy. The efficacy of the three first-line treatment options in inducing clinical and histological responses was not different between children and adults (**Table 1**). Additionally, no differences in efficacy were detected among empirical food elimination diets, PPIs, and oral steroids between pediatric and adult patients. Finally, endoscopic dilations performed in children and adults (either as a standalone procedure or combined with other anti-inflammatory treatments) were analyzed. This procedure was performed more frequently in adults (38 patients, 11.8%) than in children (3 patients, 4.8%; $p = 0.048$).

DISCUSSION

Based on biopsy findings, this study compiles the various characteristics and differences in EoE presentation between adolescents and adults. Differences between adolescent-onset EoE and adult-onset EoE were evaluated with respect to symptoms, endoscopic findings, histological activity at diagnosis, and the use of different treatment options. Data collection enabled direct comparisons between patients of different age groups to better define the natural history of EoE and its features across age ranges. The symptoms associated with EoE and its endoscopic characteristics evolved across age groups, with notable differences even within specific age ranges. As described recently, the presentation of EoE is heterogeneous in the pediatric population, with findings varying between young children and adolescents[15].

Fibrotic features progressively develop with age, leading to a significantly higher risk of strictures and the need for endoscopic dilation in adults. Differences were noted in the first-line treatments administered to pediatric versus adult EoE patients, though the response to these treatments was similar regardless of age[16].

In a recent review, Visaggi and colleagues[17] analyzed the key differences between children and adults with EoE at the time of diagnosis, providing indirect evidence that endoscopy in children often reveals a predominantly inflammatory pattern, while adults more frequently exhibit a fibrostenotic phenotype. A recent study based on data from the European Pediatric Eosinophilic Esophagitis Registry also found that endoscopic findings of fibrosis, particularly esophageal rings, were more common in adolescents, whereas exudates were more frequent in younger children[15]. Similarly, a retrospective cohort of EoE patients recruited from 10 centers in the United States documented that a higher proportion of pediatric EoE patients displayed an inflammatory phenotype on endoscopy, while older individuals exhibited a more fibrostenotic phenotype compared to pediatric patients[18]. This difference is clearly supported by our study, which found that a fibrostenotic phenotype was nearly three times more prevalent in adults than in children. This finding may be related to a longer subclinical disease course in adults and a more extended diagnostic delay from symptom onset. Delayed diagnosis exceeding two years in EoE patients has recently been associated with

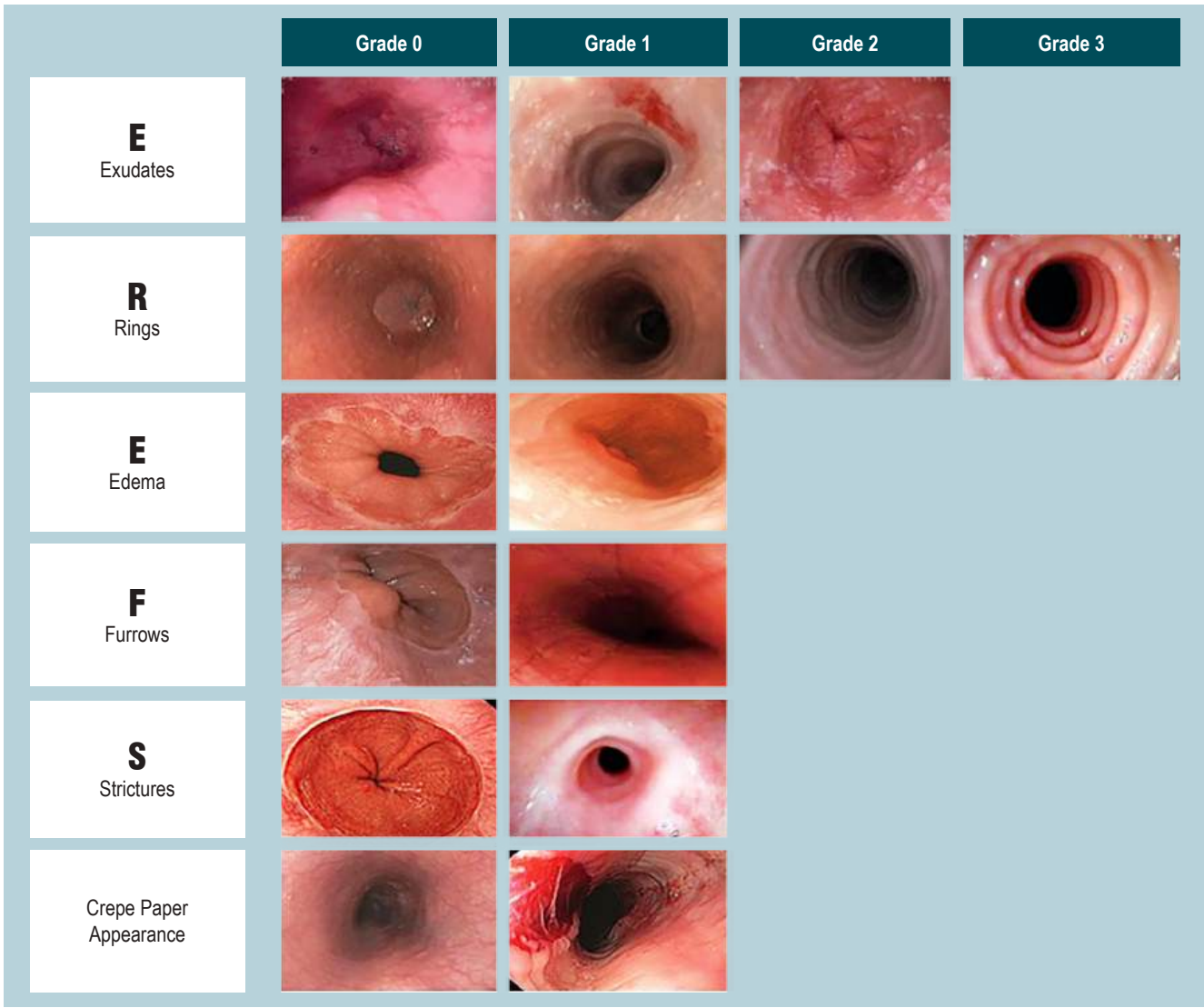


Figure 1. Endoscopic Characteristics of EREFS Scores in the Evaluation of Eosinophilic Esophagitis Author's own research.

Table 2. Endoscopic Characteristics of Eosinophilic Esophagitis in Both Groups

			Adolescents n = 62 (%)	Adults n = 272 (%)	Total n = 334	*p*-Value
Findings	Abnormal		59 (95.2)	232 (90.1)	291 (87.1)	0.036
	Normal		3 (4.8)	40 (9.9)	43 (12.9)	
EREFS score	Exudate	0	13 (21.0)	99 (36.4)	112 (33.6)	0.021
		1	17 (27.4)	80 (29.4)	97 (29.0)	
		2	32 (51.6)	93 (34.2)	125 (37.4)	
	Rings	0	20 (32.3)	153 (56.3)	173 (51.8)	0.002
		1	6 (9.7)	20 (7.4)	26 (7.8)	
		2	15 (24.1)	55 (20.1)	70 (21.0)	
		3	21 (33.9)	44 (16.2)	65 (19.4)	
	Edema	0	11 (17.7)	105 (38.6)	116 (34.7)	0.002
		1	51 (82.3)	167 (61.4)	218 (65.3)	
	Furrows	0	10 (16.1)	82 (30.1)	92 (27.6)	0.026
		1	52 (83.9)	190 (69.9)	242 (72.5)	
	Stricture	0	59 (95.2)	234 (88.2)	293 (87.7)	0.048
		1	3 (4.8)	38 (11.8)	41 (12.3)	
	Friability	0	29 (46.8)	187 (68.8)	216 (64.7)	0.082
		1	33 (53.2)	85 (31.2)	118 (35.3)	

Author's own research.

increased disease activity and progression to fibrostenosis[19]. Untreated EoE has been linked to esophageal stricture formation, with the risk of a fibrostenotic phenotype doubling for every 10-year increase in age, indicating that EoE is a progressive disease[20].

The disease phenotype may also influence symptom presentation. Most children reportedly experience nausea, vomiting, anorexia, abdominal pain, growth delay, and epigastric burning[15,17,21,22]. In contrast, dysphagia and food impaction are considered hallmark symptoms of adult-onset EoE, as previously documented[18].

Population-based epidemiological studies have described that the vast majority of EoE patients are between the first and sixth decades of life[23], although cases have been reported across all ages[24]. However, the incidence of EoE decreases with increasing age, and studies focusing on elderly patients are scarce[25]. Given that this age group is frequently excluded from clinical trials evaluating new EoE therapies, their response to different treatments remains largely unknown. A recent retrospective cohort study identified only 12 patients over 65 years old among newly diagnosed individuals treated with oral steroids in the University of North Carolina EoE database[26].

Although environmental factors are increasingly recognized as significant in the etiology of EoE[27], familial clustering of EoE in population-based studies suggests a substantial genetic contribution[28]. Our study also evaluated the presence of four atopic conditions associated with EoE—rhinitis, allergic conjunctivitis, atopic dermatitis, and asthma—and found no differences between children and adults. A prior observation by Vernon and colleagues similarly described comparable histories of allergic rhinitis, atopic dermatitis, immunoglobulin E-mediated food allergies, and familial atopy in both children and adults with EoE[29], noting only a higher prevalence of asthma in children compared to adults.

In our study, similar to other survey-based studies conducted in Europe[30,31], the United States[32], and Australia[33] regarding therapy, PPIs were the most commonly prescribed first-line therapy for EoE across all age groups. This finding is consistent with records of clinical practice[34]. However, PPIs were prescribed significantly less frequently in adolescents compared to adults. For adolescents, dietary therapy and steroids represented first-line management, while PPIs and steroids were predominant in adults ($p < 0.01$). Notably, the effectiveness of different therapies did not differ between the age groups. Regarding endoscopic dilation, it was used six

times more frequently in adults than in children, reflecting the higher prevalence of fibrostenotic EoE among adults. However, the number of dilation procedures performed did not differ by patient age, likely indicating the dominant effect of endoscopic dilation when combined with effective anti-inflammatory treatment for EoE[35,36].

Another significant finding of our study was the markedly shorter diagnostic delay among pediatric patients compared to adults (12 ± 2.9 vs. 22 ± 6.4 months; p = 0.001). Differences in diagnostic delays from symptom onset were previously reported in a 2012 multicenter study in Spain, which found delays of 28.04 ± 30 months for children and 54.7 ± 62 months for adults[37]. Data from the European EoE Registry indicate a diagnostic delay of approximately 1 year for pediatric EoE patients overall, closely matching the results of the European Registry of Clinical, Environmental, and Genetic Determinants in Eosinophilic Esophagitis (EoE CONNECT). However, these figures come from specialized centers managing EoE patients. Overall, diagnostic delays in EoE remain unacceptably long, particularly among adult patients[38].

Our study has several limitations. First, due to its retrospective nature, some data—such as details on dietary modifications or steroid medications—could not be reliably collected, limiting the evaluation of therapies in both groups. Second, as multiple centers contributed patients, there may be some heterogeneity in the treatment approaches for EoE patients, and differences in practice patterns could have influenced the treatment of both pediatric and adult cohorts. Third, this may have had a significant impact, as most treating physicians were not EoE experts and did not work in specialized EoE referral centers. Fourth, our data could not evaluate EoE disease endotypes, i.e., subtypes defined by molecular and cellular markers that may influence the identification, prognosis, and treatment response in EoE patients.

In conclusion, the largest study cohort comparing adolescent-onset and adult-onset EoE reveals that patients diagnosed at younger ages exhibit distinct clinical and endoscopic characteristics and differences in first-line therapy usage. However, treatment response rates were similar across all age groups.

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Original article

Cost-Utility Analysis of Colorectal Cancer Screening Starting at Age 45 Compared to Age 50 in Colombia

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Abstract

Background: Colorectal cancer (CRC) is among the four cancers with the highest incidence and mortality in Colombia. CRC screening is currently recommended in national guidelines starting at age 50. The American Cancer Society has suggested beginning screening at age 45. **Objectives:** To estimate the cost-utility ratio of initiating CRC screening at age 45 compared to age 50 in Colombia. **Methods:** A Markov model simulating the natural history of CRC was used to compare the initiation of screening at ages 45 and 50. The cost-utility analysis incorporated costs and utilized Colombia's per capita gross domestic product (GDP) threshold (COP 21,500,000). **Results:** Starting colonoscopy screening at age 45 was 0.33% less costly, yielded a gain of 3.49 quality-adjusted life years (QALYs), and reduced mortality by 37% compared to initiating at age 50 (costs: COP 92,364,407 vs. COP 92,669,231; QALYs: 19.40 vs. 15.91; and mortality proportion: 3.4% vs. 5.4%, respectively). **Conclusion:** Based on the Markov model analysis and the assumptions made, initiating CRC screening at age 45 was cost-effective. Costs were lower, more QALYs were gained, and the incremental cost-effectiveness ratio was below Colombia's GDP threshold. A budget impact analysis is recommended to support the implementation of policies in Colombia.

Keywords

Colon cancer, screening, cost-effectiveness, quality-adjusted life years.

INTRODUCTION

Colorectal cancer (CRC) is the third leading cause of cancer-related deaths in Colombia, following breast and prostate cancer, contributing significantly to morbidity, mortality, and high public health costs worldwide[1–3]. Approximately 80% of CRC cases are preceded by adenomatous polyps, considered precancerous lesions. When removed, these polyps significantly reduce CRC incidence[1,4,5]. Adenomas are histologically classified into tubular (87%), tubulovillous (8%), and villous (5%) types, with the latter having a higher potential for malignancy over a prolonged latency period of 10 to 15 years. Age is a known risk factor for their development[5–8].

The mortality rate from CRC in Colombia is 7.4%, and this figure has increased in recent years[1]. In 2021, 7,579 new cases were reported, with a five-year prevalence of 18,654 cases (equivalent to 36.6 cases per 100,000 inhabitants)[2]. Early-stage interventions can significantly alter cancer incidence[9–12]. According to Colombian legislation, CRC is recognized as a public health concern and a national priority. Early and integrated prevention of risk factors, along with effective, timely, and continuous detection, improves quality of life, reduces economic impact,

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and enhances social outcomes for patients (Article 5, Law 1384 of 2010)[13–16]. CRC screening is a recommended intervention outlined in local guidelines and endorsed by scientific cancer societies worldwide. Colonoscopy is the gold standard for CRC detection, offering the highest sensitivity and specificity as both a diagnostic and therapeutic tool for identifying adenomas. Colombian guidelines recommend negative-screening colonoscopies be repeated every 10 years, starting at age 50 and continuing until age 75[17]. For cases with positive adenoma findings, follow-up intervals depend on polyp size and histological characteristics. However, colonoscopy has certain disadvantages: it is invasive, requires bowel preparation, carries a risk of complications, and may be costly or have limited availability for large-scale implementation[18].

In Latin America, CRC screening is recommended starting at age 50[18–20]. The 2013 Colombian Clinical Practice Guideline (CPG) for colon and rectal cancer from the Ministry of Health and Social Protection, along with the 2015 CPG for colorectal cancer detection by the Colombian Association of Gastroenterology and the Colombian Association of Coloproctology, establish that CRC screening should begin at age 50 (a favorable recommendation with moderate-quality evidence) as a best practice. The choice of screening test should be individualized based on medical judgment. Colonoscopy is recommended as the first option, but fecal occult blood tests (FOBT), including the fecal immunochemical test (FIT) and the guaiac-based FOBT (g-FOBT), are acceptable alternatives[17]. When comparing colonoscopy to g-FOBT/FIT, colonoscopy demonstrated higher CRC detection rates (relative risk [RR]: 5.91, confidence interval [CI]: 70); however, compliance rates were higher with g-FOBT/FIT (RR: 0.57, 95% CI: 0.42–0.78)[17,18].

In 2018, the American College of Gastroenterology (ACG), the American Society for Gastrointestinal Endoscopy (ASGE), and the American Cancer Society published CRC screening guidelines recommending screening start at age 45. This was based on the rising incidence of CRC over the past two decades, which increased from 1.3% to 2.3% among individuals under 55 years of age[21]. Screening at age 45 could prevent 277,000 CRC cases and 203,000 deaths by 2030[22]. In 2019, a study conducted by Stanford University, the University of California, and the University of Pittsburgh reported that CRC screening at age 45 in a cohort of 1,000 individuals prevented four CRC cases, two CRC-related deaths, and gained 14 quality-adjusted life years (QALYs). However, earlier screening required 758 additional colonoscopies, thereby increasing costs[23]. A Colombian study documented adenoma findings in one out of every five screening colonoscopies in individuals aged 45 to 50 years (18.5% prevalence), supporting the justification for CRC screening starting at age 45[24].

Early CRC screening has economic implications for society[12]. In Europe, the economic burden of CRC is estimated at EUR 13 billion[25], while in the United States, the cost of diagnosing and treating CRC is approximately USD 100,000[26]. In Colombia, the economic burden of CRC and the cost of screening starting at age 45 remain unknown. U.S. recommendations are not directly applicable to Colombia due to differences in CRC diagnosis and treatment costs. Therefore, to evaluate and decide on the implementation of CRC screening in Colombia, cost-utility and cost-effectiveness studies using local monetary values are warranted[27].

The aim of this study was to assess whether initiating CRC screening at age 45 in Colombia is cost-effective compared to the threshold established by the World Health Organization (WHO) based on the gross domestic product (GDP). Additionally, the study evaluated its impact on mortality, QALYs, and costs.

METHODOLOGY

A microeconomic evaluation was conducted to analyze the cost-effectiveness[27] of initiating CRC screening at age 45 compared to age 50 from the perspective of a third-party payer. Costs and mortality were compared, expected outcomes for each age group were estimated using simulated mathematical modeling, and the incremental cost-utility ratio (ICUR) was calculated[28–30]. Screening was considered cost-effective when the ICUR was below the per capita GDP threshold, as defined by the Colombian Institute for Health Technology Assessment (IETS in Spanish) and the World Health Organization (WHO)[30]. A Markov model (**Figure 1**) was designed to compare three screening strategies: annual FIT-based FOBT, annual guaiac-based FOBT, and colonoscopy every 10 years. A positive FOBT result was followed by a colonoscopy.

A systematic literature review was performed using various MeSH terms in the Cochrane Library, Medline, SciELO, and Google Scholar databases. There were no language restrictions, and gray literature was included.

A 31-year time horizon was defined, starting screening at age 45 and continuing to age 76, the life expectancy in Colombia according to the National Administrative Department of Statistics (DANE in Spanish). The evaluation was conducted from the perspective of Colombia's General System of Social Security in Health (SGSSS in Spanish), incorporating the value of all direct resources associated with the use of the technology and the perceived health benefits directly experienced by patients. A

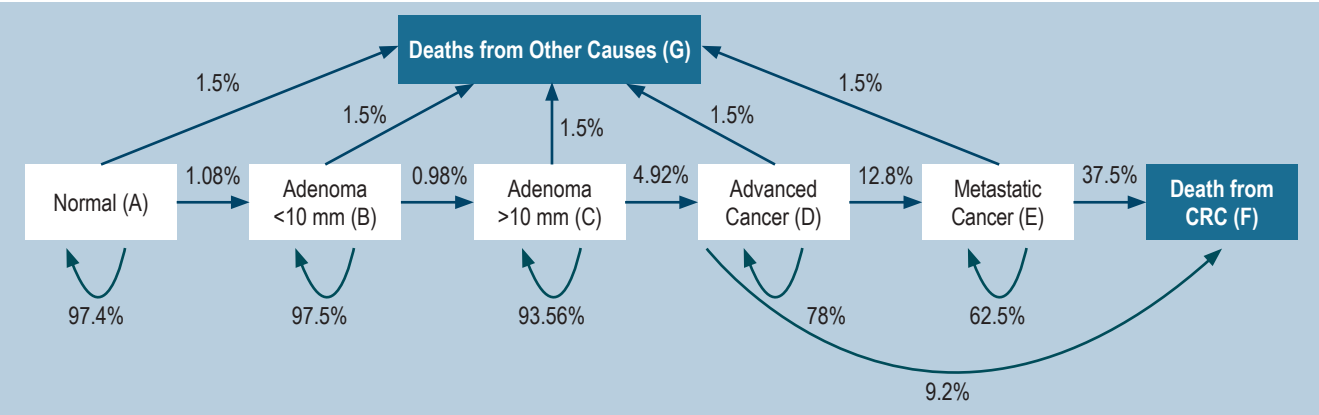


Figure 1. Markov Model Simulating the Natural History of CRC, Including Five Successive Health Transition Stages. Developed by the authors based on information from: López-Kostner F, and colleagues. Rev Med Chil. 2018;146(6):685–692[31]; Gupta S, and colleagues. Gastroenterology. 2020;158(4):1154[33]; Vatn MH, and colleagues. Cancer. 1982;49(4):819–25[34]; Williams AR, and colleagues. Gut. 1982;23(10):835–42[35]; Clark JC, and colleagues. Int J Cancer. 1985;36(2):179–86[36]; Arminski TC, and colleagues. Dis Colon Rectum. 1964;7:249–61[37]; Rickert RR, and colleagues. Cancer. 1979;43(5):1847–57[38].

5% annual discount rate, recommended by the IETS, was applied to costs and health effectiveness outcomes. The primary outcomes were the proportion of CRC-related mortality in both groups and quality-adjusted life years (QALYs).

To estimate costs, the Medication Price Information System (SISMED in Spanish) database was consulted to determine weighted averages and reported unit quantities. Micro-costing was conducted, and monetary valuation was calculated using the official fee manual of Colombia's mandatory traffic accident insurance (SOAT in Spanish). Direct costs for each stage were considered, including procedural costs and treatment costs for complications (**Tables 1–5**).

Based on published literature, frequencies for findings from screening colonoscopy were constructed, including probabilities for the health states proposed in the model for the disease at ages 45 and 50. Frequencies of findings

Table 1. Screening in Normal State (A)

Resource	Quantity	Usage Rate	Unit Cost	Source	Total Cost
General practitioner	1	100%	COP 35,100	SOAT 2020	COP 35,100
Specialist physician (family, internal or gastroenterologist)	1	100%	COP 41,300	SOAT 2020	COP 41,300
Fecal occult blood (guaiac-bases)	1	100%	COP 7,300	SOAT 2020	COP 7,300
Fecal occult blood (immunohistochemical)	1	100%	COP 17,490	Dr, Roselli Study	COP 17,490
Colonoscopy	1	100%	COP 213,040	SOAT 2020	COP 213,040

Author's own research.

Table 2. Adenoma Less Than 10 mm (B)

Resource	Quantity	Usage Rate	Unit Cost	Source	Total Cost
Specialist consultation	1	100%	COP 41,300	SOAT 2020	$ 41,300
Colonoscopy every 3, 5, and 10 years	1	100%	COP 213,040	SOAT 2020	$ 213,040

Author's own research.

Table 3. Adenoma Greater Than 10 mm (C)

Resource	Quantity	Usage Rate	Unit Cost	Source	Total Cost
Specialist consultation	3	100%	COP 41,300	SOAT 2020	COP 123,900
Colonoscopy follow-up	1	100%	COP 213,040	SOAT 2020	COP 213,040
Polypectomy (endoscopic resection of large bowel lesion)	1	100%	COP 2,446,700	SOAT 2020	COP 2,446,700

Author's own research.

in screening colonoscopy for patients aged 45 and 50 were obtained from a Chilean study (population similar to Colombia's) on a multicenter CRC screening program[31], a Colombian study on adenoma prevalence in individuals aged 45–50[24], and Korea's national cancer screening program[32] (**Table 6**).

Model Assumptions

- Screening begins at ages 45 and 50 and ends at age 76 or upon death.
- There is a probability that, after undergoing the procedure, the patient remains in the same stage they were in initially.
- Colonoscopies meet quality standards, preventing the occurrence of interval cancers within the model.
- Health stages are successive and non-reversible unless intervention with polypectomy or surgery occurs.
- The two absorbing states are death from CRC (F) and death from other causes (G).
- Colonoscopy follow-ups are conducted in the first, third, fifth, seventh, and tenth years based on the type of adenoma documented, following international guidelines on digestive endoscopy and cancer[33].

Transition Probabilities

The proposed model defines the transition probabilities for each stage, as presented in the transition probability matrix, which reflects the natural history of CRC.

The literature indicates that a patient undergoing a screening colonoscopy with normal results has a 97% probability of remaining in this normal stage for one year and a 1% probability of progressing to an adenoma smaller than 10 mm[31,32,34–38]. A person with an adenoma smaller than 10 mm has a 97% probability of remaining in the same stage for one year and a 1% probability of progressing to an adenoma larger than 10 mm[35,37,38]. A patient with an adenoma larger than 10 mm has a 5% probability of progressing to advanced regional cancer within one year and a 94% probability of remaining in the same stage[34,36–38]. A patient with advanced regional cancer identified during a screening colonoscopy has a 77% probability of remaining in this stage for one year, a 13% probability of progressing to metastatic cancer, and a 9% probability of progressing to death from CRC within one year[39]. A patient diagnosed with metastatic CRC during screening has a 62% probability of surviving for one year and a 37% probability of progressing to death within that time[39] (**Table 7**).

Using the parameters described above (**Table 8**), a transition matrix was constructed for a cohort of 1,000 patients. This included 31 cycles for patients starting screening at age 45 and 26 cycles for those starting at age 50 (**Tables 9** and **10**).

Utility Calculation

Quality-adjusted life years (QALYs) were used as the utility outcome. To calculate the quality of life for each stage, the EuroQol (EQ-5D-5L) scale was applied to patients undergoing CRC screening. A value of 1 was assigned to normal quality of life (stages A and B), 0.74 to patients undergoing interventions such as polypectomies, surgeries, hospitalizations, chemotherapy, or radiotherapy (stages C, D, and E), and 0 to patients who died (stages F and G)[40].

The cost-utility ratio (C/U) and incremental cost-utility ratio (ICUR) were calculated for the two screening strategies. Life years gained were adjusted according to the effectiveness of the two screening approaches: 0.82 for screening starting at age 45 and 0.75 for screening from ages 50 to 76 (**Tables 9** and **10**).

Table 4. Treatment of Advanced Regional Colorectal Cancer (D)

Resource	Quantity	Usage Rate	Unit Cost	Source	Costo total
Oncologist consultation	6	100%	COP 41,300	SOAT 2020	COP 247,800
Radiotherapist consultation	2	100%	COP 41,300	SOAT 2020	COP 82,600
Gastroenterologist/Coloproctologist	4	100%	COP 41,300	SOAT 2020	COP 165,200
Hemogram	6	100%	COP 24,300	SOAT 2020	COP 145,800
Liver profile	6	100%	COP 394,400	SOAT 2020	COP 2,366,400
Renal function (urea)	6	100%	COP 11,700	SOAT 2020	COP 70,200
Renal function (creatinine)	6	100%	COP 1,400	SOAT 2020	COP 8,400
LDH	6	100%	COP 17,300	SOAT 2020	COP 103,800
Abdomen and pelvis CT	3	100%	COP 670,900	SOAT 2020	COP 2,012,700
Chest X-ray	1	100%	COP 70,200	SOAT 2020	COP 70,200
Chest CT	1	100%	COP 509,700	SOAT 2020	COP 509,700
Two-dimensional M-mode echocardiogram	1	100%	COP 422,500	SOAT 2020	COP 422,500
Renal ultrasound	1	100%	COP 137,800	SOAT 2020	COP 137,800
Radiotherapy	1	100%	COP 868,400	SOAT 2020	COP 868,400
Polychemotherapy (full protocol cycle) with any protocol schedule	1	100%	COP 557,100	SOAT 2020	COP 557,100
Surgical Management (D)					
- Colectomy	1	100%	COP 2,889,700	SOAT 2020	COP 2,889,700
- Colostomy/Ileostomy; includes cecostomy, transversostomy, colostomy, sigmoidostomy	1	100%	COP 1,596,700	SOAT 2020	COP 1,596,700
- Retroperitoneal/pelvic lymphadenectomy	1	100%	COP 2,611,500	SOAT 2020	COP 2,611,500
Hospitalization and Treatment Complications (D)					
- Emergency consultations	258	100%	COP 63,244	SOAT 2020	COP 16,316,952
- Hospitalization, number of days due to treatment or treatment complications (third level). Shared room, 3 beds)	15	100%	COP 268,300	SOAT 2020	COP 4,024,500
- Intermediate care hospitalization, number of days (second and third level)	3,1	100%	COP 779,500	SOAT 2020	COP 2,416,450
- Intensive care hospitalization, number of days (second and third level)	5,6	100%	COP 1,454,500	SOAT 2020	COP 8,145,200
Palliative Care (D)					
- Palliative care consultation	6	100%	COP 41,300	SOAT 2020	COP 247,800
- Medications	6	100%	COP 2,294,145	María Ximena León and colleagues	COP 13,764,870
- Sympathetic block by region (e.g., hypogastric, celiac plexus)	1	100%	COP 2,446,700	SOAT 2020	COP 2,446,700

LDH: Lactate Dehydrogenase; Rx: X-Ray; SOAT: Mandatory Traffic Accident Insurance; CT: Computed Tomography. Author's own research.

Table 5. Metastatic Colorectal Cancer (E)

Resource	Quantity	Usage Rate	Unit Cost	Source	Costo total
Oncologist consultation	6	100%	COP 41,300	SOAT 2020	COP 247,800
Radiotherapist consultation	2	100%	COP 41,300	SOAT 2020	COP 82,600
Gastroenterologist consultation	1	100%	COP 41,300	SOAT 2020	COP 41,300
Hemogram	6	100%	COP 24,300	SOAT 2020	COP 145,800
Liver profile	6	100%	COP 394,400	SOAT 2020	COP 2,366,400
Renal function (urea)	6	100%	COP 11,700	SOAT 2020	COP 70,200
Renal function (creatinine)	6	100%	COP 1,400	SOAT 2020	COP 8,400
LDH	6	100%	COP 17,300	SOAT 2020	COP 103,800
Abdomen and pelvis CT	3	100%	COP 670,900	SOAT 2020	COP 2,012,700
Chest X-ray	1	100%	COP 70,200	SOAT 2020	COP 70,200
Chest CT	1	100%	COP 509,700	SOAT 2020	COP 509,700
Two-dimensional M-mode echocardiogram	1	100%	COP 422,500	SOAT 2020	COP 422,500
Renal ultrasound	1	100%	COP 137,800	SOAT 2020	COP 137,800
Radiotherapy	1	100%	COP 868,400	SOAT 2020	COP 868,400
Polychemotherapy (full protocol cycle) with any protocol schedule	1	100%	COP 557,100	SOAT 2020	COP 557,100
Surgical Management (E)					
- Colectomy	1	100%	COP 2,889,700	SOAT 2020	COP 2,889,700
- Colostomy/Ileostomy; includes cecostomy, transversostomy, colostomy, sigmoidostomy	1	100%	COP 1,596,700	SOAT 2020	COP 1,596,700
- Retroperitoneal/pelvic lymphadenectomy	1	100%	COP 2,611,500	SOAT 2020	COP 2,611,500
Palliative Care (E)					
- Palliative care consultation	12	100%	COP 41,300	SOAT 2020	COP 495,600
- Medications	12	100%	COP 2,294,145	María Ximena León and colleagues	COP 27,529,740
- Sympathetic block by region (including hypogastric, ganglion impar, celiac plexus, and splanchnic nerve in cases of hepatic metastasis)	2	100%	COP 2,446,700	SOAT 2020	COP 4,893,400
Complications from Treatment or Disease (E)					
- Emergency consultations	258	100%	COP 63,244	SOAT 2020	COP 16,316,952
- Hospitalization, number of days due to treatment or treatment complications (third level). Shared room, 3 beds)	15	100%	COP 268,300	SOAT 2020	COP 4,024,500
- Intermediate care hospitalization, number of days (second and third level)	3,1	100%	COP 779,500	SOAT 2020	COP 2,416,450
- Intensive care hospitalization, number of days (second and third level)	5,6	100%	COP 1,454,500	SOAT 2020	COP 8,145,200

LDH: Lactate Dehydrogenase; Rx: X-Ray; SOAT: Mandatory Traffic Accident Insurance; CT: Computed Tomography. Author's own research.

Table 6. Frequencies of Findings from Screening Colonoscopy in Patients Aged 45 and 50[31–33]

Health States	Patients Aged 45	Patients Aged 50
Normal (A)	81.50%	73.20%
Adenoma <10 mm (B)	13.95%	19.30%
Adenoma >10 mm (C)	4.55%	6.30%
Regional cancer (D)	0.00%	1.10%
Metastatic cancer (E)	0.00%	0.00%
Death from CRC (F)	0.00%	0.00%
Death from other causes (G)	0.00%	0.00%

Adapted from: López-Kostner F, and colleagues. Rev Med Chil. 2018;146(6):685–692[31]; Shim JI, and colleagues. Cancer Res Treat. 2010;42(4):191–8[32]; Gupta S, and colleagues. Gastroenterology. 2020;158(4):1154[33].

Table 7. Transition Probability Matrix

Health States	Normal (A)	Adenoma <10 mm (B)	Adenoma >10 mm (C)	Advanced Cancer (D)	Metastatic Cancer (E)	Death from CRC (F)	Death from Other Causes (G)	References
Normal (A)	97.40%	1.08%	0.00%	0.00%	0.00%	0.00%	1.51%	(31-36)
Adenoma <10 mm (B)	0.00%	97.50%	0.98%	0.00%	0.00%	0.00%	1.51%	(33,35,36)
Adenoma >10 mm (C)	0.00%	0.00%	93.56%	4.92%	0.00%	0.00%	1.51%	(31,35,36)
Advanced Cancer (D)	0.00%	0.00%	0.00%	76.82%	12.61%	9.06%	1.51%	(37)
Metastatic Cancer (E)	0.00%	0.00%	0.00%	0.00%	61.55%	36.93%	1.51%	(37)
Death from CRC (F)	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	0.00%	(38)
Death from Other Causes (G)	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	100.00%	(38)

Adapted from: López-Kostner F, and colleagues. Rev Med Chil. 2018;146(6):685–692[31]; Gupta S, and colleagues. Gastroenterology. 2020;158(4):1154[33]; Vatn MH, and colleagues. Cancer. 1982;49(4):819–25[34]; Williams AR, and colleagues. Gut. 1982;23(10):835–42[35]; Clark JC, and colleagues. Int J Cancer. 1985;36(2):179–86[36]; Arminski TC, and colleagues. Dis Colon Rectum. 1964;7:249–61[37]; Rickert RR, and colleagues. Cancer. 1979;43(5):1847–57[38].

RESULTS

Incremental Cost-Utility Ratio

The CRC screening strategy for Colombian adults starting at age 45 was 0.329% less expensive compared to screening starting at age 50 (COP 92,364,407 versus COP 92,669,231). Screening at age 45 yielded 19.40 QALYs, compared to 15.91 QALYs for screening at age 50, resulting in a gain of 3.49 QALYs with earlier screening.

The incremental cost-utility ratio (ICUR) was COP 87,243 per QALY for screening at age 45, making it more effective by gaining more QALYs and less costly. This positions it as a dominant strategy over screening at age 50 (**Table 11**).

Table 8. Parameter Calculation and Ranges for the Transition Matrix

Model Parameters	Minimum	Maximum	Base Case Value
Normal	31.50%	73.10%	97.40%
Adenoma <10 mm	19.70%	22.90%	97.50%
Adenoma >10 mm	43.00%	63.00%	93.56%
Advanced cancer	0.10%	1.30%	76.82%
Metastatic cancer	0.00%	1.30%	61.55%
Death from CRC	0.00%	7.40%	100.00%
Death from other causes	0.00%	34.30%	100.00%

Author's own research.

Mortality was 3.4% for screening starting at age 45, compared to 5.4% for screening at age 50. This represents a 37% reduction in mortality with earlier screening at age 45.

Validation Model and Sensitivity Analysis

To assess the influence of parameter uncertainty on the final outcome of the mathematical model, a deterministic sensitivity analysis was performed using probabilities ranging from 0 to 1. Monte Carlo simulations (1,000 iterations) were conducted in Visual Basic Excel, varying parameter values randomly according to statistical probability distributions. Seed variables were input based on the frequency table of screening findings for CRC in patients aged 45 and 50, and a probability matrix was constructed with the number of individuals transitioning through each stage, guided by the previously described transition probabilities. This iterative process continued until cycle 31 for patients starting screening at age 45 and cycle 26 for those starting at age 50, representing the point when the patient reaches 76 years of age or dies.

Once data for each screening group were collected, scenarios were created using QALY impact as the variable to observe the distribution of incremental utility data and incremental costs relative to the per capita GDP, given the absence of explicit thresholds in Colombia. Cost adjustments were calculated at 12%, and quality adjustments were based on the EQ-5D-5L scale, assigning a value of 0.617 for the stages of adenoma larger than 10 mm, advanced cancer, and metastatic cancer, following the EuroQol (EQ-5D-5L) results[41].

The sensitivity analysis revealed that colonoscopy screening for adults aged 45 generated 20.35 QALYs, compared to 19.85 QALYs for those aged 50. Additionally, with a 12% cost adjustment (applying the extreme discount rate), screening starting at age 45 was found to be less expensive than starting at age 50 (COP 48,284,262 versus COP 49,935,820) (**Table 12**).

Ethical Aspects and Limitations

This study addresses a societal need by examining a public health issue, providing results that benefit the entire population by evaluating and analyzing screening strategies and their cost-effectiveness. While the study adheres to the research guidelines of Colombia's IETS and follows economic evaluation methodology processes, it is a review study that relies on secondary sources. Therefore, its results must be interpreted cautiously and within the methodological framework to avoid conclusions or judgments that exceed the reproducibility of the findings.

To compare costs and benefits between two age groups (45 years and older versus 50 years and older), comprehensive data for all stages in both groups are necessary. A key limitation is the scarcity of studies reporting screening findings in patients over 45, as screening colonoscopy for individuals under 50 is not yet a recommended practice in Colombia.

Table 9. Cohort Transition Matrix for Screening Starting at Age 45

Health State (Age in Years)	Normal (A)	Adenoma <10 mm (B)	Adenoma >10 mm (C)	Cancer (D)	Metastatic Cancer (E)	Death from CRC (F)	Death from Other Causes (G)
Quality Adjustment	1	1	0.74	0.74	0.74	0	0
45	1000	0	0	0	0	0	0
46	815	140	46	0	0	0	0
47	794	145	44	2	0	0	15
48	773	150	43	4	0	0	30
49	753	154	41	5	1	1	45
50	734	159	40	6	1	1	59
51	715	163	39	7	1	2	73
52	696	166	38	7	2	3	87
53	678	170	37	7	2	5	101
54	660	173	37	7	2	6	115
55	643	176	36	7	2	7	128
56	627	178	35	8	2	9	141
57	610	181	35	8	2	10	154
58	594	183	34	7	2	12	166
59	579	185	34	7	2	14	179
60	564	186	34	7	2	15	191
61	549	188	33	7	2	17	203
62	535	189	33	7	2	18	215
63	521	190	33	7	2	20	227
64	508	191	33	7	2	21	238
65	494	192	32	7	2	23	249
66	482	192	32	7	2	24	260
67	469	193	32	7	2	26	271
68	457	193	32	7	2	27	282
69	445	193	32	7	2	29	292
70	434	193	31	7	2	30	302
71	422	193	31	7	2	32	312
72	411	193	31	7	2	33	322
73	401	192	31	7	2	35	332
74	390	192	31	7	2	36	342
75	380	191	31	7	2	38	351
76	370	191	31	7	2	39	360

Adapted from: Gupta S, and colleagues. Gastroenterology. 2020;158(4):1154[33]; Vatn MH, and colleagues. Cancer. 1982;49(4):819–25[34]; Williams AR, and colleagues. Gut. 1982;23(10):835–42[35]; Clark JC, and colleagues. Int J Cancer. 1985;36(2):179–86[36]; Arminski TC, and colleagues. Dis Colon Rectum. 1964;7:249–61[37]; Rickert RR, and colleagues. Cancer. 1979;43(5):1847–57[38].

Table 10. Cohort Transition Matrix for Screening Starting at Age 50

Health State (Age in Years)	Normal (A)	Adenoma <10 mm (B)	Adenoma >10 mm (C)	Cancer (D)	Metastatic Cancer (E)	Death from CRC (F)	Death from Other Causes (G)
Quality Adjustment	1	1	0.74	0.74	0.74	0	0
50	1000	0	0	0	0	0	0
51	732	193	63	11	0	0	0
52	713	197	61	12	2	1	15
53	694	199	59	12	2	3	30
54	676	202	57	12	3	5	45
55	659	204	56	12	3	7	59
56	642	206	54	12	4	9	73
57	625	208	53	12	4	12	87
58	609	210	51	12	4	14	101
59	593	211	50	12	4	17	114
60	578	212	49	11	4	19	127
61	563	213	48	11	4	21	140
62	548	214	47	11	4	24	153
63	534	214	46	11	4	26	165
64	520	215	45	10	4	29	177
65	507	215	44	10	4	31	189
66	493	215	44	10	3	33	201
67	481	215	43	10	3	35	213
68	468	215	42	10	3	37	224
69	456	215	42	10	3	39	235
70	444	214	41	9	3	42	246
71	433	214	41	9	3	44	257
72	421	213	40	9	3	46	268
73	410	212	40	9	3	48	278
74	400	212	39	9	3	50	288
75	389	211	39	9	3	51	298
76	379	210	38	9	3	53	308

Adapted from: Gupta S, and colleagues. Gastroenterology. 2020;158(4):1154[33]; Vatn MH, and colleagues. Cancer. 1982;49(4):819–25[34]; Williams AR, and colleagues. Gut. 1982;23(10):835–42[35]; Clark JC, and colleagues. Int J Cancer. 1985;36(2):179–86[36]; Arminski TC, and colleagues. Dis Colon Rectum. 1964;7:249–61[37]; Rickert RR, and colleagues. Cancer. 1979;43(5):1847–57[38].

Table 11. Cost-Effectiveness Ratio (C/E), Incremental Cost-Utility Ratio (ICUR), and Adjustment of Quality-Adjusted Life Years (QALYs) Gained for Effectiveness

Screening Strategy	Costs	Incremental Cost (45–50)	QALYs Gained	Incremental Effectiveness	C/E	ICUR (ICER)
CRC screening at 45 years	COP 171,175,412	COP -	24,012	0	COP 7,128,864	0
CRC screening at 50 years	COP 163,104,893	$8,070,519	21,64	2,37	COP 7,537,656	COP 3,401,086
Quality-Adjusted	**Costs**	**Incremental Cost (45–50)**	**QALYs Gained**	**Incremental Effectiveness**	**C/E**	**ICUR (ICER)**
CRC screening at 45 years	COP 11,093,632	COP -	19,40	0	COP 571,713	0
CRC screening at 50 years	COP 9,249,970	COP 1,843,662	15,91	3,494	COP 581,384	COP 527,672

Author's own research.

Table 12. Quality-Adjusted Life Years and Discounted Cost by Strategy

Strategy	QALYs	12% Cost Discount
CRC screening at 45 years	20.35	COP 48.284.262
CRC screening at 50 years	19.85	COP 49.935.820

QALYs: Quality-Adjusted Life Years. Author's own research.

DISCUSSION

This study arises from the need to evaluate the cost-effectiveness and cost-utility of initiating CRC screening at age 45, as recommended by the American Cancer Society, due to the increasing incidence of CRC in individuals under 50 in Colombia. On one hand, this decision has several implications for the healthcare system, such as increasing the demand for screening colonoscopies among a larger number of asymptomatic individuals, which will lead to higher resource consumption. On the other hand, the goal of screening is to diagnose precancerous lesions early, allowing for timely intervention and altering the natural history of a high-cost disease like CRC, ultimately contributing to resource savings.

The earlier screening begins, the larger the number of individuals to be screened, based on the population pyramid, and the higher the likelihood of not finding disease in these patients. To reduce this uncertainty, national studies are needed to estimate the prevalence of adenomas and CRC in individuals under 50.

Another issue to consider is that CRC screening in Colombia is opportunity-based. Consequently, there is a population of individuals over 50 who lack access to screening. It could be argued that a greater benefit might be achieved by including more patients from the 50+ age group rather than expanding the screening age range[42–45]. Healthcare organizations and government entities should prioritize cancer screening as part of their agenda, as its cost-effectiveness is well-documented. This prioritization could positively impact future healthcare cost distribution by mitigating the economic burden of advanced-stage CRC.

CONCLUSIONS

In a screening scenario based on the assumptions established in this study, initiating CRC screening at age 45 was shown to dominate the strategy of screening individuals over 50 in Colombia. This suggests that beginning CRC detection studies in this population yields greater benefits and lower overall costs, making it a cost-effective strategy.

The cost difference between the two strategies was 0.329%. Screening at age 45 resulted in higher utility measured in quality-adjusted life years (QALYs) and reduced mortality by 2% compared to starting screening at age 50.

A budget impact analysis (BIA) is required to support the decision to implement a national public health policy for universal CRC screening at age 45.

Conflict of Interest and Funding Statement

The authors declare no conflicts of interest regarding the publication of this article, and no third-party funding was received.

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Original article

Clinical Characteristics, Progression, and Outcomes of Patients with Crohn's Disease Treated at a Referral Hospital in Colombia: Longitudinal Case Series Analysis

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Abstract

Objective: To describe the two-year clinical outcomes of a Crohn's disease (CD) care program at a referral hospital in Colombia. **Materials and methods:** This longitudinal study was based on a case series of patients managed by a specialized CD program in Colombia between 2013 and 2023. Clinical characteristics, disease activity at program enrollment (Crohn's Disease Activity Index [CDAI]), treatment adjustments, and CDAI changes during subsequent follow-ups (6, 12, 18, 24, and 30 months) were reported. **Results:** A total of 22 patients were included, with a median age of 44 years (interquartile range [IQR]: 32–64); 10 (45%) were men. At enrollment, 14 patients (63.4%) were in remission, while 8 (36.6%) had mild to moderate disease activity. The median CDAI at enrollment was 124 (IQR: 52.7–211.2), with a significant reduction observed at 12 months (CDAI: 50, IQR: 10–115) and 24 months (CDAI: 24, IQR: 10–117) ($p < 0.05$). At the end of the follow-up period, 12 patients (80%) were in remission, 3 (20%) had mild to moderate disease activity, 7 (31.8%) were lost to follow-up at two years, and 14 (93.3%) were on biologic therapy. **Conclusion:** This study highlights the clinical characteristics, therapeutic approaches, and outcomes of a specialized CD care program. The findings suggest that the program effectively reduces CD activity, potentially due to the use of biologic therapy. Future studies are needed to confirm the potential benefits of specialized care programs.

Keywords

Crohn's disease, biologic therapy, remission.

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract characterized by episodes of activity that lead to significant morbidity due to progressive damage. This impacts quality of life and results in disability[1]. Fifty percent of patients require surgical treatment within 10 years of diagnosis[2]. However, in the past decade, early diagnosis and the advent of biological therapy have improved the disease's prognosis, reducing costs associated with hospitalization and surgery[3]. Additionally, the risk of hospitalization has decreased to 26% at one year and 40% at five years, while the risk of surgery has fallen to 12%, 18%, and 26% at one, five, and ten years, respectively[4].

The disease follows a course of activity, remission, and relapse. Cumulative relapse rates have been recorded at 53%, 85%, and 90% at one, five, and ten years post-diagnosis, respectively[5]. Therefore, during follow-up, it is essential to quantify the degree of disease activity and the response to treatment to make necessary adjustments to management.

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The Crohn's Disease Activity Index (CDAI) is an objective tool used to quantify symptoms and, consequently, disease activity in CD patients[6]. It has been universally applied to assess the efficacy and response to various treatments[7–12].

In Colombia, the general population prevalence of CD has been reported as 15 per 100,000 inhabitants. The most prevalent age group is 35–39 years, with a female predominance of 60%[13] and a higher occurrence of ileal involvement followed by ileocolonic involvement[14]. While descriptive studies have reported clinical and sociodemographic characteristics, the frequency of biological and other immunomodulatory treatments[14–16], the progression and outcomes associated with treatment in specialized programs have not been documented in our setting.

This study aims to describe the clinical outcomes over two years in a CD care program at a referral hospital in Colombia.

METHODS

This is a longitudinal study based on a case series, including all adult patients (aged 18 years or older) with a previous or new diagnosis of Crohn's disease (CD), managed by the specialized institutional program at Hospital Universitario San Ignacio (Bogotá, Colombia) between 2013 and 2023. Since the diagnosis of CD requires clinical, endoscopic, and histopathological correlation[17], diagnoses were only accepted after confirmation by the Inflammatory Bowel Disease Medical Board. This board diagnoses CD based on a combination of clinical, biochemical, and endoscopic findings, cross-sectional imaging, and histology, following the guidelines suggested by ECCO[18]. The board comprises three gastroenterologists experienced in inflammatory bowel disease, one rheumatologist, one psychiatrist, and one nutritionist. Patients referred to another hospital during the initial evaluation and those who did not meet a minimum follow-up period of six months were excluded. The study was approved by the Research and Ethics Committee of Pontificia Universidad Javeriana and Hospital Universitario San Ignacio in Bogotá (Approval Minutes FM-CIE-1164-23). The STROBE checklist was used as a guideline.

Clinical, sociodemographic characteristics, and treatment adjustments were obtained from the institutional registry for inflammatory bowel disease patients at Hospital Universitario San Ignacio. This registry systematically documents information from both initial assessments and all subsequent evaluations, including outpatient visits and hospitalizations. Collected data included age, sex, type of inflammatory bowel disease according to the Montreal classification (**Table 1**)[19], symptom onset date, diagnosis date, disease activity measurements at all evaluations (CDAI), hemoglobin levels, imaging studies (computed tomography, enterography, CT enterography), extraintestinal involvement, treatments received (biologics, immunomodulators, corticosteroids), the need for treatment changes or optimization, and adverse events. Biologic treatments included infliximab, adalimumab, vedolizumab, and certolizumab. Patients on infliximab or adalimumab could receive intensified regimens in cases of loss of response to standard doses[20, 21]. For this study, missing information was directly collected from the hospital's medical records.

Table 1. Montreal Classification for Crohn's Disease

Clinical Factors	Montreal Classification
Age	A1: <16 years
	A2: 17 to 40 years
	A3: >40 years
Location	L1: Ileal
	L2: Colonic
	L3: Ileocolonic
	L4: Isolated upper gastrointestinal tract disease
Behavior	B1: Non-stricturing, non-penetrating
	B2: Stricturing
	B3: Penetrating
	p: Perineal involvement

Author's own research.

The analysis focused on the first 30 months of follow-up for each patient from the time of enrollment in the program. Disease activity was assessed using the CDAI score, which was recorded during the initial evaluation and subsequent follow-ups every six months (6, 12, 18, 24, and 30 months). Based on this score, remission was defined as a CDAI <150; mild activity as a CDAI of 150–220; moderate activity as a CDAI of 220–450; and severe activity as a CDAI >450[17]. The primary outcome was the change in CDAI.

Data Analysis

Qualitative variables were measured using absolute and relative frequencies. Quantitative variables were recorded using measures of central tendency and dispersion. Variables with normal distribution were calculated using the mean and standard deviation (SD), while those with non-normal distribution were estimated using the median and interquartile range (IQR). The Kolmogorov-Smirnov

test with a statistical significance of 5% (p <0.05) was used to determine normal distribution.

Patients were divided into two groups for comparison based on disease activity at the initial evaluation. The first group included patients in remission (CDAI <150), and the second included those with mild to moderate activity (CDAI: 150–450). No patients presented with severe activity at baseline. Depending on the characteristics of the variables, comparisons between groups were made using a Student's T test, Mann-Whitney U test, or chi-square test. As the distribution of CDAI was non-normal, changes over time in the primary outcome were evaluated using the Wilcoxon signed-rank test. Statistical analysis was performed using Stata (Stata Statistical Software: Release 16, College Station, TX: StataCorp LLC).

Ethical Considerations

The research was conducted in accordance with ethical guidelines proposed by international agreements such as the Declaration of Helsinki of the World Medical Association, as well as Resolution 008430 of 1993 from the Ministry of Health of Colombia. The study was approved by the institutional ethics and research committees of Hospital Universitario San Ignacio and Pontificia Universidad Javeriana (Approval Minutes FM-CIE-1164-23). Signed informed consent was not required as the data were anonymized, and no sensitive information was exposed.

RESULTS

A total of 22 patients were included in this case series. The median age was 44 years (IQR: 32–64), 10 (45%) were male, 9 (41%) were newly diagnosed, 14 (63.4%) were in remission, and 8 (36.6%) had mild-to-moderate activity (MMA) at the initial evaluation. Ileocolonic involvement (Montreal classification L3) was more frequent among patients with MMA compared to those in remission (50% versus 7%, $p < 0.05$). Conversely, classifications A3, L1, and B1 were more common in patients in remission at the initial evaluation (A3: 64% versus 37%, $p < 0.05$; L1: 79% versus 25%, $p < 0.05$; and B1: 57% versus 12%, $p < 0.05$) (**Table 2**).

Table 3 shows the changes in the median CDAI score at each follow-up compared to the initial consultation. Regardless of the degree of activity during follow-up, there was an average reduction in CDAI scores to remission levels. This reduction was statistically significant at 12 months (CDAI: 50, IQR: 10–115) and 24 months (CDAI: 24, IQR: 10–117) ($p < 0.05$) (**Figure 1**). When evaluating CDAI progression based on initial activity levels, patients in remission showed a statistically significant improvement in CDAI at the 12-month follow-up (CDAI: 46, IQR: 10–70.7, $p < 0.05$). Patients with initial mild-to-moderate activity (MMA) exhibited a statistically significant improvement in CDAI at the 6-month (CDAI: 128, IQR: 62.5–226) and 12-month follow-ups (CDAI: 115, IQR: 12–221) ($p < 0.05$). By the end of the follow-up, 80% of patients were in remission, and 20% had MMA, while seven patients (31.8%) discontinued follow-up. Although there were no statistically significant differences in corticosteroid use during follow-up, there was a notable increase in the use of biologic therapies, from 36% at the initial consultation to 82.3% at 24 months ($p < 0.05$).

DISCUSSION

This study describes the baseline characteristics of patients with Crohn's disease (CD) and their two-year follow-up. Several noteworthy aspects emerge: first, the clinical characteristics of our case series suggest a profile of greater disease severity; second, by the end of the follow-up, 93.3% of the patients were on biologic therapy, a higher percentage than reported in our setting and in Latin America, indicating greater disease complexity in our program; and third, care provided by this specialized program demonstrated a reduction in disease activity during follow-up.

Various clinical predictors are associated with a worse prognosis in CD, including disease severity, age at presentation (<40 years), and ileocolonic involvement[5,22–24]. These variables influence hospitalization rates, the need for surgery, and the type of medical treatment required. Perianal involvement and extraintestinal manifestations are also associated with greater severity and a higher need for immunosuppressive therapy[22,25–28]. Penetrating disease, in particular, has been directly linked to a higher need for surgery and earlier recurrence compared to stricturing disease[22].

Our study shows a higher frequency of poor prognostic predictors compared to other studies in Colombia. The average age was 41 years, which was even lower among patients with mild-to-moderate activity (MMA) at 34 years, contrasting with other cohorts where the median age ranged from 45 to 47 years[14,16]. Among patients in remission at the initial evaluation, older age (>40 years), ileal involvement, and non-stricturing, non-penetrating behavior (Montreal classification A3, L1, B1) were more common, findings comparable to other Colombian cohorts[14–16]. However, these findings differ for those with MMA, who more frequently presented between 17 and 40 years of age, with ileocolonic involvement and stricturing behavior (Montreal classification A2, L3, B2). Additionally, 18% of our patients had perianal involvement, a higher frequency than previously reported (1.7%–9.8%)[14,15]. Finally, 9% of our population had upper gastrointestinal tract involve-

Table 2. Clinical Characteristics at Initial Evaluation of Crohn's Disease Patients at HUSI by Disease Activity

Variable	Total n = 22	Remission n = 14	Mild-to-Moderate Activity n = 8	*p*-Value
Age at consultation, median (IQR)	44 (32-64)	47 (39-63)	34 (25-67)	0.66
Male sex, n (%)	10 (45.5)	7 (50.0)	3 (37.5)	0.66
Newly diagnosed, n (%)	9 (40.9)	4 (28.6)	5 (62.5)	0.12
Initial outpatient visit, n (%)	18 (81.8)	14 (100)	4 (50.0)	0.06
Initial emergency visit, n (%)	4 (18.2)	0 (0.0)	4 (50.0)	0.06
Surgical management, n (%)	3 (13.6)	0 (0.0)	3 (37.5)	0.16
Prior surgical history, n (%)	4 (18.2)	3 (21.4)	1 (12.5)	0.76
Extraintestinal manifestations, n (%)	6 (27.3)	4 (28.6)	2 (25.0)	0.92
Hemoglobin (g/dL), median (IQR)	14.7 (12.7-15.8)	15 (13.7-16.2)	12.8 (11.4-15.2)	0.07
Montreal Classification, n (%)				
- A1	0 (0.0)	0 (0.0)	0 (0.0)	1
- A2	10 (45.5)	5 (35.7)	5 (62.5)	0.22
- A3	12 (54.5)	9 (64.3)	3 (37.5)	0.01
- L1	13 (59.1)	11 (78.6)	2 (25.0)	0.01
- L2	2 (9.1)	1 (7.1)	1 (12.5)	0.67
- L3	5 (22.7)	1 (7.1)	4 (50.0)	0.02
- L4	2 (9.1)	1 (7.1)	1 (12.5)	0.67
- B1	9 (40.9)	8 (57.1)	1 (12.5)	0.04
- B2	9 (40.9)	4 (28.6)	5 (62.5)	0.11
- B3	3 (13.6)	2 (14.3)	2 (25.0)	0.53
p-value	4 (18.2)	2 (14.3)	2 (25.0)	0.71

A1: <16 years; A2: 17–40 years; A3: >40 years; HUSI: Hospital Universitario San Ignacio; L1: Ileal; L2: Colonic; L3: Ileocolonic; L4: Isolated Upper Gastrointestinal Tract Involvement; B1: Non-Stricturing, Non-Penetrating; B2: Stricturing; B3: Penetrating; p: Perianal Involvement; IQR: Interquartile Range. Author's own research.

ment, which has not been reported in other Colombian cohorts[14–16]. Only one study in our setting has reported extraintestinal involvement, with higher percentages than observed in our study[15].

The fact that a significant proportion of patients in this study (36%) were already receiving biologic therapy at the initial evaluation may reflect a more severe disease course. In Colombia and Latin America, the reported frequency of biologic therapy use ranges from 8% to 40%[13–15,29]. By the end of follow-up, 93.3% of our population was on biologic therapy, a percentage consistent with the adoption of biologic therapy in countries with a higher prevalence of inflammatory bowel disease. A retrospective study in the United States observed an increase in biologic use in CD from 21.8% in 2007 to 43.8% in 2015[30]. Similarly, a French referral center reported that 60% of CD patients received at least one anti-TNF agent[31]. In our population, the high percentage of biologic use likely reflects the greater severity of the disease in our program. Considering that our hospital is a referral center for inflammatory bowel disease, most patients treated here have already been evaluated at other institutions and are referred either due to a lack of response to other immunomodulatory therapies or because of disease severity.

Tabla 3. Change in Median CDAI Score at Semiannual Consultations Compared to Initial Consultation in a Crohn's Disease Case Series

Variable	Initial Consultation n = 22	6-Month Follow-Up n = 22	*p*-value*	12-Month Follow-Up n = 19	*p*-value*	18-Month Follow-Up n = 19	*p*-value*	24-Month Follow-Up n = 17	*p*-value*	30-Month Follow-Up n = 15	*p*-value*
CDAI Crohn's disease, (IQR)	124 (52.7-211.2)	78.5 (47.7-188)	0.17	50 (10-115)	<0.05	71 (25-254)	0.29	24 (10-117)	<0.05	58 (30-153)	0.11
Initial Activity Level, CDAI Median (IQR)											
Remission	73 (40.7-122)	74.5 (42-173.5)	0.44	46 (10-70.7)	<0.05	60.5 (8.5-219.2)	0.97	11 (7-107.2)	0.07	50 (16-61)	0.13
Mild-to-moderate activity	216 (195.7-382.2)	128 (62.5-226)	<0.05	115 (12-221)	<0.05	170 (45-297)	0.06	170 (46-376.5)	0.14	145 (132.2-379)	0.46
Patients in remission at each consultation, n (%)	14 (63.6)	15 (68.2)	0.75	17 (89.5)	0.052	12 (63.2)	0.98	14 (82.3)	0.19	12 (80)	0.28
Treatment, n (%)											
Corticosteroid use	2 (9)	7 (31.8)	0.06	1 (5.3)	0.63	1 (5.3)	0.65	2 (11.8)	0.77	3 (20)	0.34
Biologic use	8 (36)	14 (63.6)	0.07	16 (84.2)	<0.05	15 (78.9)	<0.05	14 (82.3)	<0.05	14 (93.3)	<0.05

*These values were obtained by comparing activity levels at each follow-up with initial activity. CDAI: Crohn's Disease Activity Index; IQR: Interquartile Range. Author's own research.

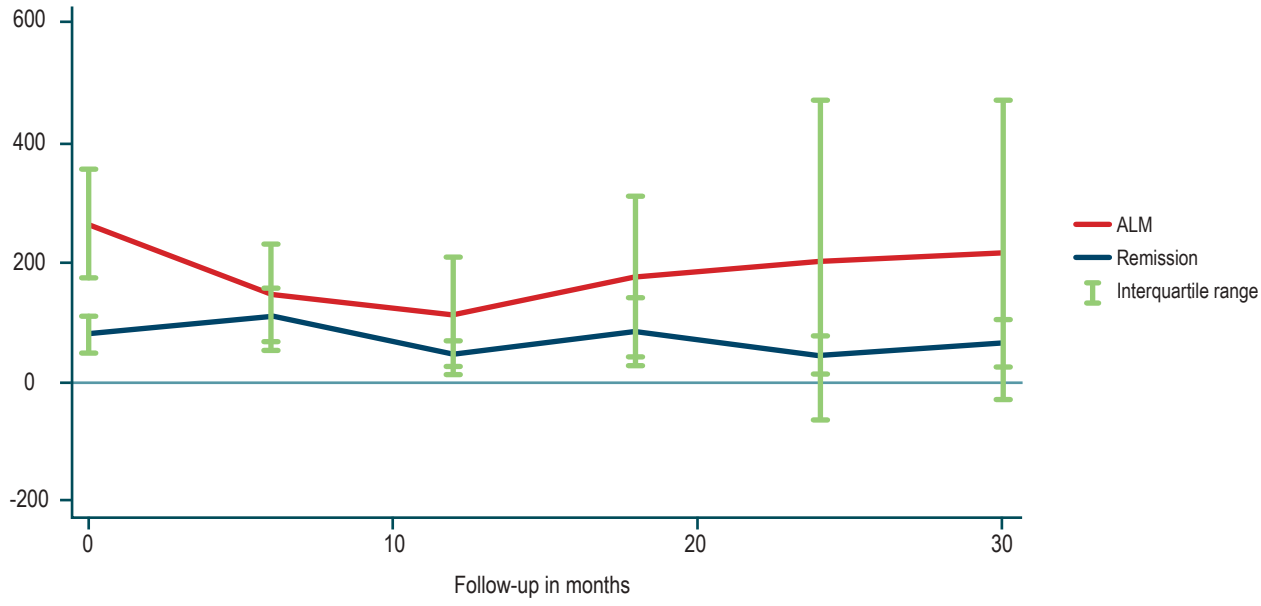


Figure 1. Average change in CDAI score over time. Author's own research.

By the end of follow-up, 20% of the patients continued to have mild-to-moderate activity (MMA) despite being on biologic therapy. This may be explained by variability in remission rates among different treatments. For example, in patients with mild disease activity, budesonide 9 mg/day achieved clinical remission in 46.7% to 61% of cases. In moderate-to-severe disease, prednisolone induced clinical remission in 59.8% of patients. Regarding TNF inhibitors, a remission rate of 25.5% was observed, with a relative risk (RR) of 1.66 (1.17–2.36) in patients with moderate-to-severe activity who had not responded to conventional therapy[17]. Therefore, although corticosteroids and biologic therapies are essential tools for managing Crohn's disease (CD), they are not 100% effective.

In our population, the Crohn's Disease Activity Index (CDAI) score showed a statistically significant reduction at the 12- and 24-month follow-ups. By the end of the follow-up period, 80% of patients were in remission. This response could be attributed to two factors: the high use of biologic therapy (93.3%) (as previously discussed) and the multidisciplinary approach of this program compared to standard care. This program enables early treatment adjustments, nutritional evaluation, mental health support, and assessment of extraintestinal involvement (e.g., rheumatology) during the same consultation.

Although disease activity improved during follow-up in both patients who started in remission and those with MMA at the 12- and 24-month evaluations, this reduction was not statistically significant at all time points. This finding could have three potential explanations:

- Previous data prior to the advent of biologic therapy demonstrated that disease relapse is common. The IBSEN cohort reported cumulative relapse rates of 53%, 85%, and 90% at one, five, and ten years post-diagnosis, respectively[5]. However, long-term data on relapse rates with biologic therapy are limited. A Danish population-based cohort of CD patients followed for a median of 7.7 years found cumulative recurrence rates of 40%, 63%, and 66% at one, five, and seven years after diagnosis, respectively[32]. These findings highlight the importance of strict follow-up for CD patients, as many may not respond to available treatments or may relapse during follow-up.
- Around 30% of patients discontinued follow-up during the study. This may have introduced selection bias, as patients with lower disease activity may have left the program, while those with higher activity levels may have continued follow-up.
- The small sample size may have limited the detection of statistically significant differences. Further studies with larger sample sizes are needed to evaluate the natural history of CD in our setting.

A key strength of this study is the reliable diagnosis of Crohn's disease (CD), as all diagnoses were confirmed through a multidisciplinary board. Additionally, follow-up through a specialized program ensures high data reliability due to the maintenance of an institutional registry for these patients. However, this series has limitations, including the small number of patients, which restricts the precision of CDAI change estimates. Moreover, due to the study's methodology, hypothesis testing should be considered only as a basis for generating hypotheses for future research. Nonetheless, this is the first reported case series of CD with longitudinal follow-up in Colombia. Another significant limitation is the lack of continuous follow-up for some patients. Therefore, further multicenter studies are recommended to evaluate the natural history of CD patients in our setting.

CONCLUSION

This study presents the clinical characteristics, therapeutic approaches, and outcomes of a specialized CD care program. Our findings suggest that this program achieves a reduction in CD activity, possibly associated with the use of biologic therapy. Future studies are needed to confirm the potential benefits of specialized care programs.

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Conflict of Interest

None.

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Original article

Eradication of *Helicobacter pylori* with First-Line Treatment at a High-Complexity Hospital in Southwestern Colombia

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Abstract

Introduction and Objectives: Confirming the eradication of *Helicobacter pylori* is essential due to increasing antimicrobial resistance to various treatment regimens. The primary objective of this study is to determine the eradication rate of *H. pylori* using the carbon-14 (^{14}C) urea breath test. **Materials and Methods:** A cross-sectional study with an analytical component was conducted by retrospectively reviewing medical records of patients who received eradication treatment for *H. pylori* and subsequent confirmation of eradication through the ^{14}C urea breath test. The study was carried out at Hospital Universitario Fundación Valle del Lili between January 2019 and June 2022. **Results:** A total of 360 patients met the inclusion criteria. Women represented 66.9% of the sample, with a median age of 51 years (interquartile range [IQR]: 39–61). A negative ^{14}C urea breath test result was obtained in 84.4% of cases, with a median interval of eight weeks (IQR: 5–12) between the end of treatment and test performance. Almost all patients received 14 days of treatment. **Conclusions:** An acceptable eradication rate was observed in our setting, even with the standard triple therapy, which remains the most commonly used regimen. Antimicrobial susceptibility studies are needed to guide treatments based on local epidemiology.

Keywords

Helicobacter pylori, eradication, breath test, microbial resistance, treatment adherence.

INTRODUCTION

The significance of *Helicobacter pylori* lies in its classification as a Group I carcinogen by the International Agency for Research on Cancer, making it a critical agent in public health[1]. In addition, it has the potential to cause pathologies such as chronic gastritis, peptic ulcer, MALT lymphoma, unexplained iron deficiency anemia, refractory thrombocytopenia and vitamin B_{12}[2]. Globally, the prevalence of *H. pylori* infection in the six regions defined by the

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World Health Organization (WHO) has decreased from 58.2% (1980–1990) to 43.1% (2011–2022). This reduction is more pronounced in younger populations, in high-income countries, and in settings with universal health coverage[3]. In Colombia, studies report a prevalence of *H. pylori* ranging from 36.4% to 83.1%, with variations depending on the geographic region studied[4–7].

Guidelines and consensus documents of the greatest impact strongly recommend the eradication of *H. pylori* due to the aforementioned effects[8–15]. The eradication rate varies depending on the treatment regimen used and the local pattern of antimicrobial susceptibility. By the late 20th century, triple eradication therapy (proton pump inhibitor [PPI], amoxicillin, and clarithromycin or metronidazole) was the first-line treatment. However, a concerning decrease in susceptibility has been observed, based on studies of antimicrobial resistance, genetic polymorphisms, and metabolomics. Currently, there is an urgent need to implement treatments that achieve at least an acceptable eradication rate[16].

Confirmation of eradication is recommended for all treated patients. The most widely used and guideline-recommended non-invasive test is the breath test, which is based on the chemical reaction of *H. pylori* urease. This enzyme cleaves urea to produce carbon dioxide (CO_2) and ammonium hydroxide (NH_4OH); these compounds then react with a labeled carbon isotope, which is exhaled and subsequently measured[17]. Two carbon isotopes (^{13}C and ^{14}C) are used for the breath test. The ^{13}C isotope requires more complex equipment (including a mass spectrometer), which makes the test more challenging to perform compared to the less complex and less costly ^{14}C isotope[18]. Importantly, this does not compromise the sensitivity and specificity of the test, which are 96% and 93%, respectively[19–22].

The objective of this study was to describe the results of *H. pylori* eradication using the ^{14}C breath test in adult patients who received various treatment regimens at a high-complexity institution.

MATERIALS AND METHODS

This was a cross-sectional study with an analytical component, involving retrospective data collection through a review of medical records. The study was conducted at Fundación Valle del Lili and approved by the institution's Biomedical Research Ethics Committee. Patients over 18 years old diagnosed with *H. pylori* infection via biopsy obtained through upper gastrointestinal endoscopy (performed either at the institution or externally) were included. After receiving treatment (whether or not provided by the institution), these patients underwent a confirmatory urea breath test between January 2019 and June 2022. Patients with more than one year between the end of treatment and the breath test were excluded.

Procedure Description

As part of the institutional protocol, the following pre-procedure checks were conducted: verification of fasting status, allergies, absence of antibiotic, PPI, or antacid use in the past 30 days, no smoking in the last 8 hours, and the date of the last *H. pylori* treatment dose. If the patient was pregnant, suspected to be pregnant, or exhibited signs of acute or recent gastrointestinal bleeding, the procedure was postponed. The required materials included the Heliprobe® system (Kibion AB, Uppsala, Sweden), which uses the 37kBq HeliCap™ capsule (2.5 µSv of radiation per capsule), the Heliprobe® BreathCard® (a device to capture exhaled ^{14}C), and the Heliprobe® Analyzer (for detecting ^{14}C radioactivity in the BreathCard®).

The patient was seated and instructed to swallow the HeliCap™ capsule with a glass of water, then wait for 10 minutes. After this time, the patient was asked to exhale into the Heliprobe® BreathCard® until the color indicator changed from orange to yellow. Finally, the BreathCard® was inserted into the Heliprobe® Analyzer for measurement.

Result Interpretation

The cut-off points for determining infection status were as follows:

- Heliprobe 0: non-infected/negative
- Heliprobe 2: infected/positive

The results were interpreted in writing by an institutional gastroenterology and endoscopy specialist.

Statistical Analysis

The institutional database was searched using the Unified Classification of Health Procedures (CUPS in Spanish) code corresponding to the [^{13}C urea] breath test. This search identified approximately 1,300 procedures.

The sample size was calculated based on an *H. pylori* eradication rate of 80%, with a precision of 5% and a power of 80%, requiring a sample size of 360 patients.

A simple random sampling strategy was employed using the list of 1,300 procedures recorded during the study period. From this list, 360 procedures were selected using a random number table to meet the desired precision and power. Patients who underwent the breath test one year or more after treatment were excluded. The results of the breath tests and other relevant variables were then collected through a review of medical records in the institutional

system. All data were recorded in a database maintained by the Clinical Research Center.

Descriptive statistics were used to evaluate sociodemographic variables, clinical symptoms, treatment types, time before testing, treatment duration, and breath test results. Absolute numbers and percentages were reported for qualitative variables, while medians and interquartile ranges (IQR) were reported for quantitative variables. Bivariate analysis was performed using chi-square or Fisher's exact tests for qualitative variables, Mann-Whitney U tests for non-normally distributed quantitative variables, and Student's T tests for normally distributed variables. Variables with a statistical significance of $p < 0.05$ were considered statistically significant. All analyses were conducted using RStudio statistical software, version 2022.07.2.

Ethical Considerations

This research adheres to the international agreements on biomedical research established by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the WHO, as well as Resolution 8430 of 1993 in Colombia. The study is classified as risk-free and is retrospective in nature; therefore, informed consent was not required. It is important to note that this article does not contain any personal information that could lead to the identification of patients involved.

RESULTS

The breath test results after antibiotic treatment were negative in 84.4% of patients. A total of 360 patients were analyzed, of whom 241 (66.9%) were women. The median age of the patients was 51 years (IQR: 39–61). The most commonly reported symptom was dyspepsia (79.4%), followed by gastroesophageal reflux (24.1%), and 22.0% of patients reported other symptoms such as diarrhea, gastrointestinal bleeding, halitosis, vomiting, and belching. No statistically significant differences were observed regarding symptoms. The median time between the end of treatment and the breath test was eight weeks (IQR: 5–12). No statistically significant differences were found in the test results based on the time interval studied. However, a higher proportion of positive results was observed in tests performed before week 8. After this period, the proportion of positive results varied but was generally lower. No patients exceeded 10 months between the end of treatment and the breath test. The treatment duration was 14 days for both groups (**Table 1**).

Eighty-six point one percent of the patients in the study received a triple regimen of amoxicillin/clarithromycin/PPI; among these, 86.4% had a negative result. The treatment regimens of amoxicillin/clarithromycin/PPI/bismuth, amoxicillin/levofloxacin/PPI, and amoxicillin/levofloxacin/PPI/bismuth yielded negative results in 83.3%, 72.4%, and 54.5% of cases, respectively. All four patients treated with the regimen of metronidazole/clarithromycin/bismuth/PPI had negative results (**Table 2**).

Regarding the time interval between the end of the treatment regimen and the breath test, among the 296 cases with available data, negative results exceeded 80% across all groups: 80% for the group tested at 4 weeks, 87.9% for the group tested between 5 and 12 weeks, and 80.2% for the group tested after more than 12 weeks (**Figure 1**).

DISCUSSION

This study identified an overall eradication rate (encompassing all treatment regimens) of 84.4%. Currently, there are uncertainties and a lack of consensus on fundamental aspects such as what constitutes an acceptable eradication rate. The most recent guidelines from the World Gastroenterology Organization propose a minimum acceptable eradication rate of 80% by intention-to-treat, although this value is described in the document as "arbitrary"[23]. Previously, Graham and colleagues proposed categorizing treatment efficacy as excellent (≥95% eradication), good (≥90%), borderline acceptable (85%–89%), or unacceptable (<85%)[24]. Other authors suggest that treatment regimens should be based on therapies achieving cure rates above 90%[11,25]. Antimicrobial resistance plays a significant role and varies geographically. A systematic review and meta-analysis across WHO regions reported global bacterial resistance rates of *H. pylori* (based on genotypic and phenotypic testing) to metronidazole, amoxicillin, clarithromycin, and levofloxacin as 91%, 38%, 15%, and 14%, respectively. According to international guidelines, a resistance rate above 15% is considered high[1]. Previously, amoxicillin resistance was thought to be low; however, in Colombia, it has been reported to range from 3.8% to 20.5%[26–28]. Resistance to clarithromycin is much more variable, ranging from as low as 2.2% in cities like Pereira[29] and Armenia, to as high as 63.1% in Bogotá[26–28,30,31], mostly associated with point mutations in the 23S rRNA gene. Metronidazole has the highest resistance rate, reaching up to 97.6%[27,31–33].

The most recent Maastricht VI/Florence Consensus recommends that in the absence of susceptibility testing, first-line treatment in areas with high (>15%) or unknown resistance to clarithromycin should be quadruple therapy with bismuth. In areas with low resistance and locally confirmed efficacy rates above 90%, triple therapy with amoxicillin/clarithromycin/PPI may still be recommended[11]. In this study, triple therapy remains the most commonly used regimen in our setting (86.1%), with a negative breath test

Table 1. Patient Characteristics According to Breath Test Results

Característica	n	Overall n = 360	Negative n = 304	Positive n = 56	*p*-value*
Age	360	51 (39-61)	51 (39-60)	55 (39-62)	0.24
Sex, n (%)	360				0.43
Female		241 (67.0)	201 (66.1)	40 (71.4)	
Male		121 (33.0)	103 (33.9)	16 (28.6)	
Symptoms					
Dyspepsia, n (%)	350				0.9
Negative		72 (20.6)	61 (20.7)	11 (20.0)	
Positive		278 (79.4)	234 (79.3)	44 (80.0)	
Gastroesophageal reflux, n (%)	349				0.73
Negative		265 (75.9)	223 (75.6)	42 (77.8)	
Positive		84 (24.1)	72 (24.4)	12 (22.2)	
Other symptoms, n (%)	359				0.19
Negative		280 (78.0)	240 (79.2)	40 (71.4)	
Positive		79 (22.0)	63 (20.8)	16 (28.6)	
Time between treatment and breath test (weeks)*	351	8 (5-12)	8 (6 -12)	8 (4-20)	0.817
Duration of treatment (days)*	354	14 (14-14)	14 (14-14)	14 (14-14)	0.054

*Median (interquartile range [IQR]). **Wilcoxon rank-sum test (Mann-Whitney U test); Pearson's chi-square test; Fisher's exact test. Author's own research.

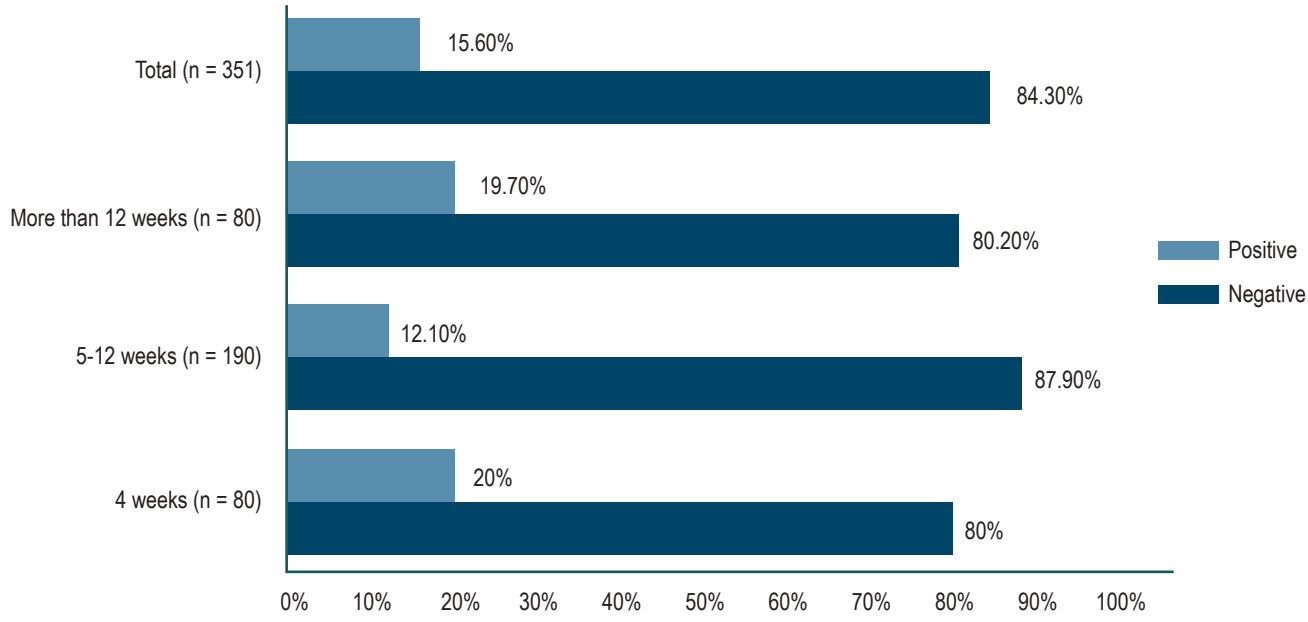


Figure 1. Breath Test Results by Time Interval Between End of Treatment and Breath Test. Author's own research.

Table 2. Breath Test Results by Treatment Regimen

	n	%
Total (n = 360)		
- Negative	304	84,4
- Positive	56	15,5
Amoxicillin/clarithromycin/PPI (n = 310)		
- Negative	268	**86,4**
- Positive	42	13,5
Amoxicillin/levofloxacin/PPI (n = 29)		
- Negative	21	**72,4**
- Positive	8	27,6
Amoxicillin/clarithromycin/PPI/bismuth (n = 6)		
- Negative	6	**54,5**
- Positive	5	45,4
Amoxicillin/levofloxacin/PPI/bismuth (n = 4)		
- Negative	5	**83,3**
- Positive	1	16,6
Metronidazole/clarithromycin/bismuth (n = 4)		
- Negative	4	**100**
- Positive	0	0

Author's own research.

rate of 86.4%, classifying it as an acceptable eradication therapy. Interestingly, quadruple therapy with metronidazole/clarithromycin/bismuth/PPI achieved the highest eradication rate (100%), which is inconsistent with the extremely high resistance rates reported for metronidazole. However, the number of patients receiving this regimen was limited. Additionally, quadruple therapy with amoxicillin/clarithromycin/PPI/bismuth showed a notable eradication rate below 85%.

It is evident that treatment regimens containing levofloxacin have eradication rates as low as 54.6% and 72.4%, consistent with the increasing resistance to levofloxacin reported by Trespalacios and colleagues in Bogotá (from 11.8% in 2009 to 27.3% in 2014), which would preclude its use as first-line therapy[34]. The same study discusses that even in *H. pylori*-naive patients, the widespread use of this antibiotic for urinary, respiratory, and gastrointestinal infections may influence resistance. To date, there are no antimicrobial susceptibility studies for *H. pylori* in Valle del Cauca, and considering the epidemiological significance, it is imperative to conduct bacterial resistance studies to determine whether it remains safe to continue using triple therapy, currently the most widely employed regimen.

The second most important factor influencing treatment success is poor adherence, which is affected by factors such as treatment complexity, potential side effects, patient willingness and motivation, and socioeconomic status[35]. In Colombia, Salazar and colleagues reported an adherence rate of 84%, which is suboptimal. Factors most significantly impacting adherence included adverse drug reactions, dosing frequency, and the number of tablets taken during the treatment period[36]. Adherence is considered excellent if it reaches or exceeds 90%. In our study, nearly all patients underwent a 14-day treatment regimen; however, this was not evaluated using validated strategies to confirm adherence. Only four patients received treatment lasting less than 14 days, three of whom had positive follow-up tests. This finding aligns with the Maastricht consensus, which states that shorter treatment durations are associated with lower effectiveness[37].

In a prospective study conducted in Peru by Vargas-Cárdenas and colleagues, a much lower adherence rate (65%) was reported using the Morisky-Green test. Poor adherence was more frequent in patients under 50 years of age, those with lower education levels, and those experiencing adverse reactions[38]. These factors could be extrapolated to the Colombian context, as it is also a developing country, highlighting the need for a prospective study on treatment adherence using validated strategies. Other factors that reduce the likelihood of eradication include disparities in healthcare access, age-related changes in the gastrointestinal microbiota, and prior exposure to specific antibiotics and *H. pylori* strains. These factors warrant further study in our local context.

The median age was 51 years, consistent with findings by Correa and colleagues, who reported that individuals aged 40 to 59 years accounted for nearly 40% of positive cases[6]. Some studies have described no significant differences in infection rates between sexes, with prevalence being similar in both men and women[39,40]. However, in our study, there was a notable predominance of women regardless of the breath test result. This finding aligns with reports from Sepúlveda and colleagues in Cali, where diagnostic positivity for *H. pylori* was based on upper gastrointestinal endoscopy and, in some cases, post-treatment follow-up[7]. Conversely, a study in China by Ren and colleagues found a slight predominance in men (44.9% compared to 42.0%)[41].

The median time between the end of treatment and the breath test was eight weeks for both positive and negative cases, with no statistically significant differences. This

value exceeds guideline recommendations. It is important to note that no studies have reported potential diagnostic performance alterations when more than four weeks elapse between the end of treatment and testing, and there is no consensus on the maximum tolerable interval. Additionally, the characteristics of the local healthcare system often do not allow adherence to the specified timelines. In our study, no significant differences were observed among the subgroups of 4 weeks, 4 to 12 weeks, and more than 12 weeks (as outlined in guidelines); in all cases, the percentage of negative results was equal to or greater than 80%. However, it is crucial to consider various causes of false positives, such as the presence of other urease-producing bacteria, including *Helicobacter heilmannii*, *Proteus mirabilis*, *Citrobacter freundii*, and *Staphylococcus aureus*, as well as false negatives due to factors like antibiotic and bismuth compound use within the last four weeks, proton pump inhibitor (PPI) and sucralfate use within the last two weeks, testing conducted less than four weeks after treatment, infection predominantly in the gastric body, and previous gastric surgery[42,43].

Given the results of this study and the high variability in clarithromycin resistance rates, triple therapy with amoxicillin/clarithromycin/PPI remains a potentially acceptable first-line treatment option in our setting while awaiting local epidemiological data on antimicrobial susceptibility.

STRENGTHS AND LIMITATIONS

This study represents one of the first descriptive analyses of *H. pylori* eradication with first-line treatment in a high-complexity hospital in southwestern Colombia, providing valuable insights into eradication outcomes via the breath test and addressing an informational gap in the region. However, some limitations must be noted. In several cases, both the diagnosis and the indication for a specific eradication treatment were made outside our institution, with patients visiting Fundación Valle del Lili solely for the post-eradication breath test. Nevertheless, the physician conducting the procedure collected detailed information on the type and duration of the treatment received. Additionally, due to administrative issues with their health insurance providers (EPS in Spanish), some patients did not undergo the follow-up test within the recommended time frame (less than one year). Finally, it was not possible to measure treatment adherence due to the retrospective nature of the study and the reliance on patient-reported information, which could affect the accuracy of some collected data.

CONCLUSION

In our setting, the eradication rate aligns with the acceptable threshold proposed by the World Gastroenterology Organization, even with standard triple therapy, which remains the most widely used regimen. The findings of this study highlight the high variability in clarithromycin resistance rates. Against this backdrop, triple therapy including amoxicillin, clarithromycin, and a PPI emerges as a potentially acceptable first-line treatment option in our context, where epidemiological data on antimicrobial susceptibility are still being gathered.

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Conflict of Interest

The authors declare no conflicts of interest.

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Original article

Challenges in the Diagnosis of Gastroparesis: Divergence Between Gastric Emptying Scintigraphy Results for Liquids and Solids

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Abstract

Introduction: Gastric emptying scintigraphy with solid food is the recommended gold standard for studying gastroparesis in patients after mechanical obstruction has been ruled out, according to the latest clinical guidelines. Although gastric emptying for liquids can also be assessed, the results of these two phases may not always align. **Objective:** To determine the level of concordance between gastric emptying scintigraphy results for solids and liquids in the evaluation of gastroparesis at three nuclear medicine centers in Bogotá, Colombia. **Methodology:** Data from all patients who underwent both phases of the study were reviewed. Patients under 18 years of age, those with accelerated results in either phase, or those with incomplete data were excluded. Cohen's kappa coefficient was calculated to assess agreement between the tests. A bivariate analysis was performed to examine the association between test results, the level of agreement, and sociodemographic and clinical variables. **Results:** A total of 210 patients met the inclusion criteria. Delayed results were observed in the solid phase in 86 patients (41%) and in the liquid phase in 181 patients (86%). The kappa value was κ = 0.082 (95% confidence interval [CI]: 0.005–0.16), with statistically significant results ($p < 0.05$). The most common pattern of divergence was normal solid-phase emptying with delayed liquid-phase emptying, observed in 102 patients (48.6%). **Conclusion:** The level of concordance between gastric emptying scintigraphy for liquids and solids is low. The solid phase is considered the gold standard, and the results of the liquid phase should be interpreted with caution, taking into account the clinical context of each patient.

Keywords

Gastroparesis, gastric emptying, scintigraphy, food.

INTRODUCTION

Gastroparesis is a syndrome characterized by delayed gastric emptying associated with upper abdominal symptoms in the absence of mechanical gastric obstruction[1]. It falls under the category of functional gastrointestinal disorders, which are highly prevalent and poorly understood, significantly impacting healthcare and socioeconomic systems[2]. Regarding its etiology, the disorder is primarily idiopathic but is also linked to diabetes *mellitus*, postsurgical conditions, and, to a lesser extent, autoimmune diseases, paraneoplastic syndromes, neurological conditions, medications, and eating disorders[3].

The true prevalence of gastroparesis is unknown, though data is available for specific countries. For instance, in the United Kingdom, a prevalence of 13.8 per 100,000 inhabitants and an incidence of 1.9 per 100,000 inhabitants were reported in 2016[4]. Similarly, a study analyzing 43,827,910 medical records in the United States found a prevalence of 0.16% in the general population[5]. In Colombia, no specific data is available; however, worldwide prevalence has been found to range between 20% and 40% in diabetic patients,

with studies consistently reporting a significantly higher prevalence in women compared to men[6].

Gastric emptying scintigraphy (GES) is a nuclear medicine test used to evaluate gastric emptying by consuming a standardized caloric meal containing a total of 255 kcal. It assesses the emptying of solids (solid-phase gastric emptying, SGE) or liquids (liquid-phase gastric emptying, LGE) labeled with radioisotopes (technetium-99m in Colombia) and is currently considered the most appropriate diagnostic method for assessing gastric motility[7,8]. In 2008, the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society reached a consensus that standardized the meal and reference values for SGE (**Table 1**)[9]. However, for LGE, there is no consensus among societies on universally accepted normal values. Nonetheless, multiple studies have established varying normal ranges for the mean gastric emptying time of clear liquids, ranging from 1.5 to 25 minutes[10–13]. In nuclear medicine practice, the upper normal limit proposed by Dr. Harvey Ziessman, set at 26 minutes, is widely accepted[14].

Table 1. Reference Values for Gastric Retention in SGE

Time	Lower Limit of Gastric Retention (%)	Upper Limit of Gastric Retention (%)
1 hour	30%	90%
2 hours	-	60%
3 hours	-	30%
4 hours	-	10%

Adapted from: Abell TL and colleagues. J Nucl Med Technol. 2008;36(1):44–54[9].

Although recent guidelines, such as those published in 2020 by the European Society of Neurogastroenterology and Motility in collaboration with United European Gastroenterology[15] and in 2022 by the American College of Gastroenterology[16], specifically recommend SGE as the diagnostic method for patients with suspected gastroparesis, it is common for both phases to be performed in these patients. However, previous studies have demonstrated that the results of the two phases may not always be consistent. Notably, it has been found that a significant percentage of patients with gastroparesis symptoms and normal SGE results test positive in LGE[8,17,18]. In light of this, the objective of the present study was to determine the concordance between gastric emptying scintigraphy results for solids and liquids in diagnosing gastroparesis at three nuclear medicine centers in Bogotá, Colombia, between July 1, 2020, and July 31, 2023.

METHODOLOGY

Study Design and Population

A multicenter, cross-sectional study was conducted at the nuclear medicine centers of Clínica Universitaria Colombia, Clínica Reina Sofía, and Medicina Nuclear Palermo in Bogotá, Colombia, from July 1, 2020, to July 31, 2023. All SGE and LGE studies performed during this period were reviewed, and cases involving patients over 18 years of age who had undergone both phases were selected. Patients with a history of gastric surgery, those with accelerated gastric emptying in either phase, or those with incomplete test, clinical, or demographic data were excluded from the analysis.

Data Collection and Result Analysis

All three centers followed the protocol established by the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society for SGE[9]. This protocol standardized the test meal to include 118 mL of egg whites mixed with 1 mCi (37 MBq) of technetium-99m-labeled radiocolloid during preparation in a microwave or non-stick pan. Additionally, the meal included two slices of white bread, 30 grams of jam, and 120 mL of water. The food could be consumed either as a sandwich or separately, ensuring that the patient ate the entire meal or at least 50% within 10 minutes. Afterward, with the patient in the supine position, immediate anterior and posterior projection images were taken at one hour, two hours, and four hours. Gastric retention and emptying percentages were then evaluated with correction for radiopharmaceutical decay.

In the case of LGE, 300 mL of water labeled with 1 mCi (37 MBq) of 99mTc-DTPA was used, and a dynamic study was performed over 40 minutes with the patient in a supine position. The mean gastric emptying time was obtained and evaluated. Both phases were conducted on different days, early in the morning, after a minimum fasting period of six hours and with the discontinuation of all medications that could affect gastric motility (opioids, prokinetics, antispasmodics, and benzodiazepines) 48 hours prior to the study.

The studies provided quantitative results, and for the analysis, the reference values and criteria defined by the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society were used for the interpretation and diagnosis of SGE[9]. According to the percentages and times obtained, the final result was described as normal SGE if all values were within the normal range, or delayed SGE if at least one measurement was abnormal. For LGE, the reference was the study by Ziessman and colleagues[14], which established an upper

limit of normal at 26 minutes. Times below 26 minutes were classified as normal LGE, and times above 26 minutes were classified as delayed LGE.

The studies were conducted using Infinia™ gamma cameras (GE HealthCare) with detectors positioned in the anterior and posterior planes. Data processing was carried out on Xeleris™ workstations, applying corrections for positioning and time. Study results were visualized through the Carestream VUE PACS platform. Clinical data were obtained from the Carestream VUE RIS, AVICENA, and SOPHIA information systems.

Statistical analysis was performed using R software version 4.3.1[19] and EpiInfo version 7.2.6[20]. Cohen's kappa coefficient was calculated to assess the strength of agreement between tests, based on the study by Landis and Koch (**Table 2**)[21]. Qualitative variables were presented as absolute and relative frequencies, while quantitative variables were described using measures of central tendency and dispersion. A bivariate analysis was conducted between the results of each test and their agreement with sociodemographic and clinical variables using the Wilcoxon rank-sum test and Fisher's exact test for qualitative variables, and Pearson's chi-square test for quantitative variables.

Table 2. Strength of Agreement Based on Kappa Value

Kappa Value	Strength of Agreement
0.00	Poor
0.01-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1.00	Almost perfect

Source: Landis JR, and colleagues. Biometrics. 1977;33(1):159–74[21].

Ethical Considerations

This study was approved by the Ethics Committee for Research of Fundación Universitaria Sanitas under Approval Minutes CEIFUS 1221-23. It adhered to the current national and international regulations governing human research, including the Declaration of Helsinki, Resolution 8430 of 1993, Resolution 1995 of 1999, and Resolution 2378 of 2008.

RESULTS

During the study period, a total of 1,217 gastric emptying scintigraphies were performed across the three centers. After excluding patients under 18 years of age or those who had undergone only one phase of the test, 242 eligible patients were identified. Of these, 32 met at least one exclusion criterion, resulting in a total of 210 patients included in the analysis. The sociodemographic and clinical characteristics of the included patients are summarized in **Table 3**. The median age was 56 years (interquartile range [IQR]: 40–65), and 85% of the study population was female. Normal nutritional status, as defined by body mass index, accounted for 47% of the population. Diabetes was present in 19% of patients, and 24% had a history of autoimmune disease. Regarding the gastric emptying results, 41% of patients showed delayed solid-phase gastric emptying, while 86% showed delayed liquid-phase gastric emptying. Concordance between the two phases was observed in 101 patients (48.1%), while 109 patients (51.9%) showed discordant results.

Table 3. Demographic, Clinical, and Gastric Emptying Scintigraphy Results of Studied Patients

Variable	n = 210
Demographic Characteristics	
Age in years, median (IQR)	56 (40-65)
Sex, n (%)	
- Female	178 (85)
- Male	32 (15)
Clinical Characteristics	
Nutritional status, n (%)	
- Underweight	9 (4.3)
- Normal	99 (47)
- Obesity	25 (12)
- Overweight	77 (37)
Diabetes, n (%)	39 (19)
Autoimmune disease, n (%)	50 (24)
Scintigraphy result	
Delayed solid-phase emptying, n (%)	86 (41%)
Delayed liquid-phase emptying, n (%)	181 (86%)
Time (days) between tests	5 (2-9)

IQR: Interquartile Range. Author's own research.

Table 4 shows that being female was associated with delayed gastric emptying scintigraphy results for liquids ($p = 0.004$). No other variables showed significant differences.

Table 4. Demographic and Clinical Variables by Gastric Emptying Scintigraphy Results

Variable	Liquid-Phase Scintigraphy Results			Solid-Phase Scintigraphy Results		
	Delayed n = 181	Normal n = 29	*p*-Value	Delayed n = 86	Normal n = 124	*p*-Value
Age in years, median (IQR)	56.00 (39.00-65.00)	55.00 (43.00-65.00)	>0.9[a]	57.50 (40.00-67.75)	55.00 (39.75-64.00)	0.5[a]
Sex, n (%)			0.004			0.2[c]
- Female	159 (88%)	19 (66%)		76 (88%)	102 (82%)	
- Male	22 (12%)	10 (34%)		10 (12%)	22 (18%)	
Nutritional status, n (%)			0.3[b]			0.4[b]
- Underweight	7 (3.9%)	2 (6.9%)		6 (7.0%)	3 (2.4%)	
- Normal	89 (49%)	10 (34%)		42 (49%)	57 (46%)	
- Obesity	20 (11%)	5 (17%)		10 (12%)	15 (12%)	
- Overweight	65 (36%)	12 (41%)		28 (33%)	49 (40%)	
Diabetes, n (%)	35 (19%)	4 (14%)	0.5	16 (19%)	23 (19%)	>0.9[c]
Autoimmune disease, n (%)	45 (25%)	5 (17%)	0.4	20 (23%)	30 (24%)	0.9[c]

[a]Wilcoxon rank-sum test. [b]Fisher's exact test. [c]Pearson's chi-square test. Author's own research.

Table 5 provides a comparison of the results from both phases for all patients, stratified by the variables studied. It was found that 48.6% of patients exhibited delayed gastric emptying in the liquid phase (LGE) while presenting normal results in the solid phase (SGE), representing the most common pattern of divergence between the two tests. No statistically significant differences were identified when analyzing the results by sex, diabetes, autoimmune disease, or obesity. Cohen's kappa coefficient was calculated to assess the agreement between the results of gastric emptying scintigraphy for solids and liquids. The κ value was 0.082 (95% confidence interval [CI]: 0.005–0.16), which was statistically significant ($p < 0.05$).

DISCUSSION

Gastroparesis is a condition predominantly of idiopathic origin, and due to the non-specific nature of its symptoms, it presents a diagnostic challenge in some cases and represents a significant cause of morbidity[22]. This study evaluated the level of agreement between the two phases of the diagnostic test currently considered the gold standard for diagnosing this condition: gastric emptying scintigraphy[8].

In this study, most of the patients with gastroparesis were female, consistent with reports in the literature[6]. Female sex was the only factor associated with delayed gastric emptying in the liquid phase (LGE). However, previous studies have not demonstrated sex differences in liquid gastric emptying, unlike solid gastric emptying. For instance, a study by Lorena and colleagues showed that the solid gastric emptying time was longer in women than in men[23]. Similarly, when evaluating the divergence between the results of both tests by sex, no statistically significant differences were found.

Of note, a higher proportion of patients had a history of autoimmune diseases than diabetes, and the percentage of diabetic patients was lower than that reported in the literature, which is approximately 30%[6]. It is essential to remember that in clinical practice, diagnosing gastroparesis in diabetic individuals involves multiple criteria. Diagnosis is not based solely on symptoms, history, and the exclusion of mechanical causes; a noninvasive test confirming delayed gastric emptying is also required[24].

In some previous studies, such as the one conducted by Sachdeva and colleagues[17], both phases were assessed simultaneously using a dual-isotope radioisotopic study, where solid food was labeled with 99mTc and liquid with 111In. In Colombia, 111In is not available for dual studies, so the two phases were conducted on different days. Nevertheless, similar and adequate preparation was ensu-

Table 5. Comparison of Results from Both Phases by Studied Variables

Variables	LGE	GVS			Kappa	*p*-Value
			Delayed	Normal		
All patients		Delayed	79	102	0.08	0.03
		Normal	7	22		
Female		Delayed	71	88	0.06	0.11
		Normal	5	14		
Male		Delayed	8	14	0.12	0.32
		Normal	2	8		
Diabetes		Delayed	15	20	0.06	0.4
		Normal	1	3		
Autoimmune disease		Delayed	17	28	-0.06	0.37
		Normal	3	2		
Obesity		Delayed	9	11	0.14	0.28
		Normal	1	4		

LGE: Liquid-Phase Gastric Emptying; SGE: Solid-Phase Gastric Emptying. Author's own research.

red for both studies. Additionally, institutional protocols did not require that one specific phase be performed first, making the order of the tests irrelevant.

Although previous studies had shown that 26% to 32% of patients exhibit discordant results between LGE and SGE[14,17,18], this is the first study to evaluate the strength of agreement between the two tests. The study found a low level of agreement, likely due to the substantial proportion of patients with delayed results in LGE but normal results in SGE (**Table 5**).

A significant factor to take into account is that, during the SGE study, patients stand up from the gamma camera and remain seated between imaging sessions, whereas, for the LGE study, patients remain in a supine position for 40 minutes immediately after ingesting the radiolabeled water. It has been shown that body position and gravity can significantly influence liquid gastric emptying. Although the documented mean time for liquid emptying in the supine position is approximately 28 minutes[12], the reference time used in this study was 26 minutes.

The process of gastric emptying involves complex neuromuscular interactions that are not yet fully understood. However, it has been determined that liquid gastric emptying occurs exponentially due to the pressure gradient generated by the tone of the gastric fundus and the relaxation of the pylorus. In contrast, solids are initially retained in the proximal stomach (lag phase) before moving to the antrum, where they are triturated through phasic contractions[25].

Failures in antral contractions and inadequate pyloric relaxation are likely the primary pathophysiological disruptions in gastroparesis[25]. Ziessman and colleagues suggested that LGE might identify patients with a primary abnormality in the gastric fundus[14]. While this hypothesis remains unproven, it has been observed that delayed emptying of caloric meals involves more complex mechanisms, including alterations in gastric accommodation and antral motility index[26].

The strengths of this study include the comparison of patients against themselves, ensuring robust correlation of results. Additionally, the outcomes of both SGE and LGE are purely quantitative, which guarantees adequate reproducibility. However, the main limitation of the study is its retrospective nature, with data extracted from multiple information systems. Nonetheless, as the participating institutions operate within a common academic and clinical framework, the procedures are highly similar. Furthermore, a stratified analysis was conducted based on the study variables to control for potential confounders. Prospective studies are necessary to confirm the findings of this research.

A comprehensive understanding of the pathophysiology of gastroparesis and the mechanisms by which LGE may yield a higher rate of positive results in suspected cases of this condition still requires further scientific development. Although our findings demonstrate that this phenomenon is not limited to previously studied international populations, only the protocols and values for SGE are internationally standardized and endorsed by scientific societies. Moreover, SGE is recommended in the latest guidelines from European and American gastroenterology societies as the diagnostic test of choice[15,16].

In this study, the degree of agreement between gastric emptying scintigraphy for liquids and solids was found to be low in our population. The most common pattern of divergence was normal solid-phase results with delayed liquid-phase results. While gastric emptying scintigraphy for solids remains the gold standard, LGE results should be interpreted cautiously and within the individual clinical context of each patient. Prospective studies are warranted to investigate this discordance and the associated factors in a controlled manner.

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Conflict of Interest

The authors declare no conflicts of interest related to this work.

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Original article

Auditing Anorectal Manometric Disorders in Children with Constipation at a Hospital in Colombia

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Abstract

Introduction and Objectives: Anorectal disorders can be an underlying cause of chronic refractory constipation in pediatric patients. This study aims to identify such disorders using high-resolution anorectal manometry (HRAM) in children with chronic refractory constipation. **Materials and Methods:** A retrospective, observational, descriptive cross-sectional data analysis was conducted based on HRAM performed in patients under 18 years old with chronic refractory constipation at a hospital in Colombia between 2014 and 2018. An exploratory descriptive analysis of demographic variables and manometric parameters was performed. Conventional manometric diagnoses were compared and aligned with the London classification. **Results:** A total of 89 patients were evaluated. According to the conventional classification, 60% of the patients had abnormalities on manometry, and 8% lacked a rectoanal inhibitory reflex (RAIR). HRAM without sedation was performed in 57 patients, of whom 80% showed an abnormal balloon expulsion test (BET); 53% had alterations in sensory thresholds, and 40% exhibited dyssynergic defecation. When extrapolated to the London classification, 93% were found to have rectal sensory disorders; 84% had rectoanal coordination disorders; 39% presented tone and contractility disorders, and 11% had rectoanal areflexia. **Conclusions:** Anorectal disorders are common in children with chronic refractory constipation and are diagnosed using HRAM to guide prognosis and targeted treatments, such as for dyssynergias. A classification similar to the London system, with manometric values tailored to pediatric populations by age groups, would provide a systematic and complementary approach to traditional methods and enhance diagnostic sensitivity.

Keywords

Constipation, manometry, pediatrics, gastrointestinal motility.

INTRODUCTION

Constipation is defined as difficulty in passing stools, often requiring straining, effort, or even the use of manual maneuvers or laxatives, leading to additional symptoms such as abdominal pain, bloating, and irritability. It also encompasses changes in stool frequency, which may vary across age groups. For instance, in children older than three years, one bowel movement per day is considered normal; in children aged 1 to 3 years, the average is 1.8 bowel movements per day; for infants aged 6 to 12 months, it is two per day; and for infants aged 0 to 3 months, the average is three bowel movements daily[1–3].

Chronic constipation negatively impacts the quality of life in children and is a frequent cause of medical consultations[4]. Globally, the prevalence of constipation in the

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pediatric population ranges from 0.5% to 32.2% (with an average of 9.5%), with higher rates observed in females[1,2]. A study by Saps and colleagues reported a prevalence of 12% to 19% among school-aged Colombian children[5]. The etiology of constipation is multifactorial, encompassing nutritional, psychological, and colorectal anatomical factors, as well as systemic metabolic, endocrine, neurological, medication-related, and motility or brain-gut axis disorders[3,6].

When patients fail to respond to treatments based on clinical history, chronic intractable or refractory constipation should be considered. While the distinction between intractable and refractory constipation is not universally defined, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) defines refractory constipation as constipation unresponsive to optimal conventional treatment for at least three months[7]. Some reviews, however, characterize refractory constipation as persisting for at least three months despite maximum doses of laxatives and requiring daily rectal stimulation, enemas, or suppositories[8]. In such cases, anorectal physiological tests, such as high-resolution anorectal manometry (HRARM), are indicated[9]. This diagnostic test evaluates the neuromuscular function of the anorectal complex[1,10]. The conventional interpretation of HRARM findings classifies anorectal dysfunctions into categories such as internal or external sphincter disorders, rectal sensation abnormalities, dyssynergic defecation, absence of the rectoanal inhibitory reflex (RAIR), and abnormal balloon expulsion[11,12].

The primary indications for performing anorectal manometry in pediatrics are suspected Hirschsprung's disease, constipation persisting despite adequate treatment, evaluation of patients with fecal incontinence, and postoperative assessment following corrective surgery for anorectal malformations[13,14].

A review of normal values for high-resolution anorectal manometry (HRARM) by age in pediatrics reveals that existing studies include few patients with diverse demographic characteristics, and no global consensus has yet been established to define reference values for the interpretation of manometry in children. In the Polish study by Banasiuk, the following reference values were reported: the mean resting sphincter pressure was 83 ± 23 mm Hg, contraction pressure was 191 ± 64 mm Hg, the mean anal canal length was 2.62 ± 0.68 cm, and the volumes for first sensation, urgency, and discomfort were 25 mL, 45 mL, and 90 mL, respectively[15].

The International Anorectal Physiology Working Group (IAPWG) published the London Classification consensus[16] on the terminology and interpretation of HRARM in adults. This consensus provides an objective and accurate framework for diagnosing anorectal disorders, classifying anorectal dysfunction into four groups: anal tone and contractility disorders, rectoanal coordination disorders, rectal sensation disorders, and absence of the rectoanal inhibitory reflex (RAIR)[11,16].

There is limited information regarding the prevalence of anorectal disorders in the pediatric population in South America, and HRARM is not routinely performed in children with constipation due to the lack of standardized methodology and reference values for its interpretation[10]. For these reasons, this study aims to describe the manometric characteristics of anorectal disorders in children with refractory constipation using conventional nomenclature and proposes the development of a classification system similar to the London Classification for pediatric patients.

MATERIALS AND METHODS

This was a descriptive, observational, cross-sectional data exploration study involving patients under 18 years of age diagnosed with chronic refractory constipation who underwent high-resolution anorectal manometry (HRARM) at the gastrointestinal physiology unit of Hospital Universitario San Ignacio (HUSI), Colombia, between 2014 and 2018. The HRARM was performed using a high-resolution ManoScan™ 360 system (Given Imaging®). Patients with non-retentive fecal incontinence, chromosomal abnormalities, congenital anomalies, anal sphincter reconstruction, growth disorders, or neurodevelopmental disorders were excluded. The manometry procedures were performed by a trained nurse and interpreted by gastroenterologists. Patients were prepared with a phosphate rectal enema and underwent the procedure while fasting, in a left lateral decubitus supine position. A rectal catheter with five radial sensors spaced one centimeter apart and a proximal balloon was inserted. Five minutes later, the following parameters were measured: resting anal pressure, voluntary contraction, defecation maneuver, rectal evacuation sensation, rectoanal inhibitory reflex (RAIR), and, finally, a balloon expulsion test (BET). For patients under four years of age and some older children, HRARM was conducted under sedation, evaluating basal anal sphincter pressure and RAIR presence. All studies were re-interpreted by a pediatric resident and a pediatric gastroenterologist. In cases with discrepancies in initial readings, the unit's entire physiology group reviewed the studies to reach a diagnostic consensus.

Demographic and manometric variables were recorded in an MS Excel database. The ethics committee of HUSI approved the study, which was classified as risk-free according to Article 11 of Resolution 8430 of 1993, issued by the Ministry of Health in Colombia. Informed consent, obtained from the children's guardians, included authorization

for the academic and research use of the results, ensuring adherence to ethical principles and complete confidentiality of patient identities.

Statistical Analysis

Quantitative variables were described using measures of central tendency and dispersion, while frequencies and percentages were calculated for qualitative variables. For group comparisons, Student's T test was applied for continuous variables, and the chi-square test was used for categorical qualitative variables. For comparisons of means, Student's T test was used for samples with fewer than 30 observations, while the Z test was employed for larger samples. A p-value <0.05 was considered statistically significant for group comparisons.

RESULTS

Demographic Characteristics

The study included 110 HRARM procedures performed during the study period. Six studies were excluded due to incomplete records, one due to evaluation following colostomy closure, and 14 due to a diagnosis of fecal incontinence. Ultimately, 89 manometry procedures met the inclusion criteria (**Table 1**). Among the patients, 72% had Bristol stool scale types 1 and 2, 80% had bowel movements less frequently than every three days, and 25% had bowel movements as infrequently as once per week.

The mean resting anal sphincter pressure was 63.6 mm Hg, while the mean maximum anal pressure during squeeze was 173.1 mm Hg. Among the patients, 33% failed to achieve significant anal sphincter relaxation, and the mean volumes required to trigger first sensation, discomfort, and urgency exceeded 100 mL. Eight percent of the patients lacked RAIR. The balloon expulsion test (BET) was conducted in 56 patients, with abnormal results observed in 80% of cases.

No significant differences were observed in manometric parameters by sex; however, some differences were noted between age groups. In children under five years, the mean resting anal sphincter pressure was one-third lower than that of children older than five years (46.9 versus 69.5 mm Hg). The anal sphincter length was 30% shorter in children under nine years (1.48 versus 2.15 cm). Among children under 12 years, the mean volume required to elicit the first defecatory sensation was 32% lower (83 versus 122 mL), the volume required to generate discomfort was 30% lower (144.3 versus 205.1 mL), and the volume required to induce urgency was 34% lower (191.3 versus 253.3 mL) (**Table 2**).

Table 1. Demographic Distribution of Pediatric Patients with Chronic Constipation

Variable	Results		
Mean age	10 years (SD: 5)		
Male	46 (51.6%)		
Bristol stool scale (n = 51)	Bristol 1: 18 (35%) Bristol 2: 19 (37%)	Bristol 3: 4 (7.8%) Bristol 4: 6 (11.8%)	Bristol 5: 2 (4%) Bristol 6: 2 (4%)
Bowel movement frequency (n = 51)	Daily: 6 (11.8%) Every other day: 4 (7.8%) Every third day: 16 (31%)	Every fourth day: 10 (19.6%) Every fifth day: 2 (4%) Every sixth day: 5 (9.8%)	Every seventh day: 6 (11.8%) Every tenth day: 1 (2%) Every two weeks: 1 (2%)
Mean resting ARS pressure	63.6 mm Hg (SD: 31.6)		
ARS length	2.0 cm (SD: 1.1)		
Mean balloon volume triggering RAIR	40 mL		
Max pressure during squeeze	173.8 mm Hg (SD: 59.7)		
Patients without significant relaxation during push (n = 57)	19 (33%)		
Mean volume for first defecatory sensation	100 mL		
Mean volume for first discomfort	150 mL		
Mean volume for urgency	200 mL		

SD: Standard Deviation; ARS: Anorectal Sphincter; RAIR: Rectoanal Inhibitory Reflex. Source: Author's own research.

In 32 patients, manometry was performed under sedation, assessing RAIR presence and resting anal sphincter pressure. These patients demonstrated a 25% lower resting anal sphincter pressure compared to non-sedated patients, with no significant differences in anal sphincter length (**Table 3**).

Of the total manometry procedures performed, 60% were abnormal. Among these, 8% lacked a rectoanal inhibitory reflex (RAIR), 6% exhibited anal sphincter hypertonia, and 3% had anal sphincter hypotonia. Among the 57 manometry procedures conducted without sedation, the diagnoses included abnormal balloon expulsion test (BET) in 80%, sensory threshold alteration in 53%, dyssynergic defecation in 40%, and external anal sphincter dysfunction in 2% (**Figure 1**).

Patients with Dyssynergia

Among patients diagnosed with dyssynergic defecation (n = 23), 39% had type I dyssynergia, 26% had types III and

Table 2. Distribution of Manometric Parameters by Age Groups and Sex

Manometric Parameters	All Ages	n	Males (53%)	n	Females (47%)	n	<5 Years	n	5 a 8 Years	n	9 a 12 Years	n	>12 Years
Mean age (years)	10 años (SD: 5)	46	9.34 (SD: 4.9)	43	11.12 (SD: 4.7)	15	2.5 (SD: 1.2)	15	6.8 (SD: 0.9)	28	10.3 (SD: 1.1)	31	15.6 (SD: 1.4)
Mean resting ARS pressure (mm Hg)	63.6 (SD: 31.6)	46	62.1 (SD: 24.9)	43	69.6 (SD: 38.8)	15	46.9** (SD: 18.1)	15	65.8 (SD: 34.6)	28	72.7 (SD: 41.9)	31	68.4 (SD: 23.7)
ARS length (cm)	2.0 SD (SD: 1.1)	46	1.9 (SD: 1.0)	43	1.9 (SD: 1.3)	15	1.4** (SD: 0.7)	15	1.5** (SD: 1.0)	28	2.0 (SD: 1.2)	31	2.3 (SD: 1.3)
Mean balloon volume triggering RAIR (mL)	20	46	29.6	41	31.7	15	28.1	15	25.3 (SD: 14.1)	27	31.9 (SD: 20.2)	30	33.3 (SD: 18.4)
Max pressure during squeeze (mm Hg)	173.8 (SD: 59.7)	25	189 (SD: 52)	32	167.9 (SD: 59.1)	1	232	6	181.1 (SD: 61.4)	22	177.1 (SD: 63.4)	28	174.2 (SD: 52.6)
Percentage relaxation during push (%)	28.3 (SD: 18.6)	23	22.7 (SD: 19.7)	32	30.8 (SD: 16.4)	1	26	5	19.4 (SD: 24.4)	21	27.5 (SD: 16.1)	28	28.8 (SD: 19.1)
Mean volume for first defecatory sensation (mL)	100	23	115.62 (SD: 77)	32	98.8 (SD: 60.7)	1	60	6	81.7 (SD: 39.2)	20	88 (SD: 57.5)	28	122** (SD: 76)
Mean volume for first discomfort (mL)	150	23	188.26 (SD: 96.0)	31	172.6 (SD: 79.5)	1	80	6	118.3 (SD: 41.7)	20	161.5 (SD: 63.6)	27	205.1** (SD: 97.5)
Mean volume for urgency (mL)	200	21	233 (92.64)	31	222.9 (SD: 86)	1	100	5	150 (SD: 50)	20	213 (SD: 69.7)	26	253.3** (SD: 93.5)

**p <0.05. SD: Standard Deviation; ARS: Anorectal Sphincter; RAIR: Rectoanal Inhibitory Reflex. Source: Author's own research.

Table 3. HRARM Parameters in Children with Constipation Under Sedation

Parameter	Non-Sedated (Mean and SD) n = 57	Sedated (Mean and SD) n = 32	Standard Error (Z-Value)
Age (years)	12.49 (3.64)	6.18 (4.08)	
Female, n (%)	32 (56%)	11 (34%)	
Mean resting ARS pressure (mm Hg)	65.7 (32.4)	48.1 (24.6)	4.23
ARS length (cm)	1.9 (1.2)	1.75 (0.8)	0.1589

SD: Standard Deviation; ARS: Anorectal Sphincter; HRARM: High-Resolution Anorectal Manometry. Source: Author's own research.

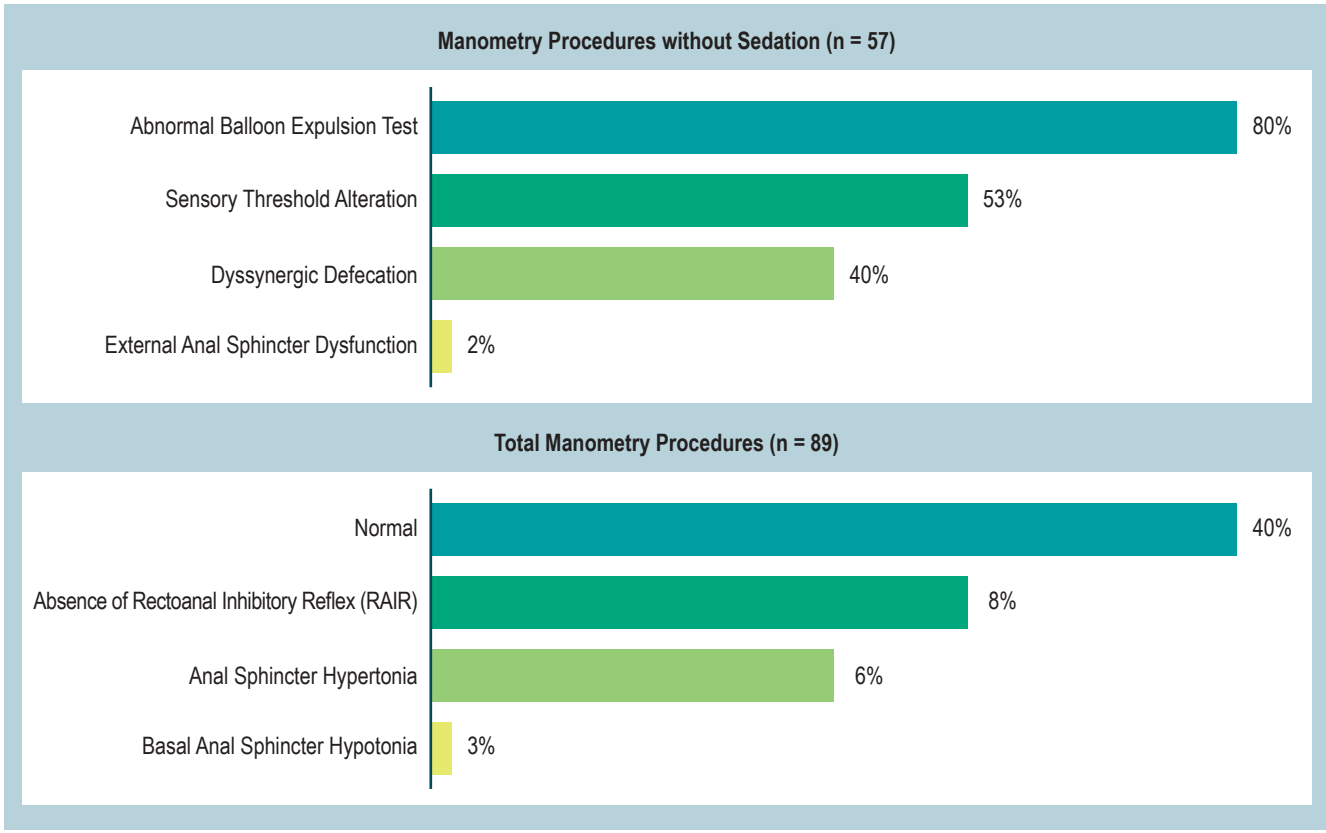


Figure 1. Results of Manometries in Children with Refractory Constipation. Source: Author's own research.

IV, and 9% had type II. No differences were observed based on age or sex. Of the patients with available Bristol stool scale data (n = 17), 88% presented with Bristol types 1 and 2 (47% and 41%, respectively). The average bowel movement frequency was every 4.7 days. The mean resting anal sphincter pressure in patients with dyssynergia was 10.7% higher compared to those with constipation but without dyssynergia (63.9 versus 70.8 mm Hg). The mean anal sphincter length was 14% greater in patients with dyssynergia (1.86 versus 2.12 cm). The mean maximum voluntary contraction pressure was 170 mm Hg. Also, 78% of patients with dyssynergia failed to achieve significant anal sphincter relaxation, 87% had an abnormal BET, and 57% exhibited sensory threshold alterations (**Table 4**).

Findings Using the London Classification Standardization

The IAPWG London Classification protocol was applied to the 57 patients evaluated without sedation (**Figure 2**).

A total of 39% (n = 22) of the patients were classified as having an anal contractility disorder. Among these, 24.5% had major disorders (17.5% with hypocontractility and normotonicity, 1.8% with anal hypotonia and normal contractility, and 5.3% with anal hypotonia and hypocontractility), while 14% had minor disorders (anal hypertonia) (**Figure 3**). In terms of rectoanal coordination disorders, 84% (n = 48) were classified as having this condition. Of these, 56% had minor disorders (14% with abnormal expulsion and dyssynergia, 25% with abnormal expulsion and poor propulsion, and 17.5% with abnormal expulsion with both poor propulsion and dyssynergia), while 28% had inconclusive disorders (25% with abnormal expulsion but normal anorectal coordination and 3.5% with abnormal expulsion and rectoanal incoordination) (**Figure 4**). A rectal sensitivity disorder was identified in 93% (n = 53) of the patients. Of these, 88% had major disorders (all with rectal hyposensitivity; none presented with rectal hypersensitivity), and 5.3% had inconclusive findings (borderline hyposensitivity) (**Figure 5**). Finally, 11% (n = 6)

Table 4. Clinical and Manometric Characteristics of Dyssynergias

Types of Dyssynergic Defecation					
Parameter	**Todos (n=23)**	**Type I (n=9)**	**Type II (n=2)**	**Type III (n=6)**	**Type IV (n=6)**
Age (SD)	12 (4)	13 (5)	11 (1)	13 (4)	11 (4)
Female (%)	52	44	100	50	67
Mean Bristol scale (n = 17)	1.82	1	2	2	2
Mean bowel movement frequency (days)	Every 4.7	Every 3	Every 7	Every 4	Every 4
Mean AS pressure (mm Hg)	70.8	60	11	62	108
Mean anal sphincter length (cm)	2.12	2.6	4.7	1.4	1.6
Mean maximum push pressure (mm Hg)	170	161	95	177	196
Patients failing to relax significantly during push (%)	78	78	50	100	67
Normal balloon expulsion test (%)	87	99	100	84	100
Sensory threshold alteration (%)	57	44	50	84	50

SD: Standard Deviation; AS: Anal Sphincter. Source: Author's own research.

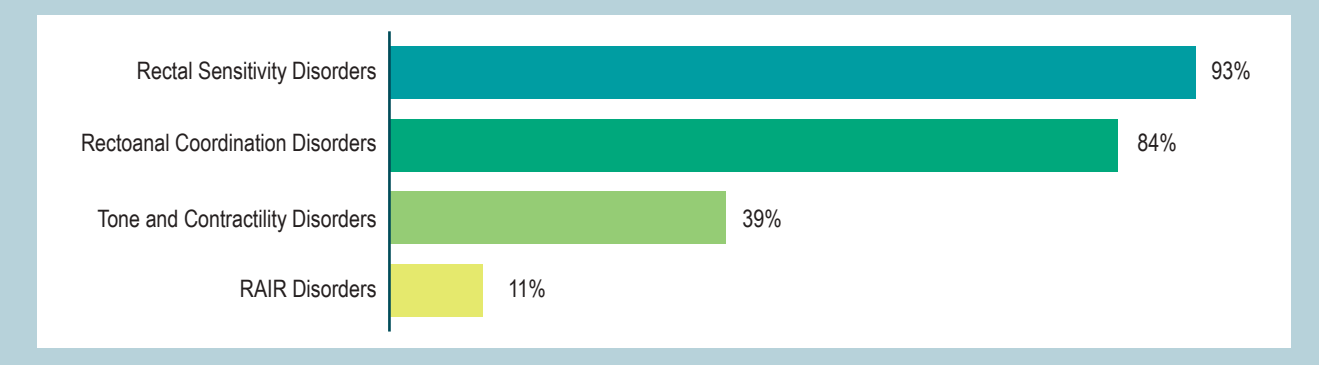


Figure 2. Manometry Results in Children with Refractory Constipation Standardized Using the London Classification (n = 57). Source: Author's own research.

were classified as having a major rectoanal inhibitory reflex (RAIR) disorder, specifically rectoanal areflexia.

DISCUSSION

Anorectal manometry measures resting anal pressure, the rectoanal inhibitory reflex (RAIR), contraction pressure, and relaxation pressure, reflecting the function of the internal and external anal sphincters[9]. This examination is commonly used in adults for diagnosing, monitoring, and guiding the treatment of functional anorectal disorders[11,17]. However, in the pediatric population, there is no consensus on baseline parameters for anal sphincter function in a healthy population stratified by age[10].

Evaluating contraction pressure and rectoanal pressure changes during a defecation attempt requires patient participation. In the present study, 36% of the patients were sedated, precluding the evaluation of contractility and sensitivity abnormalities. Under sedation, only RAIR and resting anal sphincter pressure can be measured. One of the primary objectives of HRARM in constipation is to demonstrate the presence of RAIR[10,14], which helps rule out colonic aganglionosis and other forms of neuronal dysplasia of the myenteric plexus[18], the main differen-

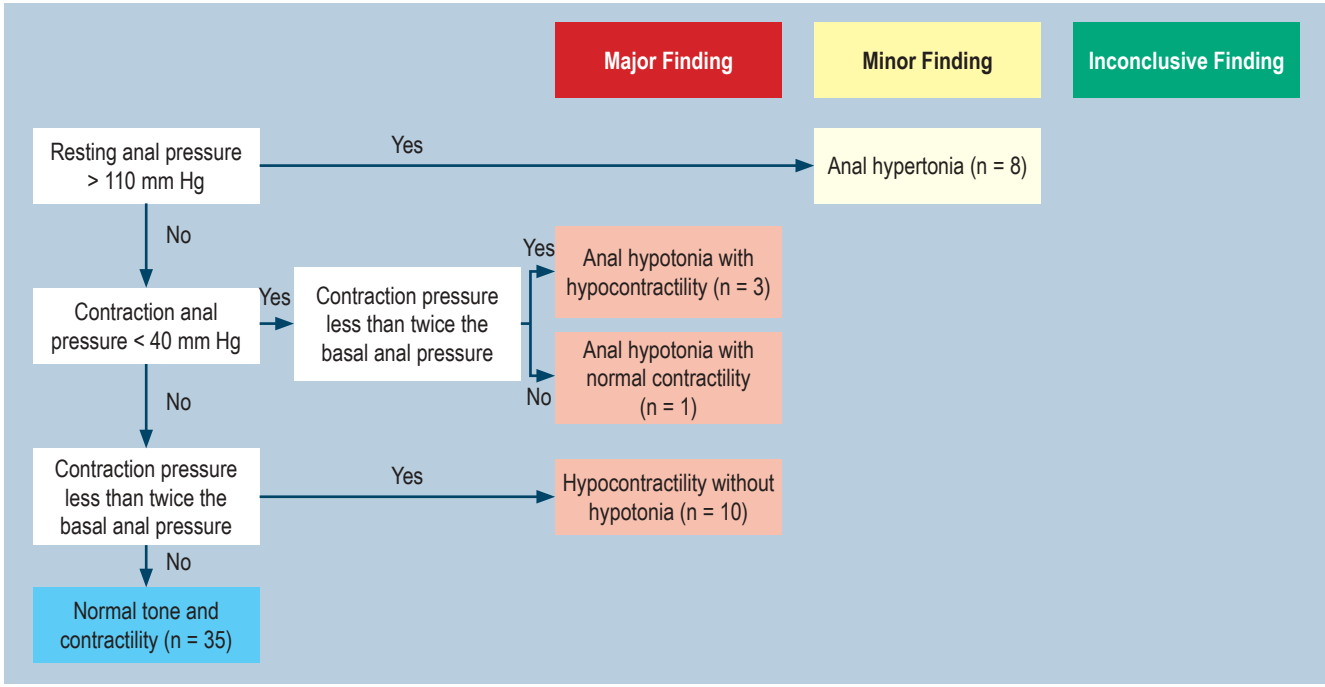


Figure 3. Anal Tone and Contractility Disorders. This figure illustrates the evaluation process for anal tone and contractility, highlighting major (red), minor (yellow), and normal (blue) manometric findings. Adapted from: Carrington EV, and colleagues. Neurogastroenterol Motil. 2020;32(1):e13679[16].

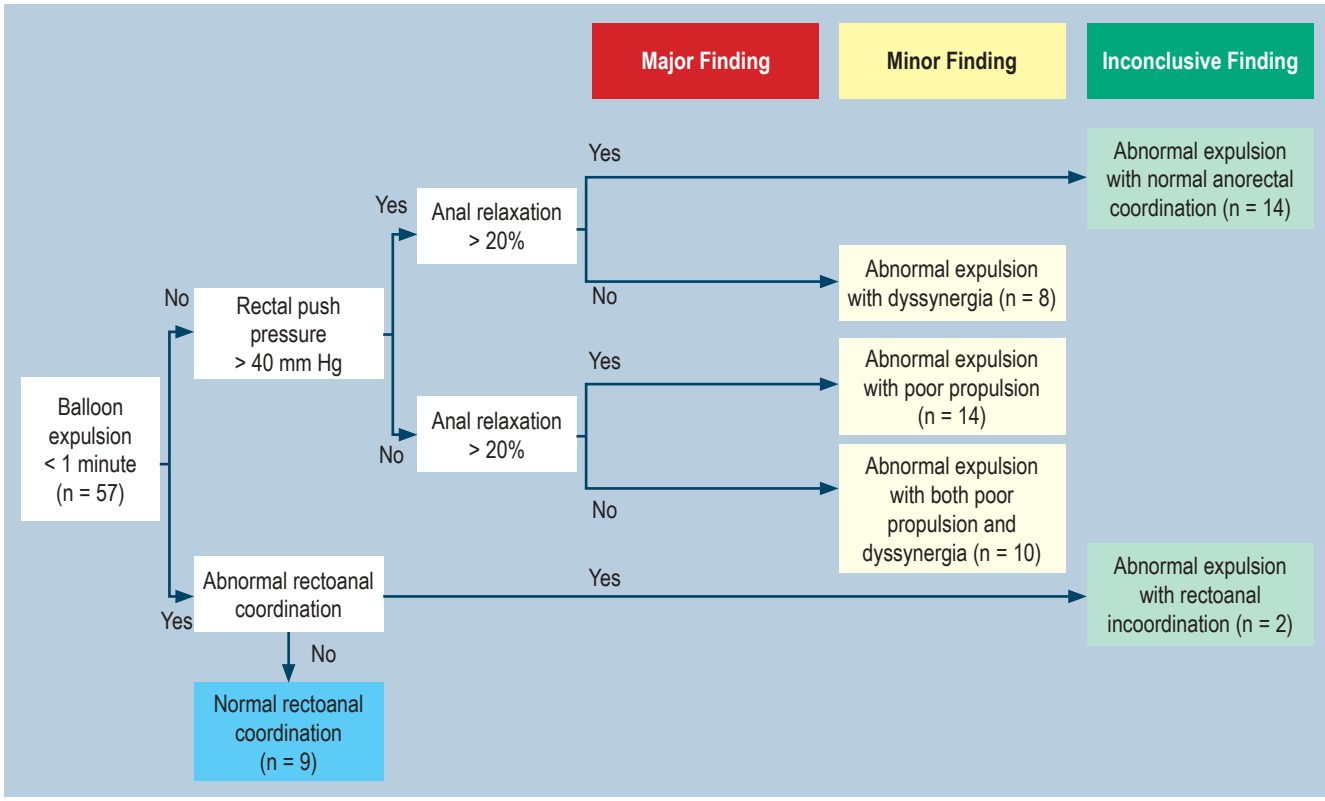


Figure 4. Rectoanal Coordination Disorders. This figure illustrates the evaluation process for rectoanal coordination, showing minor findings (yellow), inconclusive findings (green), and normal findings (blue) in patients undergoing rectoanal coordination tests. Adapted from: Carrington EV, and colleagues. Neurogastroenterol Motil. 2020;32(1):e13679[16].

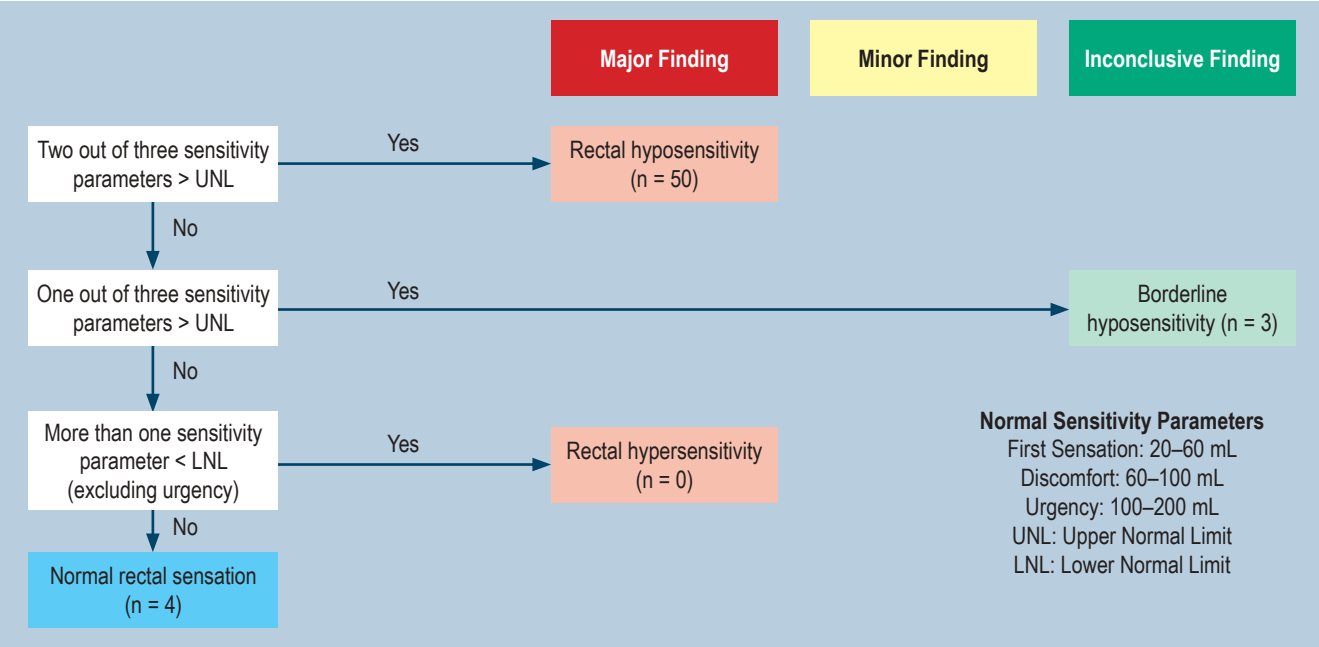


Figure 5. Rectal Sensitivity Disorders. This figure illustrates the evaluation process for rectal sensitivity, highlighting major (red), inconclusive (green), and normal (blue) manometric findings in patients undergoing rectoanal sensitivity tests. Adapted from: Carrington EV, and colleagues. Neurogastroenterol Motil. 2020;32(1):e13679[16].

tial diagnoses in a constipated child. However, in cases of significant rectal dilation, low-volume distension may not trigger RAIR in a rectum with large capacity, necessitating incremental volumes[10]. In this study, RAIR was absent in 8% of patients. Although sedation with barbiturates, benzodiazepines, chloral hydrate, and ketamine does not affect the RAIR[19], it is important to note that some studies suggest sedation might alter neuromuscular function[20]. As observed in this study, there was a difference in anal sphincter tone among sedated patients, which may indicate a limitation in detecting hypertonia in constipated patients under sedation. This finding suggests the need for different reference values for sedated versus non-sedated patients[20].

A common anorectal disorder associated with constipation is dyssynergia[21]. García-Valencia and colleagues demonstrated that in patients aged 3 to 11 years with constipation and dyssynergia, internal anal sphincter pressure and maximum tolerable volume were reduced in 97.9% of cases, suggesting that dyssynergia plays a physiological role in the development and chronicity of constipation[22]. In our study, using a conventional classification, 40% of non-sedated manometry procedures revealed dyssynergic defecation.

The London Classification, currently applied in adults, organizes HRARM interpretation by grouping disorders of tone, contractility, coordination, sensitivity, and RAIR. For pediatric populations, it is proposed that these five groups of parameters be evaluated according to age groups. Some disorders, such as RAIR, can be assessed at all ages, while others, like tone, require an alert state, and parameters like contraction, coordination, and sensitivity require a certain level of neurocognitive development to follow instructions. When extrapolating this classification to the pediatric population, 84.2% of patients had a rectoanal coordination disorder, with abnormal expulsion accompanied by dyssynergia and poor propulsion being the most common findings. Pelvic floor dyssynergia diagnosis requires confirmatory studies, such as defecography, but it can be suspected in patients with an abnormal BET. In this study, the adult parameter for balloon expulsion time (<1 minute) was applied. However, there is no consensus regarding abnormal balloon expulsion time in the pediatric population. It is likely that balloon expulsion time varies across age groups due to differences in central nervous system maturity.

Children with chronic constipation may exhibit additional involuntary contraction of the anal sphincter, possibly to avoid the painful expulsion of large, hard stools. Yan Zhao and colleagues analyzed HRARM findings in 82 adults with chronic constipation, identifying reduced resting relaxation of the anal sphincter in 24 patients and increased resting anal sphincter pressure in 36 patients[23].

Alessandrella and colleagues evaluated 29 patients aged 4 to 15 years with constipation and found higher volumes required to trigger RAIR[24]. Additionally, resting anal pressure and maximum anal contraction pressure were lower than in healthy patients. Other studies in pediatric populations have reported resting anal pressure and maximum contraction pressure values without statistically significant differences compared to healthy children[15,25].

Mortada and colleagues evaluated 50 children aged 6 to 14 years with functional constipation, observing significantly abnormal rectal sensory parameters during rectal balloon distension, including a substantially higher volume required to elicit defecatory sensation, discomfort, and urgency[26]. The need for higher volumes to trigger rectal sensations has been correlated with reduced defecation frequency. Prolonged stool retention can lead to rectal dilation and higher rectal sensation thresholds, progressively delaying the perception of the need to defecate and resulting in less frequent bowel movements. In our sample, the mean volume for the first defecatory sensation was 100 mL, for the first discomfort 200 mL, and for defecatory urgency 250 mL. These volumes are higher than the normal values established for healthy adults and pediatric populations[15,24].

Sensory threshold alterations were identified in 53% of the manometries; however, when extrapolated to the London Classification, rectoanal sensory disorders increased to 93%, an increase of 75%. This suggests potential underdiagnosis when using conventional interpretation. While there is no established London Classification for children, extrapolating these findings from our population provides a preliminary framework for future classifications and highlights the need to revisit anorectal manometric patterns in children and adolescents. Using the London Classification, our team identified a greater number of abnormal HRARM results due to associated anorectal disorders compared to conventional interpretation.

One limitation of conducting HRARM studies in pediatric populations is the lack of normal values for Colombian children, stratified by age, sex, and anthropometric measures. Retrospective observational studies can introduce information collection bias, as variables such as height, weight, and nutritional status—factors that may influence manometric parameters—were not measured. Additionally, the use of medications affecting anorectal physiology, the duration of constipation, and the presence of other symptoms were not assessed. Despite the interpretation being conducted by two gastroenterologists (adult and pediatric), including fellows, variations in manometric classification could arise due to differing interpretation parameters.

The absence of standardized values in children complicates the comprehensive understanding of anorectal physiology. Establishing reference values in a healthy pediatric population stratified by age groups remains a significant challenge. Further studies in pediatric digestive physiology are necessary to establish normative values and classify them by age groups in Latin American populations.

CONCLUSIONS

Chronic refractory constipation in children may be associated with various abnormalities in anorectal function, and HRARM proves useful for its evaluation. Additional studies on normal anorectal physiology in children, including those conducted under sedation, are needed to establish normative parameters, thereby enabling better discrimination of abnormal findings and enhancing the diagnostic utility of these tests. Although the London Classification has not been validated for pediatrics, a subgroup-based classification adapted for children could allow a targeted approach to anorectal disorders, establishing prognoses and enabling more specific, targeted treatments.

Conflict of Interest

The authors declare no conflicts of interest.

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Review Article

Eosinophilic Esophagitis: State of the Art in 2024

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Abstract

Eosinophilic esophagitis (EoE) is an immune-mediated and allergic disease categorized as a primary eosinophilic gastrointestinal disorder. Its incidence and prevalence have increased over the past decades, alongside growing awareness of the condition among gastroenterologists. EoE is more common in young males with a history of atopy. Diagnostic criteria include symptoms and esophageal histology showing a count of ≥15 eosinophils per high-power field or > 60 eosinophils/mm², with eosinophilia restricted to the esophagus and other causes of eosinophilia excluded. Treatment follows the "3 Ds" approach: diet, drugs, and endoscopic dilation. Recently approved biological therapies, such as dupilumab, and novel therapeutic strategies are under investigation for managing this condition.

Keywords

Eosinophilic esophagitis, esophagitis, eosinophilia, diagnosis, treatment.

INTRODUCTION

The term *eosinophil* was introduced by Paul Ehrlich to describe cells with granules that displayed an affinity for eosin and other acidic dyes[1]. Eosinophilic gastrointestinal (GI) disorders are characterized by eosinophilic infiltration of the GI tract accompanied by GI symptoms, in the absence of other known causes of eosinophilia[2]. Eosinophilic esophagitis (EoE) is classified as one of the primary eosinophilic disorders[2]. The first case of EoE was described in 1978 by Landres and colleagues, who interpreted it as a motility disorder resembling achalasia[3]. Subsequently, in 1982, eosinophilia in the esophagus was documented, although it was misinterpreted as a diagnostic biomarker for gastroesophageal reflux disease (GERD)[4]. It took two decades for EoE to be recognized as a distinct entity, following the publication of two case series. The first, by Attwood and colleagues in the United States in 1993, reported 12 patients with dysphagia, esophageal eosinophilia, and normal 24-hour pH monitoring; the second, by Straumann and colleagues in Switzerland in 1994, involved 10 patients with dysphagia. Both series identified EoE as more prevalent in males with atopic conditions and noted endoscopic findings distinct from those observed in GERD patients[5,6]. The first expert consensus on the diagnosis and management of EoE, published in 2007, significantly advanced the recognition and diagnosis of this condition, shaping current practices[7,8]. This review provides a com-

prehensive overview of the epidemiology, pathophysiology, diagnosis, and treatment of EoE.

EPIDEMIOLOGY

The incidence and prevalence of EoE are increasing globally in both pediatric and adult populations. A recent systematic review, encompassing 40 studies conducted between 1976 and 2022, included data from 288 million participants and 147,668 EoE cases across 15 countries spanning five continents. The global incidence of EoE was found to be 5.31 cases per 100,000 person-years (95% confidence interval [CI]: 3.98–6.63), while the global prevalence was 40.04 cases per 100,000 population (95% CI: 31.10–48.98). The condition is more common in males and in developed countries, with higher prevalence observed in North America compared to Europe, and its incidence and prevalence have increased over time—27.2- and 9.1-fold, respectively, compared to studies conducted before the year 2000[9]. This trend may be attributed to a global rise in immune-mediated diseases, increased awareness and interest in EoE, recent changes in diagnostic criteria, environmental factors such as modifications in food production (e.g., milk processing), antibiotic overuse, and improved diagnostic capabilities. Enhanced suspicion of EoE, greater access to upper endoscopy, and routine esophageal biopsy collection by gastroenterologists also contribute to these findings[10,11].

There is a male predominance in EoE, with a male-to-female ratio of 3:1[12]. More than 65% of cases occur during childhood and adolescence, with a peak prevalence between 30 and 44 years of age[13]. In Latin America, there is a scarcity of published epidemiological data. A Colombian study conducted in children and adolescents, which included 46 patients (31 males), found an average age of 11.8 years (range: 11 months–18 years), with 69% of the cases occurring in adolescents[14]. Another recent study involving a Colombian adult population, which included 152 patients (58.6% male), reported an average age of presentation of 43.3 years (range: 18–79 years), with 51.3% of cases occurring in the fourth and fifth decades of life[15].

A strong familial association has been observed, with a relative risk ranging from 10- to 64-fold, particularly in siblings, parents, and males. Concordance rates have been reported as 57.9% in monozygotic twins, 36.4% in dizygotic twins, and 2.4% in non-twin siblings. However, an analysis of twin cohorts revealed a significant role of shared environmental factors (81%) compared to genetic heritability (14.5%)[16]. A recent study identified 35 cases (14.6%) of EoE among 239 relatives of 37 EoE patients, with a higher prevalence in males than females ($p = 0.027$) and in individuals with atopic symptoms[17]. Numerous genome-wide association studies (GWAS) have been conducted to identify associated genetic *loci*, with particular focus on chemokine ligand 26 (CCL26) and calpain 14 (CAPN14)[18].

PATHOPHYSIOLOGY

EoE is a chronic inflammatory disease driven by a type 2 cellular response, in which type 2 helper T cells (T_h2) play a central role in the adaptive immune response. Type 2 cellular responses are involved in defense against parasites, venoms, and toxins, as well as in allergic diseases. It is thought that type 2 cellular responses are initiated in epithelial tissues through the production of alarmins (interleukin [IL]-25, IL-33, and thymic stromal lymphopoietin), which can activate both innate and adaptive immune responses. Alarmins released by the epithelium activate innate lymphoid cells, which subsequently release large amounts of IL-5, IL-9, and IL-13, thereby activating effector cells such as eosinophils, macrophages, basophils, and mast cells. Mast cells and basophils serve as additional sources of type 2 cytokines, particularly IL-4 and IL-13. IL-5 is critical for the development, growth, maturation, activation, and survival of eosinophils. IL-4 and IL-13 play key roles in T_h2-mediated inflammation, significantly affecting epithelial barrier permeability. IL-4 inhibits eosinophil apoptosis and induces their chemotaxis by upregulating eotaxin-3 expression, while both IL-4 and IL-13 contribute to tissue remodeling, including collagen deposition and angiogenesis[20,21]. EoE is characterized by the expression of a unique esophageal transcriptome[21].

There is also evidence supporting an allergic etiology in EoE. A high prevalence of atopic diseases, such as bronchial asthma, has been documented in these patients. Furthermore, eliminating certain foods from the diet induces clinical remission of the disease, with recurrence upon reintroduction of the same foods[21]. This condition is characterized by non-IgE-mediated food hypersensitivity, with increased expression of IgG4[22,23]. A summary of the pathophysiology is provided in **Figure 1**[24].

DIAGNOSIS

EoE is a chronic immune-allergic inflammatory disease. In a 2018 expert consensus, EoE was defined as a condition characterized by symptoms of dysphagia or food impaction in adults, and feeding difficulties, abdominal pain, or vomiting in children. Histologically, it is identified by eosinophil counts of ≥15 eosinophils per high-power field (HPF) or >60 eosinophils/mm² in esophageal tissue, with eosinophilia restricted to the esophagus[25]. The presence of atopic conditions and endoscopic findings—such as rings, longitudinal furrows, mucosal edema, white exudates, strictures, and mucosal tears—heightens diagnostic

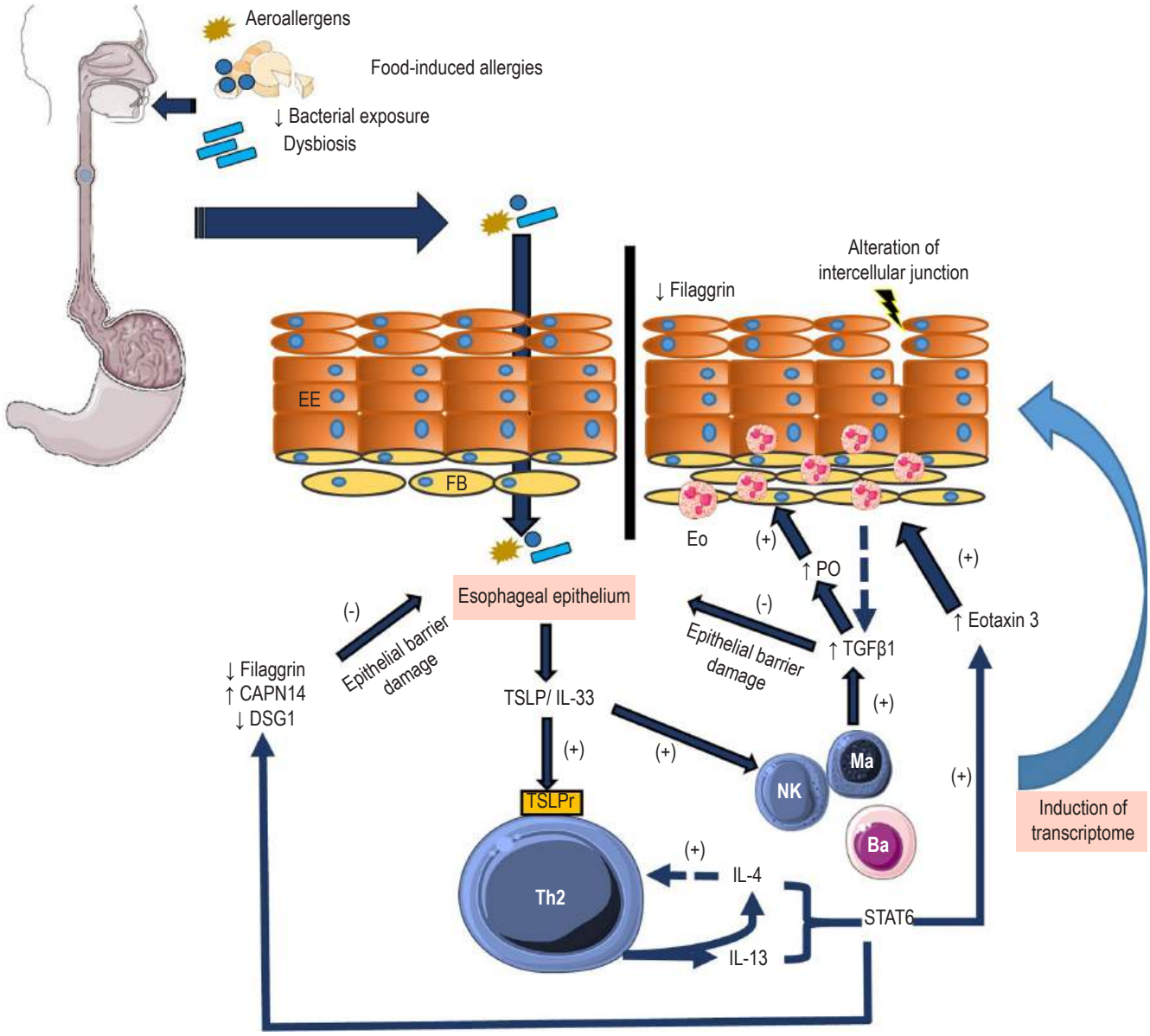


Figure 1. Pathophysiology of Eosinophilic Esophagitis. Ba: Basophils; CAPN14: Calpain 14; DSG1: Desmoglein-1; EE: Esophageal Epithelium; Eo: Eosinophils; FB: Fibroblasts; IL: Interleukin; Ma: Mast cells; NK: Natural Killer Cells; PO: Periostin; STAT6: Signal Transducer and Activator of Transcription 6; TGFβ1: Transforming Growth Factor Beta 1; Th2: Type 2 T Helper Cells; TSLP: Thymic Stromal Lymphopoietin; TSLPr: Thymic Stromal Lymphopoietin Receptor. Adapted from: Gómez-Aldana A, and colleagues. World J Gastroenterol. 2019;25(32):4598–4613[24].

suspicion. Additionally, other causes of eosinophilia, including achalasia, Crohn's disease, celiac disease, drug reactions, graft-versus-host disease, connective tissue diseases, eosinophilic gastroenteritis, vasculitis, and infections (e.g., fungal or viral), must be ruled out. EoE and GERD are not mutually exclusive conditions, and a therapeutic trial with proton pump inhibitors (PPIs) is not required to establish an EoE diagnosis[25]. A diagnostic algorithm is shown in **Figure 2**[11].

The three pillars of EoE diagnosis are symptoms, histology, and endoscopic findings. In young children, symptoms are non-specific, including nausea, vomiting, food refusal, abdominal pain, and growth retardation. In older children and adults, the disease manifests with heartburn, chest pain, dysphagia for solids, and food impaction. Several indices are available to quantify dysphagia in EoE, with the Dysphagia Symptom Questionnaire (DSQ) being the most frequently mentioned[11,26]. In patients presenting

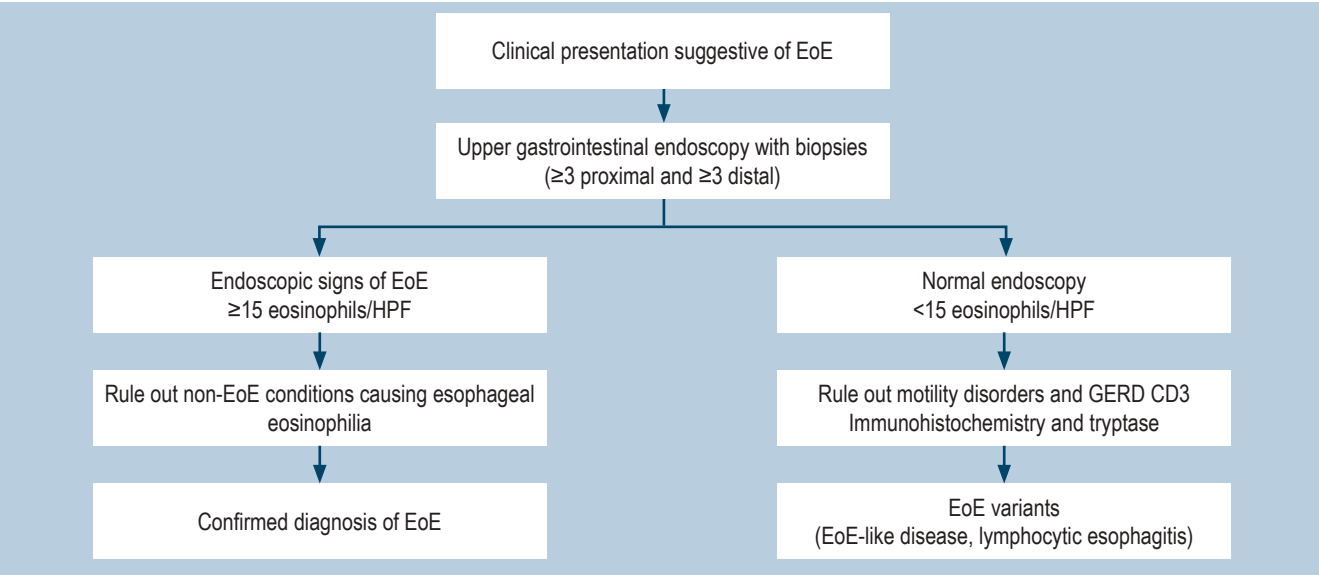


Figura 2. Diagnosis of Eosinophilic Esophagitis. HPF: High-Power Field; EoE: Eosinophilic Esophagitis; GERD: Gastroesophageal Reflux Disease. Adapted from: Biedermann L, and colleagues. Nat Rev Gastroenterol Hepatol. 2023;20(2):101–119[11].

with dysphagia for solids, the initial study is an upper digestive endoscopy. In EoE, only 5% of esophageal mucosa appears endoscopically normal.

An endoscopic scoring system has been developed to assess disease severity, known as the Endoscopic Reference Score (EREFS). This score evaluates five key endoscopic features (**Figure 3**): edema, rings, exudates, furrows, and strictures. The score ranges from 0 to 9, with higher scores indicating greater severity. The EREFS score is the standard tool that should be routinely used to ensure uniform terminology among gastroenterologists when describing endoscopic findings in EoE patients[27]. A recent endoscopy consensus on EoE recommends taking three biopsies from the proximal esophagus and three from the distal esophagus for diagnostic confirmation and patient follow-up[28]. Beyond the threshold of ≥15 eosinophils per high-power field (HPF), additional histological changes such as spongiosis, basal zone hyperplasia, mastocytosis, and papillary elongation are often observed in EoE patients[29]. A new severity index for EoE (I-SEE), proposed by a multidisciplinary consensus of international experts, integrates clinical, endoscopic, and histological aspects to determine disease severity during consultations. A score of 0–6 indicates mild disease, 7–14 indicates moderate disease, and ≥15 indicates severe disease[30].

TREATMENT

The goals of EoE treatment are to control symptoms and inflammation to prevent complications such as the development of strictures and food impaction. To achieve these objectives, the 3D rule (diet, drugs, and dilation) has been recommended. Among these, diet is the only intervention targeting the underlying cause, while endoscopic dilation is solely symptomatic, with no effect on inflammation or the disease course. Observation is not a treatment option for EoE; once diagnosed, patients must begin therapy to induce and maintain remission due to the high risk of recurrence[11].

Diet

The inflammatory response in EoE patients is triggered by exposure of the esophageal epithelium to food proteins. Consequently, elemental diets have demonstrated high rates of clinical, endoscopic, and histological remission. The first study on exclusive amino acid-based diets dates back to 1995, involving 10 children with EoE initially attributed to refractory GERD[31]. A systematic review of six observational studies reported histological remission with elemental diets in 93.6% of patients, compared to 13.3% with placebo (relative risk [RR]: 0.07; 95% confidence interval [CI]: 0.05–0.12)[32].

Despite this, maintaining dietary management in EoE patients remains challenging due to the lack of reliable tests to identify specific food triggers. International guidelines also do not recommend such tests, leaving the choice of foods to restrict largely empirical, based on their allergenic potential. Strict adherence to dietary restrictions is difficult as it significantly impacts patients' quality of life. The goal of dietary management in EoE is to minimize exposure to inflammatory

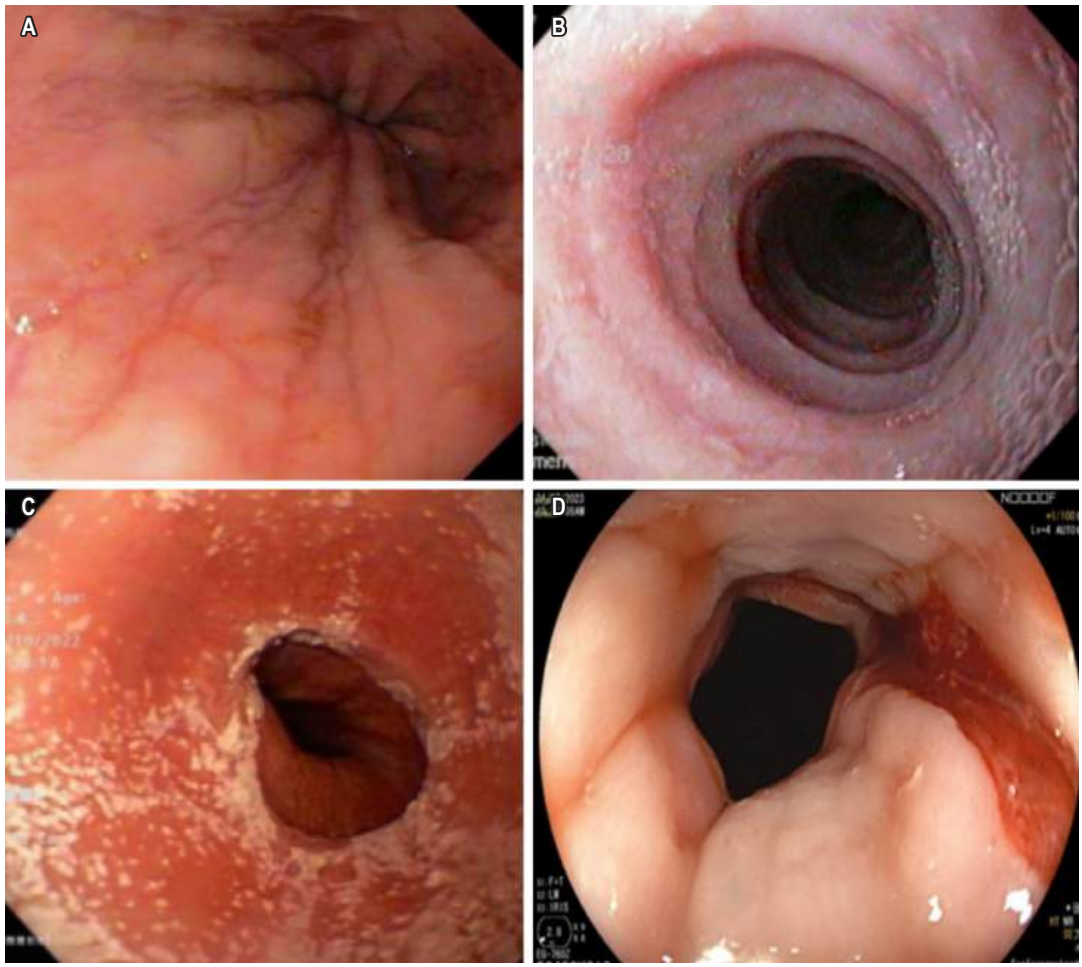


Figure 3. Endoscopic Findings in Eosinophilic Esophagitis. **A.** Edema and longitudinal furrows. **B.** Rings. **C.** White exudates. **D.** Mucosal tear. Author's file.

triggers while ensuring adequate nutrition and preserving patients' quality of life to the greatest extent possible[11].

The six-food elimination diet (SFED), targeting common allergenic foods (cow's milk, wheat, soy, eggs, nuts, and seafood), was the first regimen applied to both children and adults with EoE. It demonstrated better adherence than elemental diets, though reintroducing foods is time- and cost-intensive, requiring endoscopy with esophageal biopsies to identify specific triggers of eosinophilia. Nevertheless, these studies have highlighted the relative allergenicity of specific foods; for instance, cow's milk and wheat are more allergenic than nuts and seafood, leading to the exploration of less restrictive dietary approaches[33]. A systematic review of elimination diets in EoE, encompassing 34 studies and 1,762 patients, evaluated SFED, a four-food elimination diet (FFED: dairy, wheat, eggs, and soy), dairy-only elimination, and allergy-directed elimination diets. Histological remission rates were reported as 61.3% (95% CI: 53.0%–69.3%), 49.4% (95% CI: 32.5%–66.3%), 51.4% (95% CI: 42.6%–60.1%), and 45.7% (95% CI: 32.0%–59.7%), respectively, while clinical response rates were 92.8% (95% CI: 81.2%–99.6%), 74.1% (95% CI: 49.8%–92.6%), 87.1% (95% CI: 58.4%–99.9%), and 69.0% (95% CI: 50.2%–85.3%)[33]. A more recent randomized, multicenter study involving 129 adults with EoE found no significant differences in histological remission between SFED and dairy-only elimination after six weeks of follow-up (40% versus 34%; $p = 0.58$; 95% CI: 11–23)[34]. Based on these findings, it is advisable to initiate dietary treatment with dairy elimination in motivated EoE patients. Depending on the response, additional food groups can be excluded as needed.

Drugs

Steroids

The first reported experience with steroids in EoE was published in 1998, involving 20 pediatric patients with GERD symptoms refractory to antireflux treatment, who showed good response to oral methylprednisolone[35]. Subsequently, steroids administered via inhalation chambers with subsequent swallowing were used. A systematic review of eight randomized controlled trials comparing topical steroids with placebo found that 64.9% of patients achieved histological remission compared to 13.3% of those treated with placebo (RR: 0.39; 95% CI: 0.26–0.58). Adverse events occurred in 43% of the steroid group compared to 36% in the placebo group (RR: 1.0; 95% CI: 0.85–1.19)[32]. The recommended dose of fluticasone propionate is 880–1760 µg/day, administered as 2–4 puffs twice daily, with each puff containing 125–250 µg depending on the formulation. The recommended dose of budesonide is 2–4 mg/day, administered twice daily[36].

New formulations of topical swallowed steroids are now available, including effervescent orally dispersible budesonide, approved by the European Medicines Agency (EMA) in 2018, and oral viscous budesonide suspension, approved in February 2024 in the United States. Ongoing studies are investigating orodispersible fluticasone tablets[11]. Patients are advised not to eat or drink for 30–60 minutes after administration and to rinse their mouths afterward to prevent oral candidiasis. Reported adverse effects include oral candidiasis (1%), esophageal candidiasis (5%–30%), and adrenal insufficiency in 16% of patients[24].

Proton Pump Inhibitors (PPIs)

Several mechanisms explain the response of EoE patients to PPI therapy. First, PPIs have antisecretory effects, increasing the pH of refluxate, which restores esophageal mucosal integrity and prevents the dilation of intercellular spaces, reducing inflammation and restoring the epithelial barrier. Additionally, PPIs exhibit anti-inflammatory properties: they block adhesion molecules, preventing the activation of pro-inflammatory cytokines; inhibit STAT6 activation, which mediates eotaxin-3 expression for eosinophil recruitment; and block IL-13, thereby preventing eosinophil activation[37]. A systematic review of 23 observational studies found that patients treated with PPIs achieved histological remission in 41.7% of cases, compared to 13.7% with placebo (RR: 0.66; 95% CI: 0.61–0.72)[32]. Moderate (20 mg) or high (40 mg) doses of PPIs administered twice daily are recommended[38]. Most patients maintain clinical and histological remission with PPI doses of 40 mg/day or less[39].

Potassium-Competitive Acid Blockers (P-CABs)

This novel group of acid-blocking drugs may serve as an alternative for treatment. In cells from EoE patients, P-CABs have demonstrated anti-inflammatory effects similar to PPIs, seemingly mediated by a non-gastric proton pump that regulates T_h2 cytokine-stimulated eotaxin-3 secretion[40]. The first case series, published in Japan in 2016, involved four patients who failed to achieve histological remission with esomeprazole 20 mg/day over three months[41]. In a retrospective study, vonoprazan showed efficacy comparable to PPIs in terms of symptomatic, endoscopic, and histological responses in EoE patients[42].

Biologic Therapy

For patients with severe or refractory EoE unresponsive to conventional treatment, biologic therapy has been proposed. Based on the disease's pathophysiology, clinical trials have investigated agents targeting IL-4/IL-13 and IL-5 pathways. Among these, the most extensively studied is dupilumab, a humanized IgG4 monoclonal antibody that blocks the α-chain of the IL-4 receptor (IL-4Rα), shared by IL-4 and IL-13, thereby inhibiting their signaling[43]. A phase III randomized, controlled, multicenter trial involving 81 patients with EoE demonstrated histological remission in 60% of patients treated with subcutaneous dupilumab 300 mg weekly compared to 5% in the placebo group ($p < 0.001$) after 24 weeks of follow-up. The response was sustained at 52 weeks, with an acceptable safety profile[44]. A recent study in patients aged 1 to 11 years with EoE refractory to PPIs also confirmed the efficacy and safety of dupilumab compared to placebo[45]. In May 2022, the U.S. Food and Drug Administration (FDA) approved dupilumab for EoE as a first- or second-line therapy. However, in our setting, we recommend its use as a second-line treatment for patients with severe EoE refractory to conventional therapy.

Other biologics, such as anti-IL-5 monoclonal antibodies mepolizumab, reslizumab, and benralizumab, have been studied in EoE. While these agents reduce peripheral and tissue eosinophilia, their clinical efficacy—particularly for improving dysphagia—has been minimal[46–48].

Dilation

EoE is a chronic and progressive disease that, if not treated promptly and adequately, leads to esophageal wall remodeling and rigidity, resulting in stricture formation[49]. A study of 200 EoE patients demonstrated that the prevalence of esophageal strictures increases with diagnostic delay, rising from 17.2% with a delay of two years to 70.8% when the delay exceeds 20 years ($p < 0.001$)[50]. Mechanical dilation has proven effective for alleviating symptoms such

as dysphagia and is considered safe for patients, though it does not address inflammation. The two most commonly used dilation techniques are pneumatic balloon dilation and Savary-Gilliard dilators. Recently, a transparent conical device called BougieCap, available in various diameters, has been used. It attaches to the endoscope tip and enables direct visualization during dilation, showing clinical improvement and safety in a study involving 50 EoE patients[51]. A systematic review of 27 studies, encompassing 845 patients with strictures (including 87 children), evaluated the outcomes of 1,820 esophageal dilations, with an average of three dilations per patient. Clinical response was achieved in 95% of cases, with a perforation rate of 0.38%, bleeding rate of 0.05%, and hospitalization rate of 0.67%. No deaths related to dilation were reported[52]. Dilation is recommended for cases of stricture, but if active EoE is present, additional treatment modalities—such as dietary therapy, PPIs, steroids, or a combination of these—are required. Ideally, inflammation should be controlled first, with dilation reserved for patients experiencing persistent dysphagia or strictures.

PROPOSED MANAGEMENT OF EoE

Diet, PPIs, and steroids are considered first-line treatments for controlling inflammation in EoE patients. Biologic therapy with dupilumab is a second-line treatment for patients with severe, refractory EoE or concurrent atopic conditions, such as eczema, moderate-to-severe asthma, and chronic rhinosinusitis with nasal polyposis[53]. Endoscopic dilation is reserved for patients with persistent strictures despite achieving inflammation control with medical therapy.

When comparing the various therapeutic options, proton pump inhibitors (PPIs) are low-cost, easy to use, and well-tolerated. However, their response rates as monotherapy range between 30% and 50%, and they are less effective for the fibrostenotic phenotype. Elimination diets are natural and free of adverse events, with rare cases of nutritional deficiencies, but long-term adherence is challenging, and repeated endoscopies with biopsies are necessary to monitor response. Swallowed steroids are more effective than PPIs but are more expensive and associated with adverse events such as esophageal candidiasis. Dupilumab is effective but requires weekly subcutaneous injections, with potential adverse effects including injection site infections and conjunctivitis. There is no consensus on the preferred initial treatment for EoE. Therefore, medical management depends on the physician's experience, the patient's motivation (adherence), and the availability or approval of medications in each country, particularly topical steroid formulations and dupilumab. Data on combination therapies in EoE remain limited[53,54].

Similar to the approach used in inflammatory bowel disease (IBD), both a step-up treatment strategy and an aggressive early treatment strategy (top-down) have been proposed, as illustrated in **Figure 4**[54]. The top-down

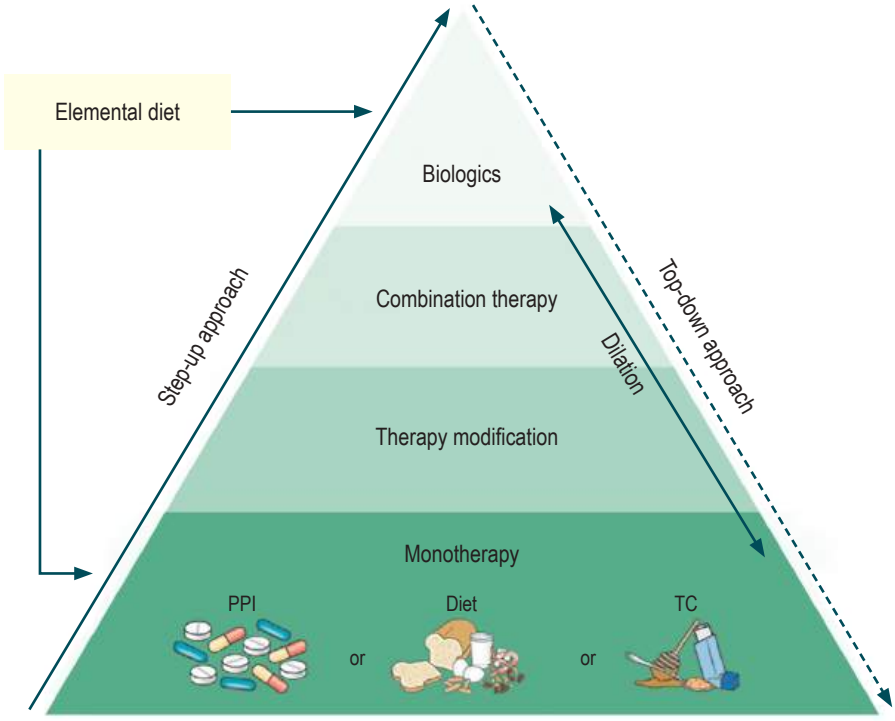


Figure 4. Therapeutic Pyramid in Eosinophilic Esophagitis. TC: Topical Corticosteroid; PPI: Proton Pump Inhibitor. Adapted from: Oliva S, and colleagues. Clin Gastroenterol Hepatol. 2024;22(9):1763–1769[54].

approach would be reserved for severe cases, fibrostenotic phenotypes, or EoE coexisting with other atopic diseases. However, further studies are needed to evaluate the utility and cost-effectiveness of this strategy[55]. A survey conducted among 228 gastroenterologists from 18 European countries reported that 82.9% use PPIs as first-line therapy, 41.6% use topical steroids, 20.6% use elimination diets, and 9.2% use combination therapies. Additionally, 21.5% do not prescribe maintenance therapy[56].

Two critical aspects in the management of EoE are the need for maintenance therapy and disease monitoring. A multidisciplinary expert consensus on EoE concludes that maintenance therapy likely reduces the risk of complications and that regular, scheduled follow-up is necessary, rather than on-demand monitoring. This is due to the moderate correlation between symptoms and histological or endoscopic disease activity. It is essential to assess disease activity, monitor adverse drug events, adjust therapy, and ensure treatment adherence in all patients. To monitor disease activity, it is necessary to evaluate symptoms, determine eosinophil counts, and assess endoscopic activity using the EREFS scoring system. Endoscopy with esophageal biopsies should be performed 8–12 weeks after initiating induction therapy. If there is a positive response, maintenance therapy should be continued. The need for re-evaluation with endoscopy should be individualized, typically within one year. However, if there is no response and treatment adjustments are made, follow-up endoscopy with biopsies should be performed within 8–12 weeks[57]. A proposed treatment algorithm is shown in **Figure 5**[53].

CONCLUSION

EoE is a type 2 immune-mediated allergic disease that is complex, multifactorial, chronic, and progressive. It is a relatively recent discovery, with defined diagnostic criteria, and its prevalence and incidence are increasing worldwide. Timely diagnosis and appropriate treatment are essential to prevent long-term complications. Key therapeutic approaches include dietary management, topical steroids, and PPIs, with endoscopic dilation required in cases of strictures. New biologic therapies, such as dupilumab, have demonstrated efficacy and safety in EoE, and innovative therapeutic strategies for the management of this condition are under investigation.

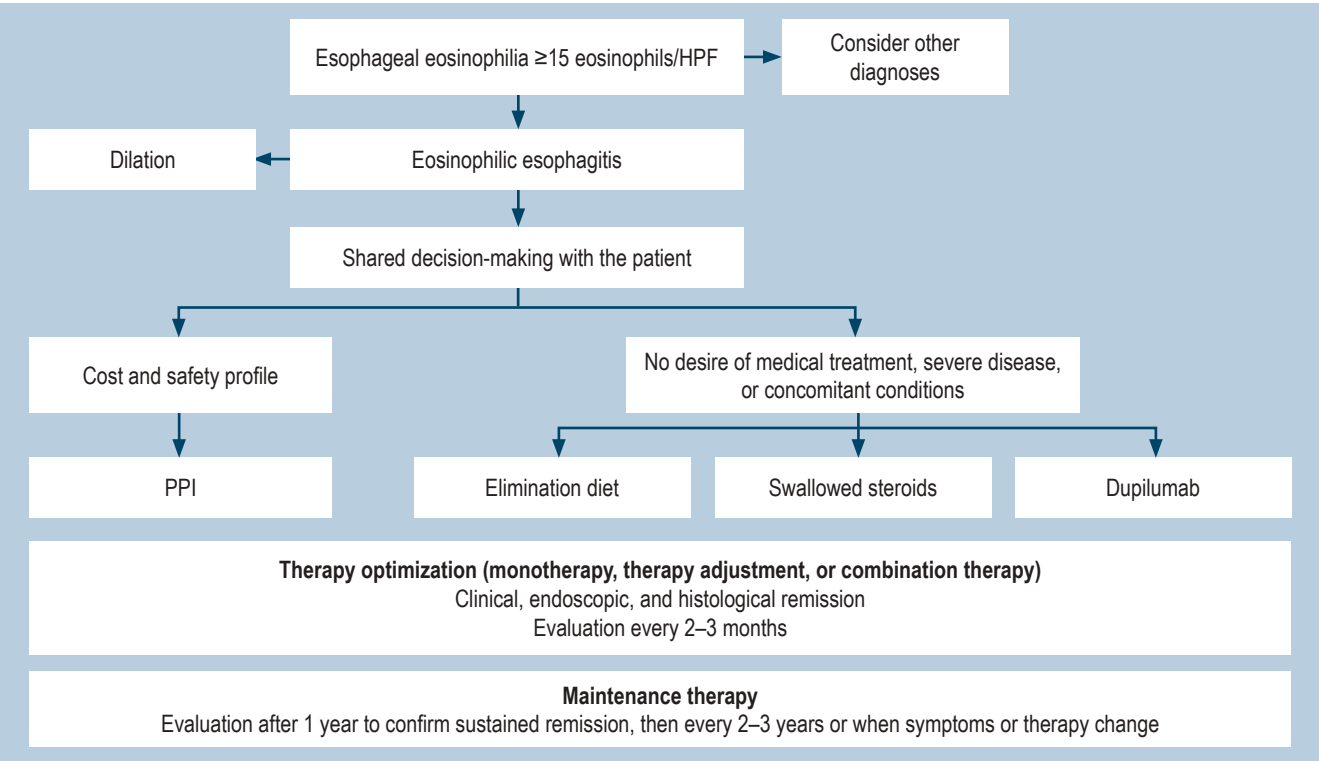


Figure 5. Management of Eosinophilic Esophagitis. HPF: High-Power Field; PPI: Proton Pump Inhibitor. Adapted from: Sauer BG, and colleagues. Am J Gastroenterol. 2023;118(5):780–783[53].

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Review Article

How to Write and Publish Research Findings

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Abstract

Introduction: Research findings are a central part of any publication and must address the proposed objectives with explicit reasoning that answers the research question. **Objective:** To highlight the core elements of an article to be published as the result of a research study. **Results:** A review of the literature is conducted to identify the key, practical, and most useful elements for presenting the results of a research study intended for publication. Additionally, common mistakes to avoid in the presentation are highlighted. **Conclusions:** Practical aspects within the context of a scientific publication are emphasized, aiming to streamline the process and prevent errors in presenting research findings.

Keywords

Methods, results, tables, research.

INTRODUCTION

It is recommended that the ultimate outcome of any scientific research should be a publication that facilitates its dissemination. Scientists or researchers are recognized not for their knowledge or expertise but for what they publish. A scientific experiment, no matter how remarkable its results, is not complete until it is published. In essence, the cornerstone of the philosophy of science is based on the premise that research must be published, as this is the only way to verify the validity of the results and contribute to scientific knowledge. A properly published manuscript allows results to be reproduced, which lends credibility to scientific research[1,2]. In other words, a scientist must not only conduct research but also write about it with impeccable clarity, ensuring the research question, the methods used to address it, and the results are effectively communicated. Poor writing can undermine the significance of the research[2].

In summary, when preparing a publication, we should ask ourselves: Is it relevant to publish the available data? Do the data address the study's hypothesis and objectives? Are the conclusions important, plausible, and reproducible?

Depending on the type of research and study design, publications can take the form of a case report, a case series, a topic review, an original article, or a meta-analysis. Choosing the appropriate journal involves evaluating whether it is indexed in national or international databases and its impact factor (citation rate). However, the key determinant for selecting a journal should be its alignment with the research objectives[3].

There are various methods and suggestions for drafting the final article. An easy way to remember the structure of a scientific publication is the acronym IMRAD (Introduction, Methods, Result Analysis, and Discussion), starting with the abstract in both Spanish and English, along with keywords to facilitate indexing[4]. It is essential to understand that the structure and organization of the article must vary depending on the type and nature of the study as well as the target journal, considering that each journal has its own publication guidelines. Generally, in all journals, the first section is the abstract, which must be written in the original language and in English. This is followed by an introduction to the topic, mentioning the origin of the research question. The methodology section then explains how the study design was selected to address the research question.

The subsequent sections of a scientific article intended for publication will present the results and highlight the core findings[5].

SECTIONS OF A SCIENTIFIC ARTICLE

Introduction and Background

This section should clearly and concisely explain the rationale for conducting the research, the research question, and the current state of the art on the topic. The introduction serves to present the research question and establish the relationship between the study and the existing evidence, offering a brief description of the study's purpose, including the hypothesis and objectives.

Materials and Methods

This section describes how the study was conducted in sufficient detail to allow replication by another researcher. It must explicitly state the type of study or design, the inclusion and exclusion criteria, the variables defined to achieve the objectives, the measurement methods, the sample size calculation, the statistical methods used, and the ethical considerations. If any interventions were performed or equipment, reagents, or medications were used, these should be described. Visual aids such as diagrams and figures are recommended to enhance clarity and comprehension.

For the hypothesis testing to be robust, the sample size calculation must be precise to ensure plausible results and valid hypothesis testing. In technical terms, this involves controlling the beta error.

Results

This section presents the study's findings clearly and is written in the past tense, avoiding the first person to ensure all authors' contributions are acknowledged. Tables and figures should be used effectively to support the narrative, with the text developed around them.

The first paragraph should succinctly summarize the study's primary finding in a clear and direct statement, and the results should be presented in the same order as described in the methodology. Begin by describing the sample or population, followed by the most significant findings that either confirm or refute the study's hypothesis.

Tables and figures must have appropriate titles and clear, concise content. Graphs are particularly useful for illustrating trends and should adhere to the journal's formatting guidelines[6,7].

Analysis

This section involves the mathematical and statistical methodologies used to organize, describe, analyze, and interpret data in a valid manner, establishing probabilities to allow extrapolation. In other words, it enables data-driven decision-making[8].

Discussion

The discussion explains the significance of the results and is typically written in the present tense. It is recommended to begin with a statement that addresses the initial research question, followed by a comparison of the findings with those in the existing literature. This should include identifying studies that support the results and those that do not, explaining the reasons for discrepancies, and illustrating how the results can improve medical practice. This section should also acknowledge potential methodological flaws and discuss how they could be addressed in future research to produce more robust findings, thus paving the way for new research areas.

In summary, a well-constructed scientific article should:

1. Present relevant findings.
2. Explain the importance of the results and compare them with those of other authors.
3. Discuss the results.
4. Acknowledge the study's limitations.
5. Suggest new research questions or lines of inquiry.
6. Provide conclusions.

KEY POINTS TO HIGHLIGHT IN THE RESULTS SECTION

The results section should include the following elements[6]:

1. An introduction outlining the research question.
2. A report on data collection, recruitment, or study participants, specifying whether inclusion and exclusion criteria were applied. This often includes a table summarizing the demographic, clinical, and other relevant characteristics of the study subjects.
3. A description of the data collection methods and the statistical approach chosen based on the type of study conducted. The most relevant results should be presented in a logical order consistent with the methods section.
4. Graphs and tables accompanied by sufficiently informative captions should be included. A general description of the experiments should be provided, and the data should be presented in a sequence that highlights significant associations or correlations.
5. A review and adherence to the specific requirements of the journal to which the manuscript will be submitted.
6. The presentation of figures, tables, and flowcharts to capture the reader's attention. These elements must be cited in the text and numbered in the order in which they are introduced. Non-textual components should include concise identifying text, and each figure or graph should be self-explanatory regarding the findings it depicts.
7. Inclusion of significant secondary results or subgroup analyses, if applicable.
8. Presentation of the frequency of events and their relationship to variables within the study and the research question, using tables and figures to summarize statistical analysis results.
9. Results should directly address the research question and study objectives. They should be analyzed straightforwardly and expressed in clear, concise language.

Writing a scientific article is not a solo endeavor; co-authors must contribute and review the manuscript to avoid frequent errors in this section[6,7], such as:

- Including raw or redundant data; instead, results should be summarized.
- Repetitive presentation of information— data included in tables or figures should not be repeated in the text.
- Reiterating information from the materials and methods section.
- Misalignment between methods and results.
- Omitting negative results or findings that do not support the conclusions. This raises ethical concerns in the work done, leading to a loss of consistency and validity. All relevant results must be reported, even if they do not support the predictions or hypotheses. Negative results are valuable and can serve as a guide for future research on the topic.
- Discussion or interpretation of the results: This should be addressed in the discussion section.
- Errors in figures and tables: These are varied and common.

The results form the core of the study and substantiate its claims. It is crucial to take sufficient time to organize them effectively and to design and prepare figures and tables to convey the intended message to the reader clearly.

CONCLUSION

When submitting an article to a journal for peer review, one of the most common reasons for rejection, based on my experience as a reviewer for multiple publications, is the lack of coherence between the various sections of the article and poor writing quality. Additionally, while most journals follow the Vancouver citation style, each journal may have its own specific requirements.

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Case report

Binasal Hemianopsia Secondary to Bilateral Lesions of the Lateral Geniculate Bodies in Post-ERCP Pancreatitis: A Case Report and Literature Review

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Abstract

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is currently the standard procedure for treating pancreatobiliary conditions. As its use has increased, so has the incidence of associated complications, such as pancreatitis, bleeding, and perforation. Post-ERCP acute pancreatitis is the most common complication. While most cases are mild, some can be severe and, in very rare instances, may result in bilateral lesions of the lateral geniculate bodies, as in this case. **Case Report:** A 28-year-old woman with a history of obesity presented with acute cholangitis due to choledocholithiasis. She underwent ERCP with bile duct stone removal and placement of a plastic stent. Forty-eight hours after the procedure, she developed severe post-ERCP pancreatitis and concurrent incongruent binasal hemianopsia. Brain magnetic resonance imaging revealed bilateral lesions of the lateral geniculate bodies (LGB). Ischemic, infectious, hydroelectrolytic, and autoimmune causes were ruled out. The patient's clinical evolution was favorable. **Discussion:** Although the mechanisms underlying lateral geniculate body lesions are not fully understood, in this case, severe post-ERCP acute pancreatitis and multiorgan involvement secondary to systemic inflammatory response syndrome (SIRS) are proposed as the likely etiology.

Keywords

Acute pancreatitis, endoscopic retrograde cholangiopancreatography, geniculate bodies, visual fields, visual acuity.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is currently considered the standard procedure for managing pancreatobiliary conditions. Various studies have demonstrated its safety and efficacy, leading to an increase in the number of procedures performed. Consequently, this has resulted in a rise in reported complications[(1)]. Among post-ERCP complications, pancreatitis is the most common. Although most cases are mild to moderate (95%) with complete patient recovery, it remains a notable cause of mortality[(2)], including the occurrence of rare complications, as described in this report.

Acute bilateral lesions of the lateral geniculate bodies represent a rare entity with unclear pathophysiology. These lesions are associated with various conditions, such as inflammatory processes and vasculitis[(3)], osmotic demyelination secondary to electrolyte imbalances[(4,5)], and ische-

mia due to systemic hypoperfusion[6]. This report presents the first case described in Latin America of a patient who developed visual deficits and radiological findings indicative of attenuation in the lateral geniculate bodies within the context of severe acute post-ERCP pancreatitis.

A CASE REPORT

The patient is a 28-year-old female with a body mass index (BMI) of 32 kg/m^2 and no other relevant medical history. She was referred from a lower-complexity facility where she had presented with a three-day history of epigastric abdominal pain. The pain was described as sharp, with an intensity of 7/10 on the pain analog scale, radiating to the right dorsal region. The symptoms were accompanied by nausea and three episodes of vomiting, followed by the onset of jaundice and dark urine; however, she did not report pale stools or fever. Upon admission, vital signs were within normal ranges: heart rate (HR), 62 beats per minute [bpm]; blood pressure (BP), 116/82 mmHg; oxygen saturation (SpO_2), 92%; respiratory rate (RR), 18 breaths per minute; and temperature, 36°C. Physical examination revealed mucocutaneous jaundice and tenderness in the right hypochondrium, with no other abnormal findings.

Laboratory tests performed at the referring institution revealed marked leukocytosis (16,280 cells/μL) with neutrophilia (80%), a negative pregnancy test, and, notably, normal bilirubin and alkaline phosphatase levels. As part of the abdominal pain workup, a complete abdominal ultrasound was performed at the referring site, which identified cholelithiasis without signs of cholecystitis and multiple diffuse focal lesions predominantly affecting the right hepatic lobe. To better characterize these findings, a contrast-enhanced magnetic resonance imaging (MRI) of the abdomen was conducted, revealing hypointense areas with geographic contours, primarily in the right hepatic lobe. At our institution, laboratory tests showed alterations in liver biochemistry consistent with a cholestatic pattern (total bilirubin: 4.59 mg/dL, direct bilirubin: 3.38 mg/dL, alkaline phosphatase: 279 U/L, aspartate aminotransferase [AST]: 976 U/L, alanine aminotransferase [ALT]: 1,553 U/L). Tests for hepatotropic viruses were negative, and coagulation times, renal function, and electrolyte levels were within normal limits. Given the persistence of abdominal pain, the cholestatic biochemical pattern, and focal liver lesions, choledocholithiasis was deemed highly probable despite its absence in prior imaging studies. Consequently, endoscopic ultrasound (EUS) was performed, which revealed hyperechoic lesions consistent with microabscesses in the right hepatic lobe and dilation of the distal common bile duct (CBD) to 9 mm, with a 6 mm hyperechoic image in its distal third suggestive of biliary lithiasis. During the same anesthetic session, an ERCP was performed without rectal administration of nonsteroidal anti-inflammatory drugs (NSAIDs). Purulent fluid was observed, and the CBD measured 6 mm in diameter. A 5 mm stone was successfully extracted. As adequate clearance of the contrast medium was not achieved, a plastic biliary stent was placed without complications (**Figure 1**). In light of cholangitis,

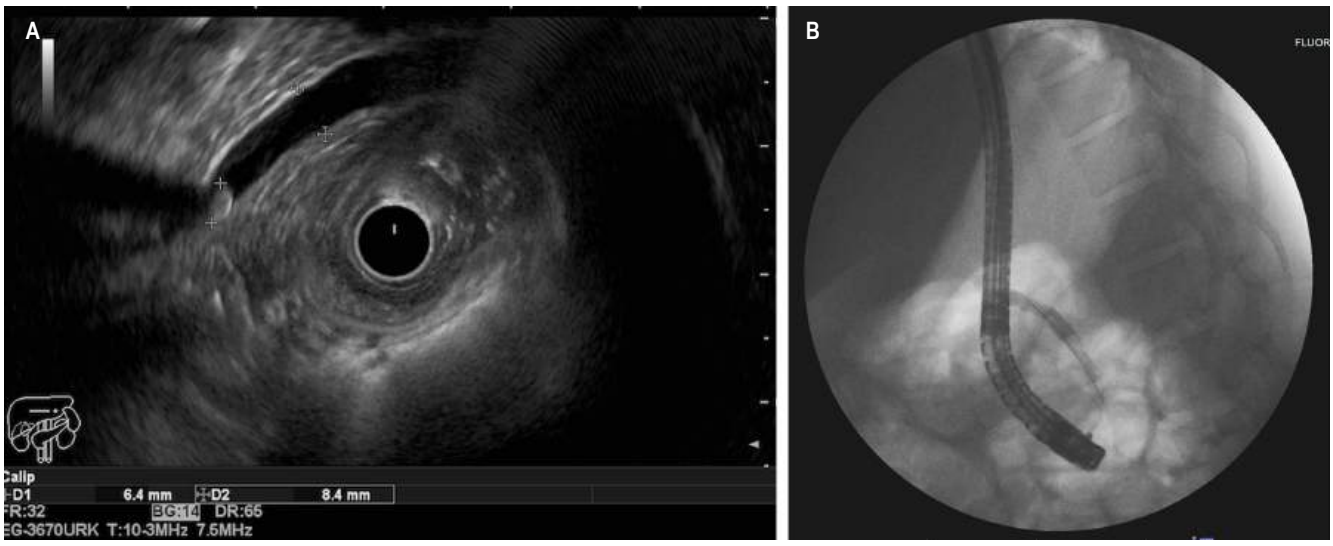


Figure 1. Diagnostic Imaging. **A.** Endoscopic ultrasound of the biliopancreatic region showing distal common bile duct dilation to 8.4 mm with a 6.4 mm biliary stone in its distal third. **B.** Fluoroscopic image from ERCP showing a 6 mm CBD and a 5 mm stone, successfully extracted without complications. Author's File.

antibiotic therapy with intravenous piperacillin/tazobactam 4.5 mg every six hours was initiated.

Forty-eight hours after the procedure, the patient developed upper abdominal pain radiating to the back, requiring opioid analgesics. Serum amylase levels were noted to be elevated to 18 times the upper normal limit, leading to a diagnosis of post-ERCP pancreatitis. On the same day, the patient reported bilateral visual field disturbances, which caused difficulty reading and perceiving objects. A neuro-ophthalmology evaluation revealed normal visual acuity on physical examination but an incongruent binasal visual field defect with left-sided predominance, observed through confrontational visual field testing and better characterized with the Amsler grid (**Figure 2**). A contrast-enhanced brain MRI was requested, showing diffusion restriction in both lateral geniculate bodies (LGBs), with low values on the apparent diffusion coefficient (ADC) map and hyperintensity in fluid-attenuated inversion recovery (FLAIR)/T2 sequences localized to the lateral aspect of the LGBs (**Figure 3**). Infectious and autoimmune causes were ruled out, and no metabolic or electrolyte disturbances were observed during hospitalization to account for the lesions. These findings were attributed to the inflammatory process associated with severe acute post-ERCP pancreatitis, which was also characterized by multiple pancreatic collections on abdominal CT. These collections showed favorable clinical evolution, and the patient's pain resolved completely. Upon discharge, the patient still exhibited persistent incongruent binasal hemianopia. However, during outpatient follow-up at 12 weeks, she reported improvement in her visual field defects.

DISCUSSION

ERCP is a diagnostic and therapeutic tool for various biliopancreatic pathologies[7]. Over the past two decades, the use of ERCP for therapeutic purposes has increased, while its use as a diagnostic tool has declined[8]. ERCP is an invasive procedure associated with adverse events, with an overall incidence rate of approximately 10%, varying across studies based on patient characteristics, procedural complexity and volume, endoscopist experience, and prophylactic measures employed[9].

Among post-ERCP complications, pancreatitis is the most common, occurring in 5%–15% of cases, followed by hemorrhage (0.3%–9.6%), cholecystitis (0.5%–5.2%), cholangitis (0.5%–3%), and perforation (0.08%–0.6%). Rarely, outbreaks of infections linked to contamination of duodenoscope equipment have also been reported[1]. Although the majority of post-ERCP pancreatitis cases are considered mild (95%), this complication can carry a mortality rate of up to 2.8%[2].

The concept of post-ERCP pancreatitis was introduced in 1991, and its definition has since evolved[2]. Currently, the diagnosis is considered in patients who develop new or worsening abdominal pain 24 hours after undergoing ERCP, associated with serum amylase or lipase levels exceeding three times the upper normal limit, or imaging evidence of pancreatitis, requiring hospitalization or prolongation of the hospital stay, as observed in the present case[10]. Notably, this patient presented symptoms 48 hours after the procedure, which is unusual and suggests the need

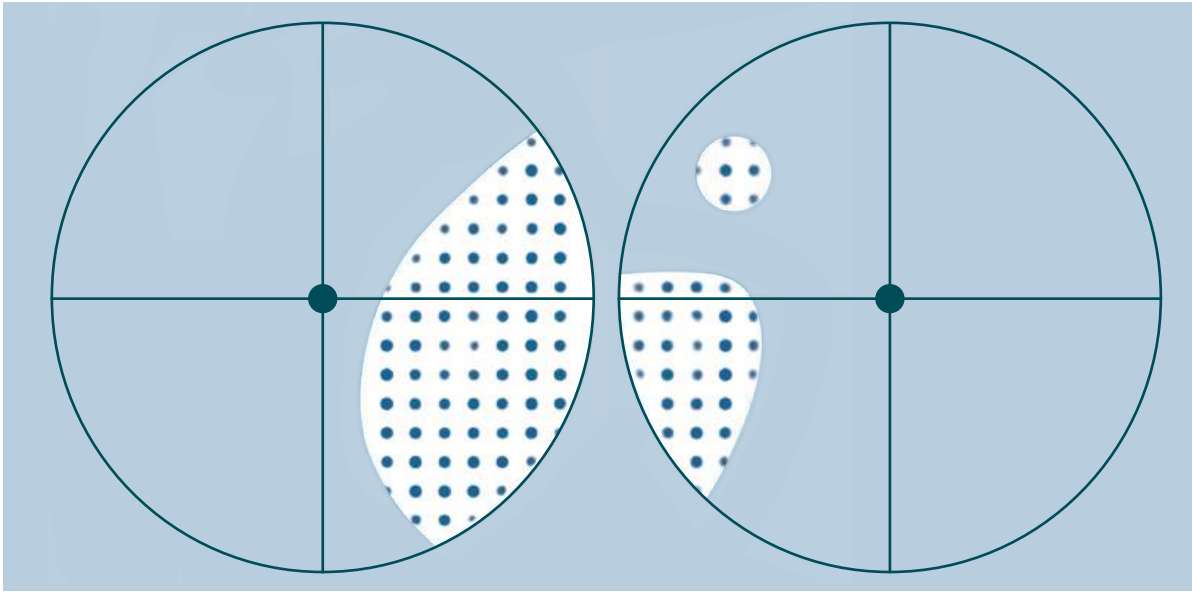


Figure 2. Diagram of the Patient's Visual Fields Based on the Amsler Grid. Author's own research.

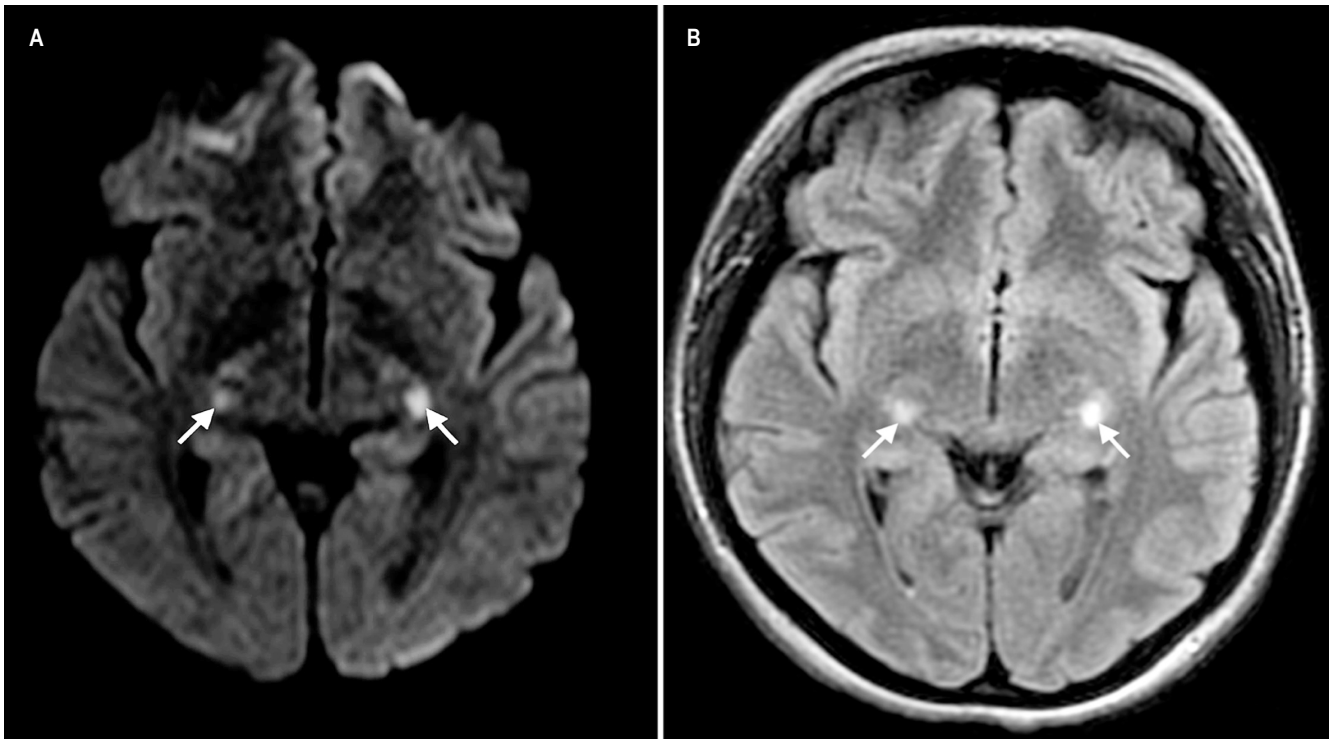


Figure 3. Brain MRI Findings. **A.** Diffusion-weighted imaging (DWI) showing signal enhancement in the lateral geniculate bodies, predominantly on the left side (arrows). **B.** FLAIR images with hyperintensities in the same distribution. Author's File.

for longer observation periods for such patients, particularly in outpatient settings.

Post-ERCP pancreatitis should be suspected in cases of post-procedural abdominal pain, with evaluation of serum amylase or lipase levels to distinguish it from other post-ERCP complications, such as perforation, cholangitis, or unresolved biliary lithiasis. Diagnostic imaging may also be warranted to rule out structural causes of pancreatitis[2]. In confirmed cases, the revised Atlanta classification is recommended to describe local and systemic complications, as it may better predict the severity and mortality of post-ERCP pancreatitis compared to consensus criteria[2].

While the pathophysiological mechanisms of acute pancreatitis are not fully understood, intra-acinar signaling events play a critical role. These include elevated cytosolic calcium levels, mitochondrial depolarization, and cytochrome C leakage, alongside nuclear factor-κB activation via IkB dissociation and proteasomal degradation, culminating in nuclear translocation of p65. This process promotes the synthesis of inflammatory mediators (cytokines and chemokines), leading to neutrophil infiltration in the pancreas[11]. Concurrently, lysosomal dysfunction, zymogen granule alterations, and increased oxidized glutathione due to reactive oxygen species (ROS), coupled with concurrent deleterious mechanisms and impaired autophagy, perpetuate acinar injury[11]. Additional mechanisms include loss of apical microvilli, inhibition of apical secretion, F-actin reorganization, basolateral vesicle formation, release of damage-associated molecular patterns (DAMPs) activating inflammasomes, and leakage of exocrine enzymes such as trypsin and pancreatic lipase. These enzymes cause unregulated hydrolysis of adipocyte triglycerides, resulting in fat necrosis and the production of unsaturated fatty acids that inhibit mitochondrial complexes I and V, thereby reducing adenosine triphosphate (ATP) production. This exacerbates local injury and systemic inflammatory responses[11]. These insights elucidate the multi-organ involvement of acute pancreatitis and the emergence of unusual manifestations, as seen in the present case.

In the presented clinical case, the diagnosis of post-ERCP pancreatitis was confirmed based on the onset of abdominal pain, marked elevation of serum amylase, and imaging findings showing bilateral lesions of the lateral geniculate bodies (LGBs), which coincided with acute visual field deficits.

The LGBs are thalamic nuclei located in the dorsolateral thalamus[12] and are critical in the visual pathway. They receive retinal projections and send signals to the primary

visual cortex[13]. Measuring 4–6 mm in diameter[14], the LGBs are structured into six cellular layers. Layers 2, 3, and 5 receive ipsilateral input (temporal retina), while layers 1, 4, and 6 receive contralateral input (nasal retina). Each layer is composed of distinct neuronal populations characterized by their size: magnocellular neurons are found in layers 1 and 2, while parvocellular neurons are located in layers 3 through 6[15]. The layers have a retinotopic organization, with macular vision represented centrally, the superior visual field in the lateral horn, and the inferior visual field in the medial horn of the LGB[16]. The LGBs are connected to retinal ganglion cells through their axons, which travel via the optic nerves and optic tracts[16].

Projections from the LGBs predominantly terminate in the primary visual cortex via optic radiations, with a smaller proportion reaching extra-striate cortical areas such as the thalamic reticular nuclei[16]. The LGBs are vascularized by dual arterial supply: the anterior choroidal artery, a proximal branch of the internal carotid artery, which supplies the medial and lateral horns, and the posterior choroidal artery, a branch of the posterior cerebral artery, which irrigates the hilum of the LGB[16]. These structures are also considered centers of signal modulation and integration[17], with roles that extend beyond simple signal relay. They regulate the flow and strength of visual information sent to the cortex, control extraretinal afferent input to the LGB[18], encode visual attention[19], and perform additional integrative functions[17].

Lesions of the LGBs are rare. Unilateral involvement typically causes congruent bilateral homonymous hemianopia[20] or partial homonymous anopia. In the context of multiple sclerosis, such lesions result from demyelinating processes. However, thromboembolic events have also been described, leading to variability in visual defects due to the anatomical diversity of LGB vascularization and anastomoses[21].

As presented in this case, bilateral lesions of the lateral geniculate bodies (LGBs) have been infrequently described in the literature (**Table 1**), and the underlying mechanisms for their involvement remain poorly understood. The first known report was published in 1933 by MacKenzie and colleagues, who described these lesions in the context of anterior choroidal arteritis secondary to syphilis[22]. Since then, various mechanisms have been proposed to explain such injuries. Among these are hypoperfusion and ischemia resulting from hemodynamic changes secondary to massive hemorrhage or anaphylactic shock, as the LGBs lie in a vascular border zone supplied by the anterior, middle, and posterior arterial territories[22]. Other proposed mechanisms include posterior circulation cerebral infarcts in patients with microangiopathic hemolytic anemia, traumatic brain injury, and methanol-induced cytotoxicity (pancreatitis and renal necrosis). Due to the histological similarity between the LGBs and the brainstem pons, it has been hypothesized that the tightly interwoven neuronal and oligodendroglial networks in the LGBs hinder cellular expansion during rapid sodium level increases, resulting in bilateral extrapontine geniculate myelinolysis due to overly rapid correction of hyponatremia[23]. Additional etiologies reported include aseptic lateral geniculitis, H1N1 influenza, severe preeclampsia, inflammatory bowel disease, and anaphylactic shock[24].

Interestingly, recent reports of such lesions frequently occur in the context of acute abdominal pain or pancreatitis, often as complications of ERCP. Six cases were identified in the reviewed literature[23,24,28–31]. Another notable case was reported by Pun and colleagues, where vision loss occurred as a complication of ERCP, though central nervous system lesions could not be documented because the patient declined neuroimaging (**Table 1**)[32].

It is noteworthy that, to date, since the first case reported in 1933, 92% of patients in the literature with bilateral LGB lesions have been female; only a single case has been reported in a male patient[29]. The reason for this relationship remains unknown, or it could represent an incidental finding. In our patient, the only preexisting condition was obesity, similar to the case reported by Murugesan and colleagues[31], which also identified acute pancreatitis as a possible etiology. However, unlike our case, their patient was diagnosed with associated thrombotic microangiopathy. In our case, there were no hemodynamic disturbances or electrolyte imbalances requiring correction, no history of traumatic brain injury, and infectious, autoimmune, and autoinflammatory causes were excluded. Based on these findings, we propose severe post-ERCP acute pancreatitis and multiorgan involvement secondary to the underlying systemic inflammatory response as a plausible etiology. The damage to the blood-brain barrier caused by the release of trypsin, elastase, lipase, and phospholipase A2 may allow the infiltration of leukocytes and proinflammatory cytokines (tumor necrosis factor-alpha [TNF-α], interleukin-1β, and interleukin-6), potentially explaining neuronal edema, demyelination, or hemorrhagic necrosis in these structures, as has been suggested in cases of pancreatic encephalopathy[33].

Conflict of Interest

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

Table 1. Reported Cases of Bilateral LGB Lesions

Year	Author	Age (years)	Sex	Proposed Etiology	Remarks
1933	Mackenzie and colleagues[34]	No data	Female	Syphilitic arteritis	Motor deficit resolved completely; pathology revealed syphilitic gummas
1972	Merren[25]	37	Female	Pancreatitis, microangiopathy, methanol toxicity (?)	Associated renal failure; LGB pathology showed coagulative necrosis
1995	Donahue and colleagues[4]	37	Female	Myelinolysis due to rapid correction of hyponatremia	Postoperative case in a patient with alcoholic cirrhosis and chronic hyponatremia
1996	Greenfield and colleagues[6]	28	Female	Lateral geniculitis due to infectious diarrhea	Diarrhea
2002	Imes and colleagues[26]	33	Female	Ischemia; shock from uterine hemorrhage	Respiratory distress was noted
2002	Moseman and colleagues[27]	21	Female	Ischemia, vasoconstriction	Patient with eclampsia
2004	Lefebvre and colleagues[22]	31	Female	Ischemia, anaphylactic shock	
2006	Baker and colleagues[28]	29	Female	Pancreatitis, transient hypotension	Post-ERCP case; high sedation dose required; history of migraine with typical aura; vision improved by day 13.
2007	Mudumbai[23]	18	Female	Pancreatitis, microangiopathy	Oral contraceptive use; acute renal failure (hemodialysis); visual acuity recovered at 32 months.
2015	Viloria and colleagues[29]	40	Male	Pancreatitis, osmotic demyelination due to hydration	Post-cholecystectomy; visual acuity recovered in 6 weeks.
2015	Bartel[24]	22	Female	Pancreatitis, ischemia, transient hypotension	Post-normal ERCP; received rectal indomethacin.
2016	Mathew et al.[30]	42	Female	Ischemia, bilateral LGB arteritis (?)	Unconfirmed systemic bacterial infection; history of psoriasis.
2023	Murugesan et al.[31]	22	Female	Pancreatitis, microangiopathy	Obesity; recent initiation of paleo diet.

Author's own research.

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Case report

Atypical Intestinal Lesions in a Patient with Neurofibromatosis Type 1: A Case Report

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Abstract

Neurofibromatosis type 1 (NF1) is a neurocutaneous disorder that can manifest as multiple tumors or plexiform lesions in the gastrointestinal tract and extra-intestinal sites. Gastrointestinal involvement occurs in 10%–25% of patients, with neurofibromas being the most common lesions, typically located in the small intestine. When multiple tumors are found in the small intestine, they are often gastrointestinal stromal tumors (GISTs). This case report presents a 55-year-old woman with a history of NF1, characterized by neurofibromas and café-au-lait spots across her body. She was evaluated as an outpatient in the endoscopy unit at Unión de Cirujanos S. A. S. in Manizales, Colombia, within the Gastroenterology Surgical Clinic Service at Universidad de Caldas. The patient underwent ileocolonoscopy after a positive fecal occult blood test. She denied abdominal pain, hematochezia, rectal bleeding, or melena. Ileocolonoscopy revealed nodular lesions ranging from 3 to 5 mm in the distal ileum. Endoscopic resection was performed on one lesion, which was sent for histopathological examination.

Keywords

Neurofibromatosis, neurofibroma, gastrointestinal stromal tumor, atypical intestinal lesions.

INTRODUCTION

Neurofibromatosis type 1 (NF1), or Von Recklinghausen disease, is a neurocutaneous disorder that may manifest as multiple tumors or plexiform lesions within the gastrointestinal tract as well as in extraintestinal locations. It is an autosomal dominant condition with a prevalence of 1 in 3,000 individuals. Approximately half of all cases have a family history, while the other half arise spontaneously. Gastrointestinal involvement occurs in 10%–25% of patients. The upper intestinal tract is the most commonly affected region, with neurofibromas representing the predominant lesion type, usually located in the small intestine. When multiple tumors appear in the small intestine, particularly in the jejunum, they are typically gastrointestinal stromal tumors (GISTs) associated with NF1. Additionally, other gastrointestinal lesions may arise in patients with NF1 and should be considered as differential diagnoses. Abdominal lesions in NF1 are often asymptomatic and, consequently, underrecognized in clinical practice[1,2].

CLINICAL CASE

We present the case of a 55-year-old woman with a medical history of NF1, characterized by neurofibromas and café-au-lait macules distributed across her body (**Figures 1** and **2**).

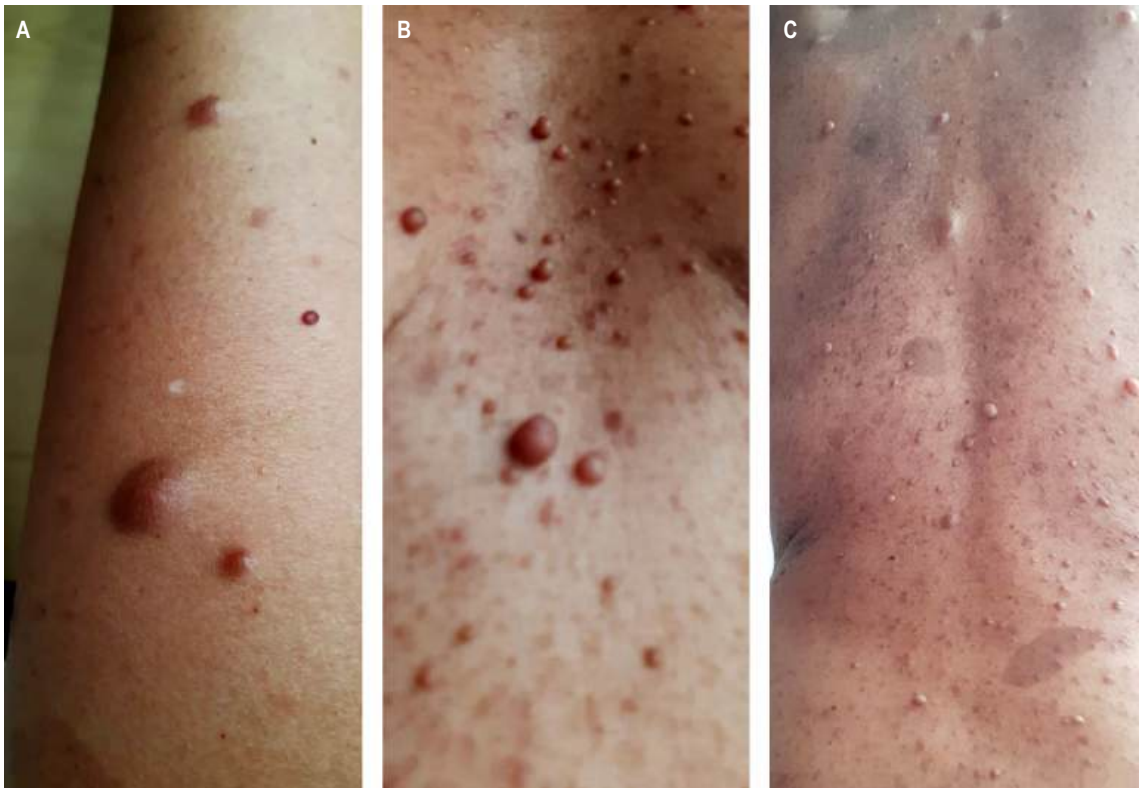


Figure 1. Café-au-lait Macules and Neurofibromas on the Skin of a Patient with Neurofibromatosis Type 1. **A.** Upper limb. **B.** Abdomen. **C.** Dorsal region. Images courtesy of Dr. Fabián Eduardo Puentes-Manosalva, Unión de Cirujanos S. A. S., Clinical-Surgical Gastroenterology Service, Universidad de Caldas, Manizales, Colombia.

The diagnosis was clinically confirmed during a genetics consultation. The patient was managed on an outpatient basis at the endoscopy unit of Unión de Cirujanos S. A. S. in Manizales, Colombia, part of the Clinical-Surgical Gastroenterology Service, Universidad de Caldas. She underwent ileocolonoscopy for the evaluation of a positive fecal occult blood test. The patient denied any abdominal pain, hematochezia, rectal bleeding, or melena.

The ileocolonoscopy revealed nodular lesions measuring 3 to 5 mm in the distal ileum (**Figures 3** and **4**). Endoscopic resection of one of the lesions was performed (**Figure 4**), and the sample was sent for histopathological analysis. The remaining segments examined, including the cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum, showed no evidence of inflammatory or tumoral lesions. Haustral markings and colonic motility were preserved. Internal hemorrhoids were observed in the anal canal, without dilation or other abnormalities.

Immunohistochemical analysis of the lesion from the ileum revealed cellular proliferation, with positivity for CD68 and focal positivity for vimentin, along with negativity for CKAE1/AE3, CD34, and cytomegalovirus. The immunophenotypic profile corresponded to reactive histiocytic cellular proliferation. Additional testing with S100 markers showed occasional positivity in histiocytes, while SOX-10 was negative. The final diagnosis indicated acute inflammation and reactive fibroblastic and histiocytic proliferation, with no evidence of neoplasia.

DISCUSSION

Neurofibromatosis is classified into three types: type 1 (NF1), also known as Von Recklinghausen disease, accounting for 90%–95% of cases; type 2 (NF2), comprising less than 10%; and type 3 (NF3), or schwannomatosis[3]. NF1 is a genetic autosomal dominant disorder with a prevalence of 1 in 3,000 individuals. It arises from a mutation in the tumor suppressor gene NF1, located on chromosome 17q11.2. This mutation leads to a reduction in the intracellular protein neurofibromin, resulting in uncontrolled activation of the RAS gene and cell proliferation pathways, along with inhibition of apoptotic pathways[3–5].

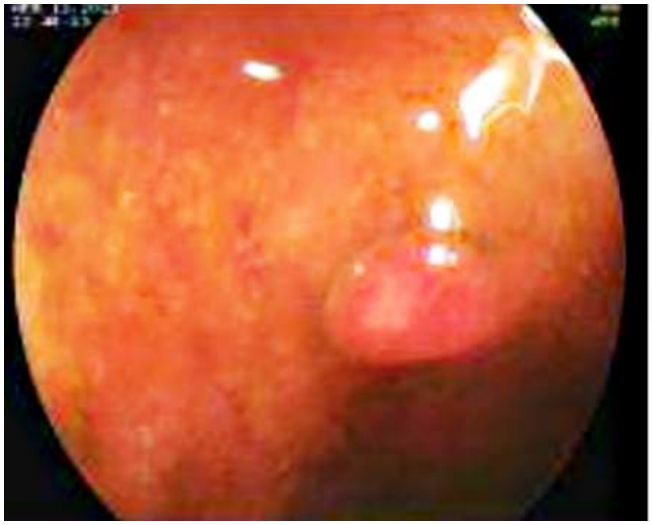
The diagnosis of NF1 is primarily clinical, with neurocutaneous manifestations being the most frequent. Diagnosis



Figure 2. Café-au-lait Macules on the Gluteal Region of a Patient with Neurofibromatosis Type 1. Image courtesy of Dr. Fabián Eduardo Puentes-Manosalva, Unión de Cirujanos S. A. S., Clinical-Surgical Gastroenterology Service, Universidad de Caldas, Manizales, Colombia.



Figure 3. Atypical Nodular Lesion in the Distal Ileum of a Patient with Neurofibromatosis Type 1. Image courtesy of Dr. Fabián Eduardo Puentes-Manosalva, Unión de Cirujanos S. A. S., Clinical-Surgical Gastroenterology Service, Universidad de Caldas, Manizales, Colombia.



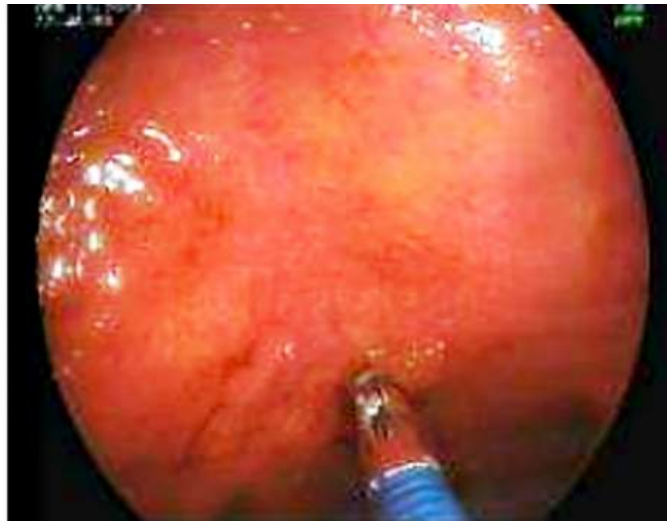


Figure 4. Atypical Nodular Lesion in the Distal Ileum of a Patient with Neurofibromatosis Type 1 and Its Endoscopic Resection. Images courtesy of Dr. Fabián Eduardo Puentes-Manosalva, Unión de Cirujanos S. A. S., Clinical-Surgical Gastroenterology Service, Universidad de Caldas, Manizales, Colombia.

requires the presence of two or more of the following criteria (**Table 1**): six or more café-au-lait macules larger than 5 mm in children or larger than 15 mm in adults, two or more cutaneous or subcutaneous neurofibromas or one plexiform neurofibroma, axillary or inguinal freckling (Crowe's sign), optic nerve glioma, two or more iris hamartomas (Lisch nodules), atypical bone lesions (sphenoid dysplasia, cortical thinning of long bones with or without pseudoarthrosis), and a first-degree family history of NF1[3,4].

The coexistence of multiple tumors of different types is common in NF1 due to the variable penetrance of the autosomal gene. Consequently, patients may present with one or more tumors synchronously or metachronously[2,3]. Gastrointestinal tract lesions are not uncommon in NF1,

occurring in 10%–25% of all cases, though only 5% are symptomatic[2,3]. These manifestations typically appear between the ages of 30 and 40 and can occur at any location within the gastrointestinal tract, although the small intestine is the most frequent site (70%), particularly the jejunum[2,3]. The most common locations of gastrointestinal neurofibromas are the jejunum, followed by the stomach, ileum, duodenum, and colon[4]. These lesions arise in the Meissner's plexus of the submucosa, the Auerbach's plexus of the muscularis propria, or even the serosa. They are generally asymptomatic but, depending on their location and the extent of mucosal involvement, may present clinically with abdominal pain, diarrhea, upper or lower gastrointestinal bleeding, palpable mass, microcytic anemia, intestinal obstruction (due to intussusception or secondary volvulus), perforation, or even obstructive jaundice[2–5].

Table 1. Diagnostic Criteria for Neurofibromatosis Type 1*

Six or more café-au-lait macules larger than 5 mm in children or larger than 15 mm in adults
Two or more cutaneous or subcutaneous neurofibromas or one plexiform neurofibroma
Axillary or inguinal freckling (Crowe's sign)
Optic nerve glioma
Two or more iris hamartomas (Lisch nodules)
Atypical bone lesions (sphenoid dysplasia, cortical thinning of long bones with or without pseudoarthrosis)
First-degree family history of neurofibromatosis type 1

*At least two criteria are required. Adapted from: Gamarra ER, and colleagues. Horiz Med (Lima). 2020;20(4):e1412[3]; SSelfa-Muñoz A, and colleagues. Rev Esp Enferm Dig (Madrid). 2012;104(2):99-100[4].

Gastrointestinal neoplasms are more frequent in patients with NF1 compared to the general population and occur in three main forms: hyperplasia of the submucosal and myenteric nerve plexuses and mucosal ganglioneuromatosis, leading to intestinal motility disorders; GIST with varying degrees of neural or smooth muscle differentiation; and neuroendocrine tumor producing somatostatin (ampullary somatostatinoma), characteristic of the periampullary region of the duodenum, containing psammoma bodies and potentially associated with pheochromocytoma[2].

Gastrointestinal lesions associated with NF1 most commonly include benign neoplasms, such as neurofibromas (52%), leiomyomas (17%), ganglioneurofibromas (5.8%), neuroendocrine tumors, and GISTs (6.5%). In NF1, GISTs are slightly more common in women and tend to appear at younger ages, although they can also manifest later in life. They are usually multiple and predominantly located in the small intestine, unlike in the general population without NF1, where GISTs are more frequently found in the stomach[5,6]. Malignant neoplasms may also occur, with 20% being adenocarcinomas. Among benign tumors, such as neurofibromas, malignant transformation occurs in 5% to 15% of cases[3], particularly in patients over 40 years of age. As a result, surgery is the treatment of choice for symptomatic tumors, while clinical monitoring may be considered for asymptomatic patients[4]. Although rare, gastrointestinal adenocarcinoma has been reported in the stomach, esophagus, duodenum, biliary tract, pancreas, and colon. However, the genetic association between adenocarcinoma and NF1 remains unclear[5]. Gastrointestinal lesions in NF1 can be visualized through endoscopic studies such as esophagogastroduodenoscopy, colonoscopy, enteroscopy, or video capsule endoscopy, as well as imaging studies like computed tomography (CT) or nuclear magnetic resonance imaging (NMRI)[5–7]. The risk of recurrence and cancer-specific mortality appears to be similar between NF1 and non-NF1 patients following surgical resection of GISTs[8].

The incidence of GIST in NF1 patients is approximately 6%–7%, but the concurrent presence of multiple GISTs is uncommon[9,10]. GISTs are the most common non-neurological tumors in NF1 patients, with an incidence 45 times higher than in the general population. When GISTs are associated with NF1, mutations in the KIT and PDGFRA genes are frequently absent, rendering imatinib ineffective. Consequently, surgical resection is the first-line treatment. The prognosis for NF1-associated GISTs is better than that for sporadic GISTs. Laparoscopic surgery is as effective as open surgery; however, it offers advantages such as reduced procedure-related pain, faster recovery, and shorter hospital stays. The recurrence rate in NF1 patients is similar to that of patients with sporadic GISTs[10]. While neurofibromas can occur in the gastrointestinal tract, they may also be found extraintestinally. Isolated neurofibromas have been documented in patients without NF1 in locations such as the colon and mesentery[11,12].

Currently, no specific treatment exists for neurofibromatosis. Management involves clinical monitoring or surgical intervention to resect neurofibromatous lesions, especially when there is functional impairment or risk of malignancy[13]. Gastrointestinal neurofibromas are generally resistant to chemotherapy and radiotherapy. As a result, pharmacological options, such as thalidomide, pirfenidone, imatinib, and tipifarnib, are being investigated for lesions that cannot be resected due to their proximity to vital structures[14].

Gastrointestinal tumors that are difficult to distinguish from neurofibromas macroscopically and radiologically include lipomas, which account for 5% of all gastrointes-

tinal tumors and 10% of benign gastrointestinal tumors. These lesions are typically located just beneath the mucosa and are usually asymptomatic. However, they can cause obstruction, intussusception, or bleeding. Lipomas may coexist with gastrointestinal neurofibromas, making them an important differential diagnosis to consider[15,16]. In the case reviewed in this article, atypical intestinal lesions were observed in the distal ileum of a 55-year-old female patient with NF1.

CONCLUSION

NF1, or Von Recklinghausen disease, is a neurocutaneous disorder that may present with multiple tumors or plexiform lesions in both the gastrointestinal and extraintestinal regions. Gastrointestinal lesions are not uncommon in NF1, occurring in 10%–25% of cases, with only 5% being symptomatic. These manifestations typically appear between the ages of 30 and 40 and can be found throughout the gastrointestinal tract, although the small intestine is the most commonly affected site. Benign tumors such as neurofibromas may undergo malignant transformation in 5%–15% of cases, particularly in patients over 40 years old. GIST should be suspected in NF1 patients presenting with gastrointestinal symptoms.

Multiple GISTs located outside the stomach should raise suspicion for NF1, and gastrointestinal lipomas should be considered as an important differential diagnosis. A thorough medical history and careful physical examination are essential. Endoscopic studies, such as esophagogastroduodenoscopy, colonoscopy, enteroscopy, or video capsule endoscopy, as well as imaging studies like CT and MRI, are highly valuable for evaluating NF1 depending on the type and location of gastrointestinal lesions. Clinical monitoring or surgical intervention is recommended for neurofibromatous lesions, particularly when functional impairment or risk of malignancy exists. Endoscopic resection or laparoscopy can be useful for both diagnosis and treatment.

The case presented in this article highlights atypical intestinal lesions in the distal ileum of a patient with NF1. Detailed histopathological and immunohistochemical analysis demonstrated acute inflammation and reactive fibroblastic and histiocytic proliferation, with no evidence of neoplasia. This finding is significant as it introduces a new differential diagnosis for gastrointestinal lesions in patients with NF1.

Conflict of Interest

The authors declare no conflicts of interest for this article.

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Case report

Wilson's Disease with Severe Neurological Presentation: A Case Report

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Abstract

Introduction: Wilson's disease (WD) is an autosomal recessive disorder that can affect individuals of any age. Neurological involvement is reported in 30%–40% of patients, with dysarthria, ataxia, and dystonia being the primary manifestations. The presence of Kayser-Fleischer (KF) rings is observed in 77.2%–85.2% of cases. Chelation therapy demonstrates a paradoxical response in up to 50% of patients. We report a case of severe neurological presentation without KF rings, exhibiting a paradoxical response to chelation therapy. **Case Presentation:** A 23-year-old man with no prior medical history presented with a six-month history of symptoms consistent with vasovagal syncope episodes, followed by ataxia, muscle weakness, dysphagia, sialorrhea, and dysarthria. His condition progressively worsened due to sepsis of pulmonary origin secondary to an aspiration event. Investigations revealed low ceruloplasmin levels, elevated urinary copper, imaging findings consistent with thalamic and lenticular involvement, liver biopsy showing autoimmune hepatitis-like changes and features resembling non-alcoholic fatty liver disease (NAFLD), absence of KF rings, and a paradoxical response to chelation therapy. The disease course was marked by severe dystonia progression and a fatal outcome. **Conclusions:** WD is a condition with significant morbidity and a variable clinical spectrum. Isolated neurological involvement without KF rings is uncommon, and outcomes depend on early initiation of copper chelation therapy. However, paradoxical worsening of symptoms due to treatment, as observed in this case, poses an additional challenge.

Keywords

Wilson's disease, dystonia, penicillamine, copper.

INTRODUCTION

Wilson's disease (WD) is a rare condition with increasing prevalence[1,2]. It lacks a genotype-phenotype correlation and exhibits a wide spectrum of manifestations, affecting individuals aged 3 to 55 years. Neurological involvement is observed in 30% to 40% of cases and is associated with the presence of Kayser-Fleischer (KF) rings in 77.8% to 85.2% of cases[3], with similar findings reported in Colombian series (approximately 72.7%)[4]. Imaging findings in patients with neurological involvement are often non-specific, with the panda sign being the only late-stage pathognomonic finding[5]. Treatment primarily involves chelators, though the efficacy of combined therapy (chelators and zinc) remains debated due to high risks of side effects and paradoxical responses[3]. For severe neurological involvement, liver transplantation is still under discussion[6]. This report presents a clinical case of WD with less than one year of neurological manifestations, no chronic imaging findings, progression to severe dystonia, absence of KF rings, and a fatal outcome.

CASE DESCRIPTION

The patient was a 23-year-old male with no prior medical history, normal neurodevelopment, good academic per-

formance, and psychosocial functioning typical for his age. He reported no significant family medical history. Six months prior to his admission, he experienced a sudden two-minute loss of consciousness, with complete recovery, consistent with syncope. This event recurred four times in the following week, prompting multiple emergency department visits. Initial evaluations, including a positive tilt table test, supported a diagnosis of vasovagal syncope. Complementary studies, including echocardiography, carotid Doppler, non-contrast cranial CT, and 24-hour Holter monitoring, were normal.

Two months before admission, the patient developed progressive lower limb weakness, gait disturbances with an increased base of support, and incoordination of gross and fine motor activities. He also exhibited bradylalia, which progressed to mild dysarthria, dysphagia for solids and liquids, and sialorrhea. Subsequently, he experienced a tonic posturing episode involving flexion of the upper limbs, extension of the lower limbs, and retrocollis lasting one minute, with preserved consciousness and no sphincter relaxation or tongue biting. A non-contrast brain MRI revealed thalamic and lenticular nucleus lesions, hypointense on T1 and hyperintense on T2 and fluid-attenuated inversion recovery (FLAIR) sequences, with no additional abnormalities (**Figure 1**). Two electroencephalograms, one 6-hour and another 12-hour, showed no ictal activity. During clinical evolution, the patient displayed impaired attention (dysexecutive symptoms), recurrent overvalued anxious thoughts, and a labile and anxious mood, with intact memory, preserved sleep, and appetite.

The patient exhibited progressive deterioration characterized by episodes of tremors in the extremities, abnormal limb and neck posture, which became increasingly frequent and prolonged, ultimately impairing ambulation and resulting in immobility. Laboratory tests revealed mild normocytic normochromic anemia, elevated creatine phosphokinase (CPK), impaired renal function consistent with KDIGO stage II without chronic findings, and hepatic profile abnormalities with elevated transaminases, predominantly aspartate aminotransferase (AST) (**Table 1**). A repeat cranial CT scan was normal, as was a lumbar puncture with opening pressure and cerebrospinal fluid analysis. A bronchial aspiration episode led to sepsis of pulmonary origin, necessitating orotracheal intubation and prolonged invasive mechanical ventilation. Antibiotic therapy included piperacillin-tazobactam followed by meropenem.

Extended studies for Wilson's Disease (WD) revealed low ceruloplasmin, serum copper within normal limits, elevated urinary copper (766 µg/24 hours), and a liver biopsy performed due to persistent abnormal liver function tests. The biopsy showed moderate interface hepatitis, hepatocellular ballooning, and Mallory bodies (**Figure 2**). An ophthalmological evaluation found no evidence of Kayser-Fleischer (KF) rings, and imaging studies revealed no chan-

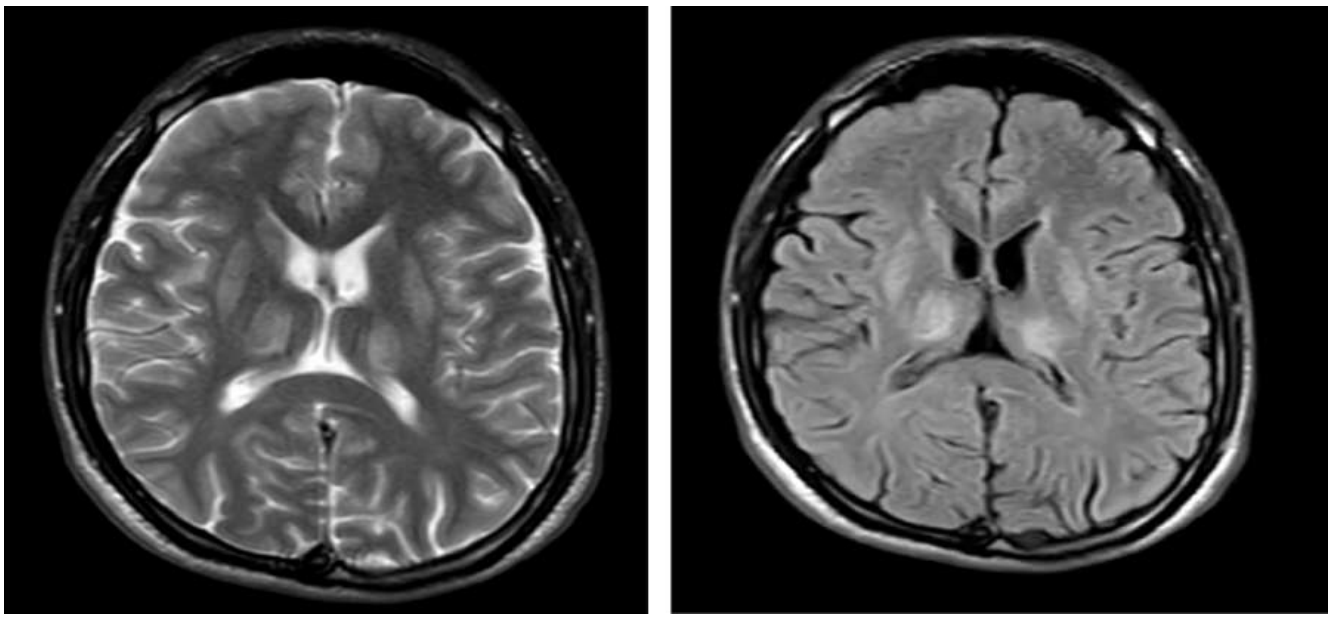


Figure 1. Brain MRI using T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences showing increased signal intensity in the basal ganglia, with greater involvement of the lentiform nucleus and thalamus bilaterally, without evidence of diffusion restriction. Source: Patient's medical records.

ges consistent with chronic liver disease. A Leipzig score of six points was calculated. Treatment included penicillamine at 15 mg/kg/day combined with zinc sulfate at 150 mg/day. Neurological deterioration occurred, marked by severe generalized dystonia predominantly affecting the oromandibular and cervical regions with pronounced retrocollis within three days of initiating chelation therapy (**Figure 3**). Intensive care unit (ICU) management involved cycles of neuromuscular relaxants combined with sedation using benzodiazepines (midazolam), baclofen, methadone, and gabapentin. Despite these interventions, clinical evolution was poor, leading to discussions with the family regarding the limitation of therapeutic efforts. The patient ultimately had a fatal outcome after four weeks of hospitalization.

This case documents WD presenting with severe neurological manifestations, secondary rhabdomyolysis, and the unique characteristic of absent ocular involvement, as no KF rings were detected. Additionally, the patient exhibited a paradoxical response to chelation therapy. This case adds to the literature with detailed observations and a review.

DISCUSSION

WD is an autosomal recessive disorder caused by mutations in the ATP7B gene on chromosome 13, with more than 700 mutations described. There is no established genotype-phenotype correlation, and epigenetic alterations play a significant role. The defect leads to impaired copper excretion, resulting in multi-organ damage due to tissue deposition[3].

Described in 1912 by Dr. Samuel Alexander Kinnier Wilson, its prevalence has increased to 30–142 cases per million[1,2]. Clinical manifestations are diverse, typically affecting adolescents or young adults, with an age range of 3 to 55 years. They include neurological involvement (30%–40%), hepatic involvement (30%–50%), psychiatric symptoms (30%–40%), and corneal KF rings[3,7].

This case presents unique features warranting analysis in the context of current knowledge. Notably, the absence of KF rings in a patient with neurological manifestations and cerebral imaging findings, despite disease onset less than a year prior, is unusual. In the literature, neurological symptoms vary widely; they are often mild or intermittent for years but can progress rapidly to severe deterioration within months. Damage predominantly affects the basal ganglia, with early symptoms including dysgraphia and gait and balance disturbances[1]. Manifestations range from involuntary movements to severe dystonia, with dysarthria being the most common symptom (46%–97%), followed by ataxia (28%–75%), dystonia (38%–69%), parkinsonism (12%–58%), and dysphagia (50%), among others[3]. There is no genotype-phenotype correlation for neurological manifestations in WD[3,8], and MRI findings do not consistently align with clinical presentation or treatment response[3].

Some significant findings indicate that up to 83.3% of patients with neurological manifestations of Wilson's Disease (WD) have documented hepatic involvement, with hepatic copper content measured by spectroscopy exceeding 250 µg/g of liver dry weight[3]. Although local

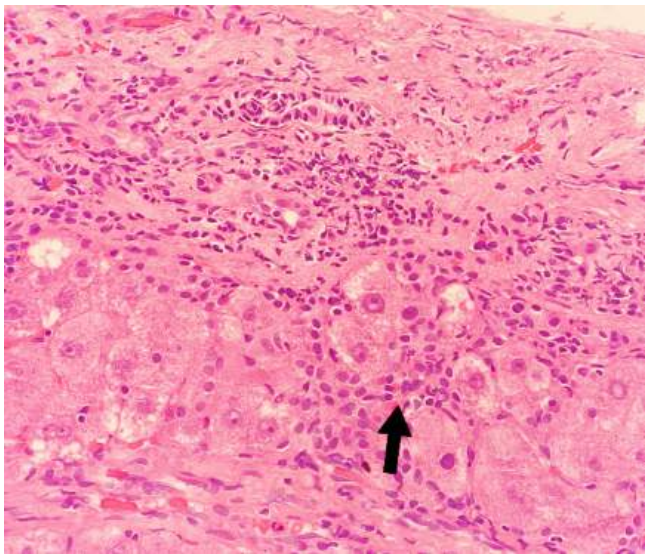


Figure 2. Liver Biopsy stained with hematoxylin and eosin, showing lymphoplasmacytic infiltrate with evidence of limiting plate destruction. Source: Patient's medical records.



Figure 3. Severe Dystonia with Pronounced Retrocollis. Source: Patient's medical records.

Table 1. Laboratory Results

Laboratory Test	Reference Range	Resultados
White blood cells (×10³/µL)	5.1-9.7	10.19
Differential Count (%)		
Neutrophils	39.6-64.6	85.9
Lymphocytes	20.7-39.6	9
Monocytes	1-12.6	3.5
Eosinophils	1-3.9	0.4
Basophils	0.01-1	0.1
Absolute Counts ×10³/µL)		
Neutrophils	1.4-6.5	8.76
Lymphocytes	1.2-3.4	0.91
Monocytes	0-0.7	0.36
Eosinophils	0-0.7	0.04
Basophils	0-0.2	0.01
Red blood cell count (×10⁶/µL)	4.5-5.5	3.77
Hemoglobin (g/dL)	14-18	11.5
Hematocrit (%)	42-56	34.2
Mean corpuscular volume (fL)	80-100	90.7
Mean corpuscular hemoglobin (pg)	27-34	30.5
Mean corpuscular hemoglobin concentration (g/dL)	31.5-35	33.6
Red cell distribution width (%)	November 15	12.9
Platelet count (×10³/µL)	150-450	145
Platelet volume (fL)	6.4-13	10
C-reactive protein (mg/L)	0-3	84
Creatinine (mg/dL)	0.67-1.17	0.54
Blood urea nitrogen (mg/dL)	July 18	15.22
Sodium (mmol/L)	135-145	143.42
Potassium (mmol/L)	3.5-5	3.29
Chloride (mmol/L)	98-107	108.84
Calcium (mg/dL)	8.5-10.1	7.75
Magnesium (mg/dL)	1.8-2-4	2.1

Laboratory Test	Reference Range	Result
Total creatine kinase (U/L)	39-308	5836
Vitamin B12 (pg/mL)	211-911	808
Total bilirubin (mg/dL)	0.2-1	0.72
Direct bilirubin (mg/dL)	0-0.2	0.23
Indirect bilirubin (mg/dL)	0-1.1	0.49
Alkaline phosphatase (UL)	58-237	107.4
Aspartate aminotransferase (U/L)	15-37	131.87
Alanine aminotransferase (U/L)	16-63	146.23
γ-glutamyl-transferase (U/L)	0-55	181.33
Prothrombin time (seconds)	11.8-16.1	13.3
International normalized ratio (seconds)	0.5-1.5	1.14
Partial thromboplastin time (seconds)	24.3-35	33.8
Serum albumin (g/dL)	3.8-4.4	2.5
Lactate dehydrogenase (U/L)	85-227	391.2
Storage Disease Screening		
- Serum copper (µg/dL)	70-140	<25
- 24-hour urine copper (µg/24h)	<60	766.53
- Ceruloplasmin (mg/dL)	20-60	5.0
- Total serum iron (µg/dL)	65-175	31.7
- Ferritin (ng/mL)	20-99	540.79
- Transferrin saturation (%)	20-50	20.98
- Iron-binding capacity (µg/dL)	250-450	151
Lipid Profile		
- Total cholesterol (mg/dL)	0-200	132.13
- High-density lipoprotein (mg/dL)	40-60	25.01
- Triglycerides (mg/dL)	<150	120.9
- Thyroid-stimulating hormone (µIU/mL)	0.55-4.78	2.98

Source: Patient's medical records.

data are limited, neurological involvement has been observed in 40% of WD patients, with parkinsonism (14%) and dystonia (11%) being the most common manifestations. Among patients with WD and documented neurological involvement, none had detectable copper deposits in liver biopsies, 72.7% exhibited Kayser-Fleischer (KF) rings, 81% had low ceruloplasmin levels, and elevated urinary copper was observed in only 54.5% of cases[4].

What makes our patient's case unusual is the absence of KF rings or sunflower cataracts. Neurological manifestations of WD without ocular involvement are rare in the literature. It has been reported that KF rings are present in 77.8%–85.2% of patients with neurological or psychiatric involvement[7,9], in 36%–62% of patients with hepatic manifestations, and in 10%–30% of asymptomatic patients[9]. Local data show that only 40% of all newly diagnosed WD cases and 72.7% of cases with neurological involvement had KF rings identified by slit-lamp exam[4]. In this case, no ocular involvement was documented, but hepatic involvement was present. This initially necessitated the exclusion of other differential diagnoses due to the atypical presentation. Optical coherence tomography of the anterior segment could have been a useful alternative to rule out ocular involvement, given the slit-lamp's sensitivity of approximately 50%[9].

The diagnosis of WD also includes evidence of hepatopathy, and abdominal ultrasonography can aid in identifying the disease. Depending on the stage of WD, abdominal ultrasound may reveal hepatomegaly or signs of chronic liver disease[10]. Liver biopsy remains essential for quantifying hepatic copper, assessing the degree of inflammation and fibrosis, ruling out other diseases, and potentially evaluating treatment response[11]. Histological findings in WD include autoimmune-like hepatitis, fibrosis, fatty infiltration, cirrhosis, hepatocellular ballooning, and Mallory-Denk bodies, among others. However, these findings are non-specific. In analyzing hepatic copper, it is important to consider its heterogeneous deposition in the liver, varying by lobe in early stages and by nodule in cirrhosis. This variability can lead to negative staining results, making such tests less sensitive, and a negative result does not exclude the diagnosis. A more reliable test is the measurement of hepatic copper concentration, where levels <50 μg/g of liver dry weight are normal, and levels >250 μg/g indicate abnormal copper deposition[3,12]. In the presented case, there were no imaging findings indicative of cirrhosis, but moderate chronic hepatitis and autoimmune-like hepatitis were observed. These findings bear similarities to changes seen in nonalcoholic fatty liver disease (NAFLD).

In magnetic resonance imaging (MRI), early abnormalities are often non-specific but can be valuable for diagnosing unexplained neurological or psychiatric symptoms. Findings may include alterations in the basal ganglia, thalami, pons, and white matter. Data show evidence of cerebral atrophy, bilateral symmetrical lesions in the caudate and putamen (characterized by concentric laminar increases in T2 signal intensity), and T2 signal hyperintensities in the substantia nigra (pars compacta), periaqueductal gray matter, pontine tegmentum, and thalamus. Additionally, T2 signal hyperintensities may be observed in the periaqueductal gray matter, substantia nigra, and around the red nuclei, which maintain their normal hypointensity. A late-stage hallmark, the panda sign, consists of T2 hyperintensity in the midbrain and has been considered pathognomonic. However, similar changes may be seen in chronic liver disease, which must be taken into account. It is clear that MRI is not useful for determining prognosis or monitoring neurological symptoms[3,5]. In the present case, the disease onset was less than 12 months, and hyperintensity in the basal ganglia was documented without evidence of the panda sign, suggesting a rapidly progressive course driven by neurological involvement.

Adverse effects at the initiation of therapy remain a major concern, particularly due to the risk of neurological deterioration after starting any of the three main medications. This occurs most frequently with penicillamine (13.8%), followed by trientine (8%) and zinc (4.3%)[13]. Neurological deterioration has been reported in up to 50% of patients initiating penicillamine, and as many as 30% of patients may discontinue therapy due to adverse events, making this drug one that requires special caution. Although most guidelines recommend starting treatment with penicillamine, recent data from a clinical trial (the Chelate trial) with 48 weeks of follow-up demonstrated that trientine tetrahydrochloride is not inferior to penicillamine and is comparable in terms of side effects[14].

There is currently no clear evidence on whether combination therapy with chelators and zinc offers advantages over monotherapy, nor are there comparative data on its safety profile. The decision to initiate combination therapy is primarily based on clinical judgment and the mechanism of action rather than efficacy or safety[3]. Another therapy under evaluation is bis-choline tetrathiomolybdate (ALXN840), which acts by forming a tripartite complex with copper and albumin, followed by biliary excretion. Preclinical and phase III studies have shown that in ATPB7(-) mice, this therapy is not inferior to D-penicillamine or trientine in reducing hepatic copper levels. However, high doses have been associated with potential mitochondrial damage. Results from ongoing studies are still awaited[15]. Additionally, methanobactin therapy in animal studies has demonstrated strong cop-

per-binding affinity and promising results in preventing copper-induced mitochondrial damage and improving histological outcomes. In terms of precision medicine, adeno-associated virus vectors encoding human ATP7B complementary DNA (cDNA) in hepatocytes of a WD mouse model have demonstrated effective ATP7B expression and reduction in hepatic copper levels. Shorter vectors have also shown long-term normalization of copper levels in mice. Furthermore, liver cell transplantation therapies have reduced fulminant hepatitis, decreased inflammation, and improved short-term survival[8].

In this case, combination therapy with zinc and penicillamine was initiated, primarily based on clinical judgment regarding the disease's progression and resource availability. However, neurological deterioration was subsequently documented, raising concerns about the optimal therapy for neurological forms of WD.

In the multidisciplinary management approach, the possibility of liver transplantation was considered based on very limited data, primarily from small cohorts in France and Italy. However, clinical outcomes remain unclear, and severe neurological involvement is still not an established indication for liver transplantation[6].

CONCLUSION

WD is a disease with significant morbidity and a wide spectrum of clinical manifestations. Neurological presentations without KF rings are uncommon. The prognosis of neurological manifestations depends heavily on the early initiation of copper-chelating therapy, despite the risk of neurological deterioration associated with treatment initiation. Liver transplantation for severe neurological manifestations remains a controversial topic.

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 Interest

The authors declared no conflicts of interest.

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Author Contributions

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

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Case report

Emphysematous Gastritis: Is Surgical Management Mandatory? A Case Report

Sandra López-Tamayo,[1*] Maryan Ruiz-Gallego.[2]

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Abstract

Introduction: The radiological finding of gas dissecting the gastric wall is rare and is associated with two conditions: emphysematous gastritis, which involves infection by gas-producing bacteria and has a severe course with a mortality rate exceeding 50%, and gastric emphysema, which is predominantly caused by mechanical factors and has a more benign prognosis. In cases of gastric pneumatosis, early diagnosis and timely treatment are crucial to preventing complications. **Case Presentation:** A 62-year-old male patient presented to the emergency department with abdominal pain, distension, and diarrhea. He was hemodynamically stable and showed no signs of peritoneal irritation. Computed tomography revealed gastric pneumatosis associated with pneumoperitoneum. The patient was managed conservatively with antibiotics and demonstrated a successful recovery, with complete resolution of symptoms and radiological findings. **Discussion:** Various etiologies can cause gastric pneumatosis; however, when associated with pneumoperitoneum, the diagnostic suspicion leans toward emphysematous gastritis, a condition that typically follows a severe course and often necessitates surgical management. Nonetheless, cases managed conservatively with positive outcomes have been reported. **Conclusion:** Early recognition of patients with emphysematous gastritis is critical to reducing complications such as gastric perforation or death. Historically, these patients warranted surgical intervention; however, recent case reports suggest that conservative management can be effective. There is no consensus on the standard approach for patients presenting with gastric pneumatosis.

Keywords

Gastritis, emphysema, gastroenteritis.

INTRODUCTION

The management of patients presenting to the emergency department with abdominal pain requires a thorough clinical evaluation to rule out surgical causes, as a wide range of medical emergencies can lead to complications when a precise diagnosis is overlooked.

Pneumatosis, defined as the presence of gas within the walls of a hollow organ, is an imaging finding generally associated with local inflammatory, ischemic, or infectious changes. Clinical discernment is crucial in determining the diagnosis and assessing the need for surgical intervention. Specifically, gastric pneumatosis has two etiologies described in the literature: gastric emphysema and emphysematous gastritis[1,2]. Gastric emphysema results from the dissection of air into the gastric wall following mucosal injury, usually of mechanical origin, with reported cases following gastroscopy, vomiting or aerophagia, gastric outlet obstruction, or even in association with pneumothorax and pneumomediastinum in some cases[3]. Emphysematous gastritis, on the other hand, typically presents as a rare manifestation of infectious gastritis due to the invasion of the gastric mucosa by gas-producing microorganisms and is most often associated with the visualization of air in the portal venous system. The most frequently isolated microorganisms include *Streptococcus spp., Escherichia coli, Enterobacter spp., Pseudomonas aeruginosa,*

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and *Clostridium perfringens*, with isolated reports also describing mucormycosis[4,5].

Both entities present a variable clinical spectrum, ranging from non-specific symptoms, such as epigastric pain and nausea with or without vomiting, to acute abdomen, systemic inflammatory response syndrome, sepsis, and, in some cases, death[6]. Elevated lactate and creatinine levels are associated with increased mortality. Furthermore, when either condition manifests as an acute abdomen, mortality rates range from 50% to 80% despite surgical treatment. For this reason, early diagnosis and timely treatment are warranted to prevent complications and reduce mortality[7,8].

CASE REPORT

We present the case of a 62-year-old male patient who arrived at the emergency department with a three-day history of abdominal pain and distension, multiple episodes of diarrhea without gastrointestinal bleeding, nausea, vomiting, and fever. The patient attributed these symptoms to the consumption of spoiled meat. Upon admission, his vital signs were within normal limits. Physical examination revealed abdominal distension and tenderness on palpation, but there were no signs of peritoneal irritation. Analgesia was administered, and laboratory tests were performed, showing normal leukocyte levels (8,700), mild neutrophilia (85%), elevated C-reactive protein (4.9), normal renal function, and adequate electrolytes and acid-base status. Due to persistent pain, an abdominal and pelvic computed tomography (CT) scan was ordered. The axial CT scan revealed gas bubbles, predominantly in the region corresponding to the hepatic dome and the left hepatic lobe, suggestive of portal venous gas (**Figure 1**). There was also liquid and gaseous distension of the gastric chamber, with air dissecting the gastric wall, particularly at the fundus and along the greater curvature (**Figure 2**), findings

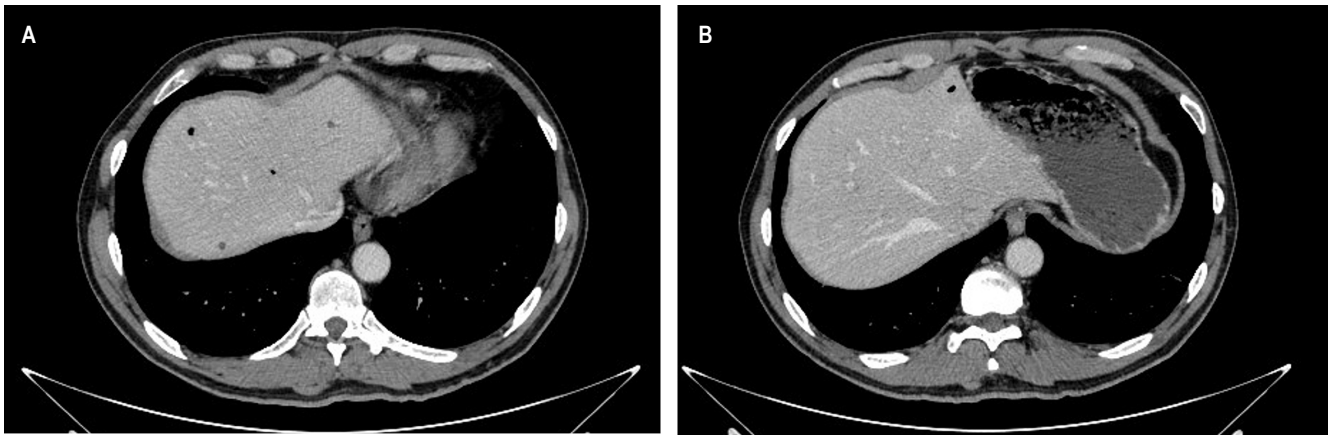


Figure 1. Gas bubbles predominantly in the hepatic dome region (**A**) and left hepatic lobe (**B**), suggestive of portal venous gas. Source: Patient's medical records.

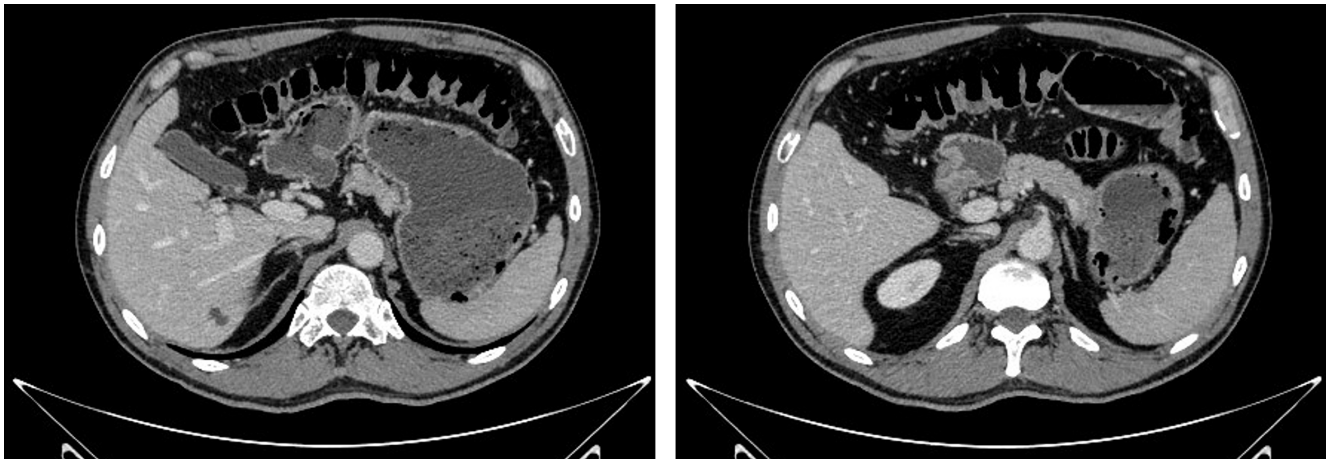


Figure 2. Air dissecting the gastric wall at the fundus and greater curvature, consistent with gastric wall pneumatosis. Source: Patient's medical records.

consistent with gastric wall pneumatosis and non-specific thickening of the gastric walls at the antropyloric region.

An upper digestive endoscopy (UDE) was performed to rule out any lesions that could explain the pneumatosis findings. The only abnormality identified was mucosal pallor of the gastric body, antrum, and duodenum, with erosions but no ulcers, consistent with signs of mild ischemia (**Figure 3**). Based on these findings, a CT angiography was conducted, which ruled out vascular ischemic involvement of the esophagus, stomach, duodenum, or intestines and confirmed vascular patency of the arterial and venous axes (**Figure 4**). Additionally, the resolution of the portal venous gas and improvement in the gastric pneumatosis were observed.

The patient's clinical course was favorable following conservative management with empirical antibiotic therapy. He received piperacillin/tazobactam upon admission, and after ruling out ischemic involvement, oral intake was reintroduced. The patient tolerated oral feeding well, with evidence of normal intestinal transit. He was subsequently discharged to complete a seven-day outpatient antibiotic course with cephalexin and metronidazole. At the two-week follow-up, the patient showed complete resolution of symptoms.

DISCUSSION

The imaging finding of portal venous gas in conjunction with gastric pneumatosis raises suspicion for mesenteric ischemia or intestinal necrosis as a consequence of advanced stages of obstruction, necrotizing enterocolitis, Crohn's disease, ulcerative colitis, or caustic ingestion. For this reason, urgent surgical management is justified when clinical suspicion points toward one of these etiologies.



Figure 3. Pallor of the distal gastric body and antrum mucosa, with erosions, consistent with mild ischemia. Source: Patient's medical records.

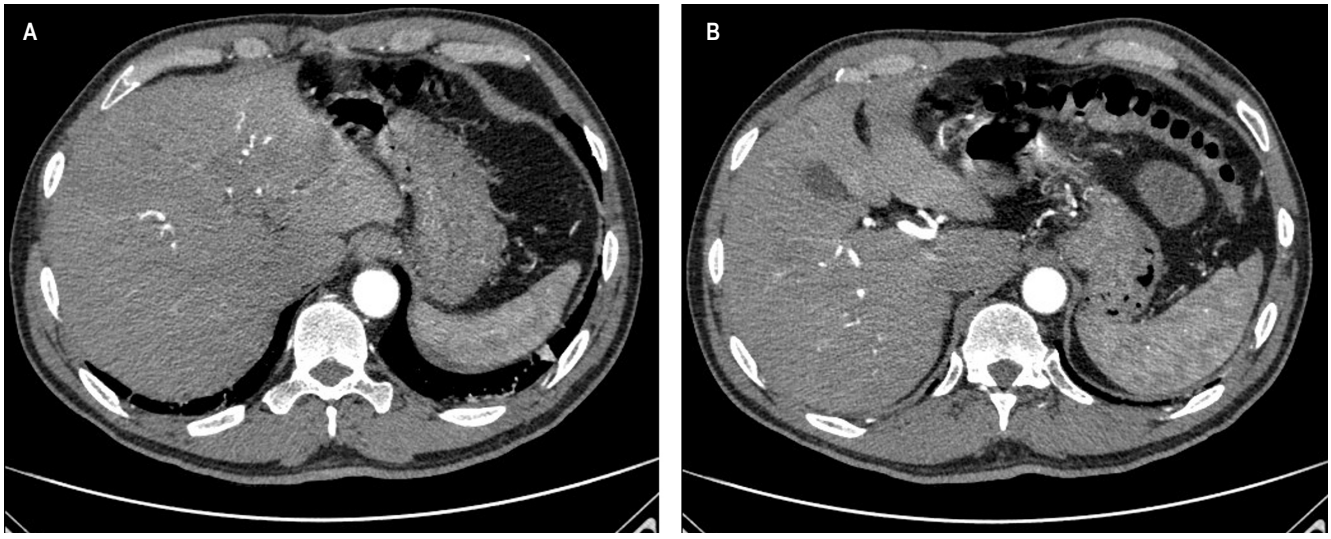


Figure 4. CT angiography. **A.** Resolution of portal venous gas. **B.** Minimal residual air in the gastric wall. Source: Patient's medical records.

In this case, the etiology of gastric pneumatosis appears to be emphysematous gastritis, as the onset of symptoms was associated with the ingestion of spoiled food, and there was no preceding mechanical trigger that could explain the dissection of air into the gastric walls. Thus, the successful outcome of this patient following conservative medical treatment is particularly noteworthy.

When emphysematous gastritis is associated with ischemia of the gastric walls, the risk of necrosis or perforation increases, thereby warranting surgical exploration to assess visceral viability, ensure adequate vascular flow, and perform segmental resections if necessary[8,9]. The decision to immediately restore gastrointestinal continuity or to perform damage control procedures depends on the patient's clinical, hemodynamic, and metabolic status.

Reports in the literature describe patients undergoing emergency gastrectomy without altering the fatal outcome, possibly due to the systemic damage and surgical morbidity involved. Risk factors associated with emphysematous gastritis have been identified, including diabetes, chronic obstructive pulmonary disease (COPD), renal failure, immunosuppression, prolonged steroid use, and alcohol abuse—none of which were documented in this patient.

Our patient presented with gastrointestinal symptoms, and CT imaging showed air in the gastric wall and portal venous system, prompting suspicion of intestinal ischemia. However, due to hemodynamic stability and the absence of peritoneal signs, endoscopy was performed to assess the mucosa, revealing only superficial ischemia without transmural involvement. Consequently, conservative management with antibiotics was chosen.

Upon reviewing the literature, there have been reports of patients who underwent surgical intervention despite showing no intraoperative abnormalities, despite signs and symptoms suggestive of intestinal ischemia and perforation, as described by Pastor-Sifuentes and colleagues[10,11]. However, successful conservative treatment with bowel rest and parenteral nutrition has also been documented, as in the case reported by Arezzo and colleagues[1]. In light of this, surgery should be reserved for patients who fail to respond to conservative management, those with transmural gastric ischemia, signs of peritoneal irritation, perforation, or extensive visceral involvement. This case illustrates the successful management of an emphysematous gastritis patient who remained stable throughout the course of the disease with medical treatment with antibiotics[12].

CONCLUSION

Emphysematous gastritis and gastric emphysema are two conditions with variable clinical outcomes. Early recognition of emphysematous gastritis, typically diagnosed via computed tomography revealing gastric pneumatosis and portal venous gas, is crucial to reducing complications such as gastric perforation or death. Historically, these patients warranted surgical intervention; however, there have been reports of negative surgical findings despite symptoms of an acute abdomen, as well as successful outcomes with conservative management involving bowel rest or antibiotic therapy.

It is important to note that there is no standardized approach for patients presenting with gastric pneumatosis, and further studies are needed to appropriately determine which patients can be managed medically and which require surgical intervention.

Ethical Responsibilities

We confirm that informed consent for the publication of this article was obtained, and authorization was granted by the bioethics committee. Additionally, no personal data that could identify the patient is included in the development of this text.

Funding Sources

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Conflict of Interest

We declare there are no conflicts of interest.

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Case report

Heterotopic Pancreas as a Cause of Intussusception and Gastrointestinal Bleeding: A Case Report

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Abstract

Introduction: Intussusception is the telescoping of one segment of the intestine into an adjacent segment, leading to obstruction, inflammation, and ischemia. In adults, it accounts for 5% of intussusception cases, representing 1%–5% of intestinal obstructions. It is typically secondary to intraluminal lesions (benign or malignant) or iatrogenic factors. **Case Report:** A 39-year-old male patient with a history of chronic gastritis presented with a three-month history of intermittent epigastric and left hypochondrial pain, which progressively increased in intensity and was associated with melena and rectal bleeding. On physical examination, he was hemodynamically stable, with mild tenderness in the left upper quadrant, no signs of peritoneal irritation, and positive findings for melena on digital rectal examination. Initial laboratory tests revealed no inflammatory response and normal hemoglobin levels. Upper gastrointestinal endoscopy and colonoscopy showed no abnormalities. Due to persistent abdominal pain, hepatobiliary ultrasound was performed, revealing a "target sign" suggestive of intussusception, which was confirmed with abdominal computed tomography. The patient underwent laparoscopic surgery, which identified an intestinal intussusception in the proximal ileum with a palpable intraluminal mass. Segmental resection and side-to-side anastomosis were performed. Histopathological analysis revealed a submucosal lipoma with ectopic pancreatic tissue. **Conclusion:** Intestinal intussusception in adults is rare and even less frequently associated with ectopic pancreatic tissue.

Keywords

Choristoma, pancreas, intussusception, gastrointestinal bleeding, laparoscopy, general surgery, case study.

INTRODUCTION

Intussusception is the telescoping of one segment of the intestine into an adjacent segment, which can lead to obstruction, inflammation, or ischemia. In adults, intussusception accounts for 5% of all cases and represents 1% to 5% of intestinal obstructions. The median age of affected individuals is 50 years, with a male-to-female ratio of 1:5[(1)]. Intussusception in adults is typically secondary to the presence of intraluminal lesions, most of which are related to neoplasms, followed by benign lesions such as polyps, lipomas, and fibromas, with only a few cases linked to iatrogenic causes[(2)].

The association with ectopic pancreatic tissue is extremely rare, and its clinical presentation is variable. It may manifest with chronic, intermittent abdominal pain accompanied by non-specific signs of intestinal obstruction, or it may present with nausea, vomiting, gastrointestinal bleeding, constipation, or abdominal distension[(1,3)]. The variability in clinical presentation and imaging characteristics makes preoperative diagnosis challenging. Nonetheless, timely diagnosis is essential, as surgical intervention is

often the definitive treatment[3]. A review of the literature identified few reports of heterotopic pancreas in Latin America[4–6], with only one case described in Colombia, located within a gastric polyp[4]. This report presents the case of a patient with ectopic pancreatic tissue as the cause of intestinal intussusception.

CASE DESCRIPTION

The patient was a 39-year-old male with a history of chronic gastritis and no other significant medical or surgical history. He was admitted to a tertiary care hospital after experiencing a three-month history of intermittent epigastric and left hypochondrial pain, which intensified one day prior to admission. The pain was rated 8/10 on the pain analog scale and was associated with two episodes of melena and one episode of rectal bleeding. He denied self-medicating or consuming herbal infusions. Upon admission, he was normotensive, tachycardic, and had an oxygen saturation of 98% on room air. On physical examination, he had anicteric sclerae, moist pink mucosa, a soft, depressible abdomen with tenderness on palpation in the epigastric and left hypochondrial regions, but no signs of peritoneal irritation, palpable masses, or organomegaly. A digital rectal exam was positive for melena. Initial laboratory tests showed a normal complete blood count without anemia, and normal creatinine and blood urea nitrogen (BUN) levels.

The general surgery team evaluated the patient and diagnosed gastrointestinal bleeding. Management was initiated with omeprazole, intravenous fluids, and analgesics. Due to his symptoms, esophagogastroduodenoscopy and colonoscopy were performed, both of which were unremarkable. However, given the persistence of abdominal pain in the epigastric and left hypochondrial regions, a hepatobiliary ultrasound was ordered, which revealed a target sign consistent with intussusception. This finding was subsequently confirmed by abdominal computed tomography (**Figure 1**). Based on imaging results, the patient underwent laparoscopic abdominal surgery, which revealed intestinal intussusception involving a proximal ileal loop and the presence of an intraluminal mass, with no macroscopic involvement of the mesentery or intestinal serosa. A 10 cm segment of the affected intestine was resected, and an anastomosis was performed using the Barcelona technique (**Figure 2**). The patient's postoperative course was uneventful, and he was discharged eight days after admission. During his follow-up visit four weeks later, he demonstrated satisfactory clinical recovery. The pathology report described intestinal intussusception with a submucosal lipoma and a focus of histologically normal ectopic pancreatic tissue (**Figure 3**).

DISCUSSION

Ectopic pancreatic tissue is defined as pancreatic tissue that lacks vascular or anatomical continuity with the pancreas itself, also referred to as heterotopic pancreas[7]. It has an incidence of 0.2% in laparotomy series and 0.5% to 3.7% in autopsy studies[8], with a higher prevalence in men during

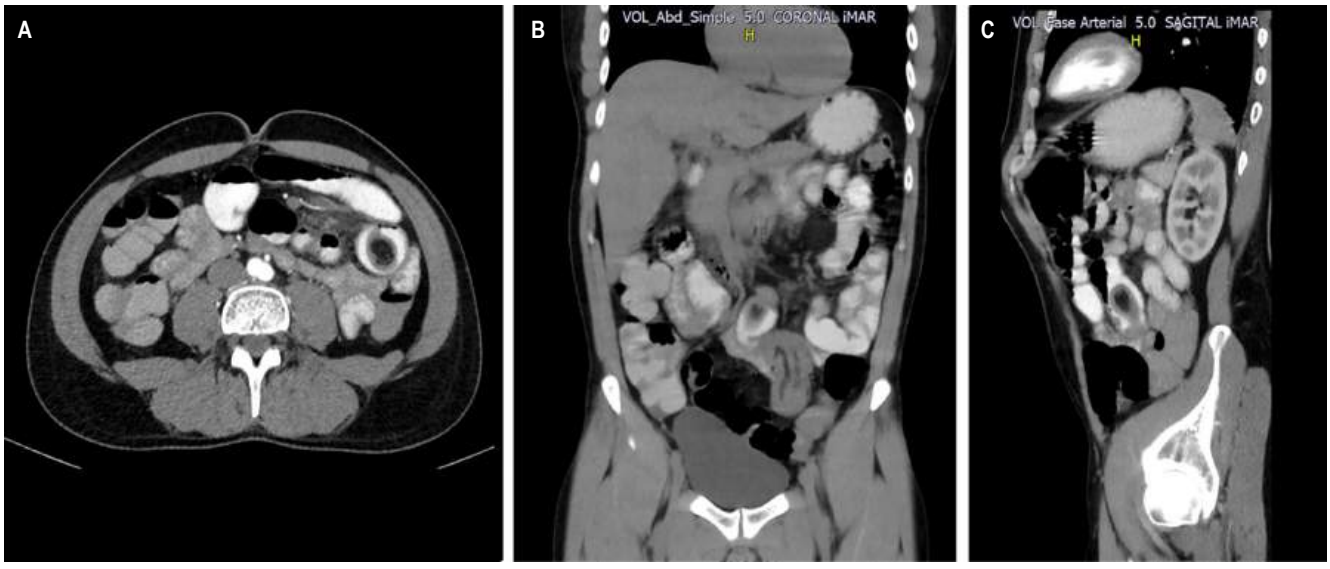


Figure 1. Axial (**A**), coronal (**B**), and sagittal (**C**) views of an abdominal and pelvic computed tomography scan with oral and intravenous contrast. The images show a target or doughnut sign in the region of the ileal loops, suggestive of intussusception. Images provided by the Ubiquo System, Hospital Universitario San José, Popayán, Colombia.

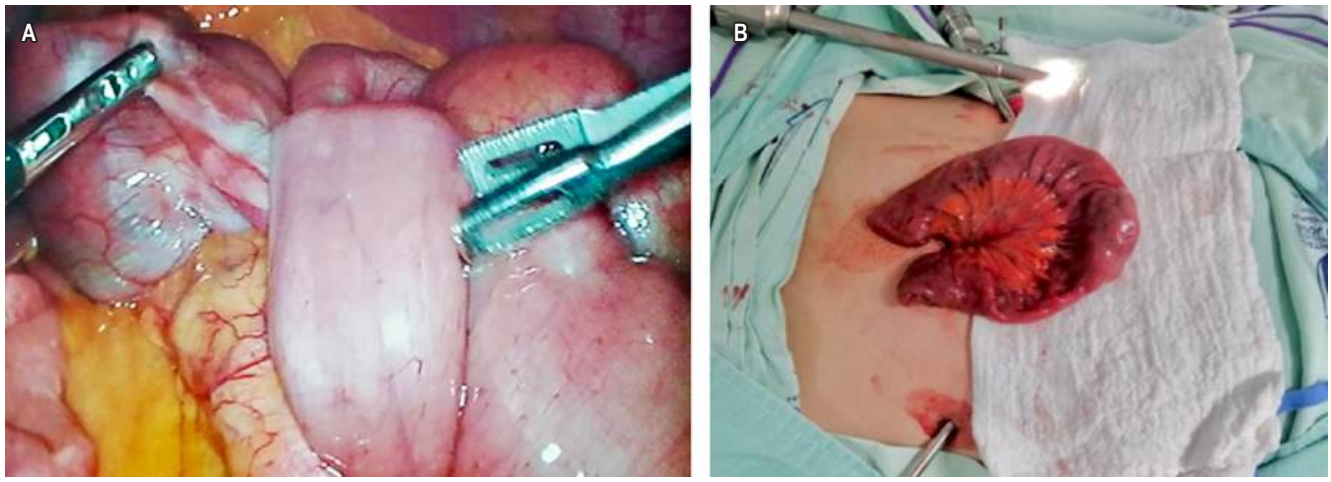


Figure 2. Intraoperative photographs from the laparoscopic approach. **A.** Proximal ileal loop showing findings consistent with intussusception. **B.** Surgical specimen following resection of the proximal ileum. Author's file.

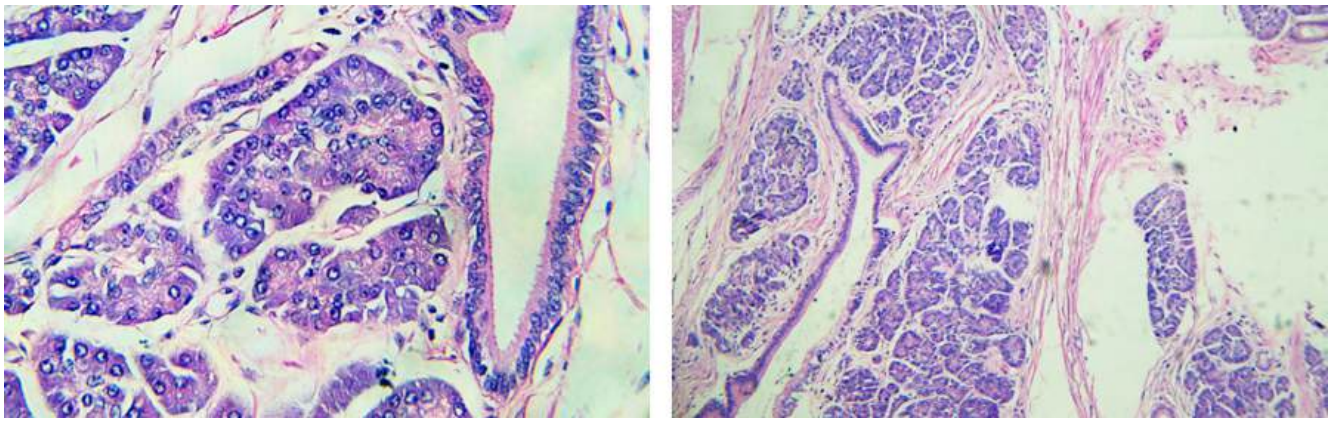


Figure 3. Histological analysis showing foci of pancreatic tissue composed of serous acini without epithelial atypia, glandular ducts with normal histological features, and histologically normal islets of Langerhans. No evidence of infiltrative tumor lesions is observed. Source: Pathology Laboratory, Hospital Universitario San José, Popayán, Colombia.

the fifth and sixth decades of life. The most common locations are the stomach (25%–38%), followed by the duodenum (17%–36%) and the jejunum (15%–21%); however, it can also be found in other sites such as the biliary tract, mesentery, and omentum[9,10]. The exact etiology remains unknown, although various theories have been proposed regarding its embryological origin[7,10,11]. In this case, ectopic pancreatic tissue was identified as the cause of intussusception in the proximal ileal loop—a location more commonly associated with pediatric cases and infrequently reported in the literature[12,13]. Geoffray and colleagues demonstrated that ectopic pancreatic tissue in the ileum occurs in only 0.2% of cases[14,15].

Most cases of heterotopic pancreatic tissue are asymptomatic and are usually incidental findings during autopsies, laparotomies, or abdominal imaging studies[9,11,16]. When symptomatic, they typically present with non-specific symptoms such as abdominal pain, epigastric pain, nausea, vomiting, and gastrointestinal bleeding. Although any intestinal condition that disrupts normal peristaltic patterns increases the risk of intussusception[1], it is rare for pancreatic heterotopia to cause intestinal obstruction or intussusception[7,10,17]. In this case, the patient's primary symptoms were abdominal pain and gastrointestinal bleeding. According to the case series and systematic review by LeCompte and colleagues, only 20% of patients with

this condition are symptomatic, with 67% presenting with abdominal pain and 9% with gastrointestinal bleeding[18].

Furthermore, only 5% of all cases of intussusception occur in adults, with 1% to 5% of these presenting with intestinal obstruction. In more than 90% of adult cases, an organic lesion (mass) is present[19,20]. Clinical manifestations are often non-specific, and the diagnosis is typically made through radiological imaging or intraoperatively[2,3]. Abdominal computed tomography (CT) is currently considered the most sensitive radiological method for confirming intussusception, with a diagnostic accuracy ranging from 58% to 100%[1,3]. CT imaging can reveal the characteristic target sign, which corresponds to a three-layered structure comprising the intestinal wall, mesentery, and enveloping bowel loop[21,22]. Additionally, CT scans can define the location, potential etiology, and relationship with adjacent structures[2]. In this case, the diagnosis was initially suggested by an abdominal ultrasound and subsequently confirmed by an abdominal CT scan, which demonstrated the classic findings of intussusception. Although abdominal ultrasound is not the diagnostic modality of choice, it is a quick, easily performed procedure that requires no preparation and can aid in detecting intussusception. Honjo and colleagues reported an ultrasound diagnostic accuracy of approximately 50%[1].

The definitive diagnosis is made through histopathological analysis, where macroscopically, a region of small yellowish nodules ranging from 1 mm to 5 cm can be observed[10]. These nodules are typically located in the mucosa and, in some cases, in the serosa. Microscopically, a few lobules of pancreatic acini are seen, containing polarized cells with basally oriented nuclei and amphophilic or basophilic granular cytoplasm. Pancreatic islets are observed in one-third of cases, while lesions composed entirely of endocrine cells are rare[17,23], as shown in **Figure 3**.

In adults, intussusception requires definitive treatment in 70% to 90% of cases, with surgical resection being the preferred approach due to its frequent association with malignancy[3]. The traditional approach to managing intestinal intussusception is laparotomy[20]; however, laparoscopy has proven to be a useful and safe method for treating this condition, with additional advantages such as improved aesthetic outcomes, reduced surgical stress, enhanced gastrointestinal tract healing, shorter hospital stays, and a lower risk of incisional hernia[24]. This is supported by the study by Zhao and colleagues, who compared laparoscopic and open surgical techniques in 162 pediatric patients—62 of whom underwent laparoscopic surgery and 100 open surgery. The results showed that the laparoscopic group had shorter times to oral intake initiation and shorter hospital stays compared to the open surgery group[25]. In contrast, no comparative studies in adult patients were identified in the literature. This report presents a rare case of ectopic pancreas in an adult patient, managed with intestinal resection via laparoscopy, resulting in a favorable outcome.

Ethical Considerations

This study was designed in accordance with current international bioethical standards, and all presented data respect the patient's confidentiality.

Approval for the case report was obtained from the ethics committee of Hospital Universitario San José de Popayán, Colombia.

Conflict of Interest

The authors declare no conflicts of interest.

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Case report

Fulminant Intestinal Amebiasis in a Young Female Patient: A Case Report

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Abstract

Intestinal amebiasis is an endemic disease in developing countries caused by the protozoan *Entamoeba histolytica*. It is typically asymptomatic, but in rare cases, it can present with severe manifestations. This is the case of a 30-year-old female patient who, two days after undergoing open appendectomy, developed rectal bleeding and abdominal pain accompanied by signs of hemodynamic instability. Colonoscopy revealed multiple necrotic ulcers in the mucosa with abundant clots. The patient experienced clinical deterioration, persistent bleeding, and signs of peritoneal irritation, necessitating exploratory laparotomy. Intraoperative findings included hypoperfused colon and cecal perforation, requiring total colectomy. Histopathological analysis confirmed acute severe ulcerative colitis caused by *E. histolytica*.

Keywords

Gastrointestinal bleeding, hematochezia, *Entamoeba histolytica*, amoebic dysentery, colectomy.

INTRODUCTION

Entamoeba histolytica is an extracellular enteric protozoan with a preference for the large intestine and is responsible for approximately 10% of all *Entamoeba* infections worldwide, with the remaining 90% attributed to other species. Its identification dates back to the 19th century when Lamb first described it. Later, Lösch named the organism *Amoeba coli* and demonstrated its ability to cause colonic ulceration and dysentery[1]. In 1883, Koch identified amoebas in an ulcerated human intestine, but it was not until 1903 that Schaudinn coined the term *Entamoeba histolytica* due to its capacity to cause tissue lysis[1,2].

Intestinal infection caused by *E. histolytica* is referred to as amebiasis, which ranks among the top three parasitic infections leading to death worldwide[3]. Approximately 90% of amebiasis cases are asymptomatic, while 10% result in invasive disease. However, its effects are not confined to the intestine; it can also cause extraintestinal disease, such as hepatic abscesses, pneumonia, pericarditis, and even cerebral amebiasis, although extraintestinal manifestations account for less than 1% of cases[4].

CASE PRESENTATION

We report the case of a 30-year-old female patient with no known medical history who, two days after undergoing an open appendectomy, developed multiple episodes of profuse rectal bleeding, accompanied by general malaise and diffuse abdominal pain. Upon admission to the emergency department, she was in poor condition, presenting with tachycardia, dehydration, and generalized pallor. Laboratory tests revealed leukocytosis (26,750 cells/μL) predominantly due to neutrophils, hemoglobin of 9.5 g/dL, platelet count of 225,000/μL, blood urea nitrogen (BUN) of 9.0 mg/dL, serum creatinine of 0.5 mg/dL, and normal coagulation times.

A total colonoscopy was performed (**Figure 1**), which revealed multiple mucosal ulcerations with necrosis, clots, and patchy ulcerations in the rectum, descending colon, and transverse colon, with diffuse bleeding that could not be controlled endoscopically. Following the procedure, the patient experienced significant rectal bleeding, prompting an abdominal CT angiography, which showed irregular, concentric mural thickening of the cecum and ascending colon without evidence of contrast extravasation. Due to the persistence of bleeding and a hemoglobin drop to 6.9 g/dL, an abdominal aortogram was performed. At the level of the right hypogastric artery, contrast extravasation was observed in the distal branch, leading to endovascular embolization of the affected vessel. Initial differential diagnoses included severe ulcerative colitis and ischemic colitis, which were rapidly ruled out based on the clinical presentation and the absence of relevant medical history or risk factors.



Figure 1. Ischemic colon with multiple ulcerations, mucosal denudation, and abundant clots observed during colonoscopy. Author's File.

The patient had a torpid clinical course despite the treatment provided. Due to the development of signs of peritoneal irritation, an exploratory laparotomy was performed, revealing peritonitis in the right two quadrants, along with a hypoperfused and pale colon and a perforation in the cecum. A total colectomy was performed (**Figure 2**), and the patient completed her recovery in the intensive care unit (ICU), where vasopressors and invasive mechanical ventilation were successfully discontinued. *Pluralibacter gergoviae* was isolated from the peritoneal fluid culture, while blood cultures were negative. She was treated with meropenem, and due to her favorable clinical progression, she was discharged from the hospital with an ileostomy. However, one week later, the patient was readmitted due to worsening abdominal pain, accompanied by nausea and fever. A review of the colon pathology report revealed severe, perforating acute colitis caused by *Entamoeba histolytica*, along with acute suppurative peritonitis (**Figures 3** and **4**). The Infectious Disease team recommended treatment with intravenous (IV) metronidazole 750 mg every eight hours for ten days, followed by oral (PO) paromomycin 500 mg every eight hours for seven days, resulting in the patient's full recovery.



Figure 2. Total colectomy. The ischemic colon is shown with fibrinopurulent membranes, multiple necrotic areas, and perforations. Author's File.

DISCUSSION

Acute lower gastrointestinal (GI) bleeding, historically defined as bleeding originating below the ligament of Treitz, has been reclassified to distinguish it from bleeding originating in the midgut. It is now limited to bleeding that arises from the colon, rectum, or anus[5,6]. Its defini-

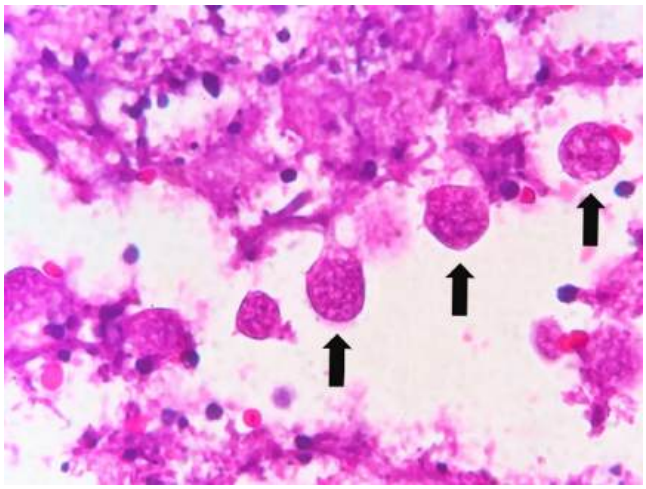


Figure 3. Abundant acute inflammatory infiltrate and multiple *Entamoeba histolytica* trophozoites (black arrows). Hematoxylin and eosin stain of a colon biopsy section at 10x magnification. Author's File.

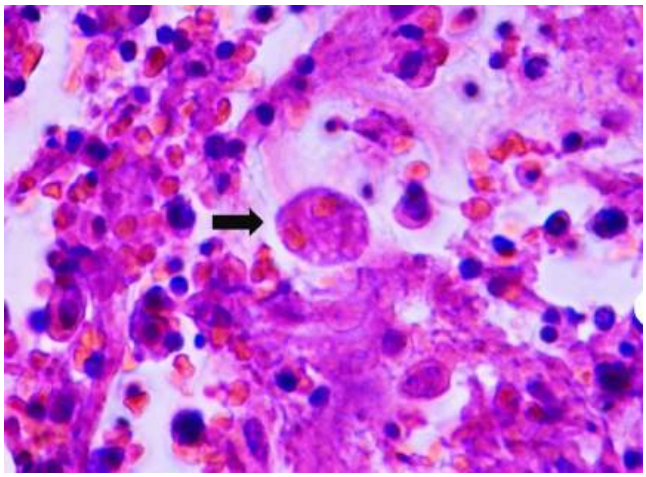


Figure 4. Abundant acute inflammatory infiltrate and a trophozoite of *Entamoeba histolytica* with erythrophagocytosis (black arrow). Hematoxylin and eosin stain of a colon biopsy section at 10x magnification. Author's File.

tion, which is somewhat arbitrary, refers to recent onset within a period of fewer than three days[5]. Acute lower GI bleeding has an incidence of 20 to 30 cases per 100,000 person-years and accounts for 20% of all GI bleeds[7]. It is most commonly associated with colonic sources, such as diverticulosis or angiodysplasia[8], and over 80% of cases resolve spontaneously[5,8]. Clinically, it often presents as hematochezia, though melena may occur less frequently. Advanced age and comorbidities are linked to higher morbidity and mortality[6].

Diverticular disease is the leading cause of acute lower GI bleeding, accounting for 30% to 65% of cases[9]. This is followed by ischemic colitis (5% to 20%), which generally affects elderly patients with cardiovascular risk factors[6,7]; hemorrhoids (5% to 20%), more common in younger individuals[6,7]; colorectal polyps and neoplasms (2% to 15%); angiodysplasia (5% to 10%), which is more prevalent in those over 60 years[6,7]; and inflammatory bowel disease (3% to 5%)[6]. Infectious colitis is one of the least common causes, accounting for only 2% to 5% of cases[6].

The first-line diagnostic tool is colonoscopy, which can provide a definitive diagnosis in 74% to 100% of cases. It also allows for a more precise description of the lesion, even in the absence of active bleeding, and in many cases facilitates therapeutic intervention[10]. The timing of colonoscopy remains a subject of debate. Although urgent or early colonoscopy (within 6 to 12 hours) has been shown to improve diagnostic yield and shorten hospital stays, it does not significantly affect major outcomes, such as mortality[10], compared to elective colonoscopy (performed within 36 to 60 hours)[10,11].

Additional studies, such as CT angiography, are reserved for hemodynamically unstable patients in whom active bleeding is suspected, as it provides a rapid and minimally invasive method to localize the bleeding site and guide subsequent endoscopic or radiological therapy. If a positive finding is observed, catheter angiography can enable embolization of the responsible vessel, thus avoiding emergency laparotomy whenever possible[12], as was the case in our patient.

Bleeding caused by infectious colitis typically presents as acute diarrhea (lasting fewer than 14 days) with blood in the stool, often in the context of recent travel to endemic areas or consumption of contaminated food[7,13]. This diagnosis is made when an invasive or non-invasive pathogen triggers diffuse mucosal inflammation of the colon. Infectious colitis should be suspected in patients with acute diarrhea, particularly when they present with heavily blood-stained stools, tenesmus, urgency, or evidence of fecal inflammatory markers. The diagnosis is confirmed when diffuse colonic inflammation is observed during colonoscopy[13]. Given that Latin America is considered an endemic region for *E. histolytica*, the presence of bloody diarrhea in this context should prompt clinicians to actively investigate for this pathogen[14].

Amebiasis is a common parasitic infection in many tropical and subtropical regions of the world, particularly in areas with poor sanitation. It can present in various forms: asymptomatic infection (90%), non-invasive symptomatic infection (6%–8%), and acute amebic colitis (dysentery)[15]. Nearly all infections are acquired through the consumption of food or water contaminated with feces containing cysts, a scenario that is relatively frequent in developing

countries[4,16]. Less common transmission routes include oral-anal sexual contact and contaminated endoscopes or enema devices[16].

Amebic cysts enter the human intestinal lumen and produce trophozoites capable of invading intestinal epithelial cells[17]. This process involves the parasite's Gal/GalNAc lectin binding to the galactose (Gal) or N-acetyl-D-galactosamine (GalNAc) carbohydrates of the host cell membrane[18]. After adhering to mesothelial cells, the amoeba employs cytotoxic mechanisms to induce cell death and tissue invasion, including apoptosis, phagocytosis, and trogocytosis[19,20]. In rare cases (<0.5% of cases), fulminant necrotizing amebic colitis occurs, leading to gangrenous necrosis of the large intestine. The mortality rate for this condition is extremely high, ranging from 55% to 100%, with secondary sepsis due to perforation-related peritonitis being the leading cause of death[15].

In our patient's case, the preceding episode of appendicitis raises the suspicion that the accumulation of parasites may have triggered acute inflammation of the appendix, even though the histopathological report of the appendix did not mention trophozoites. Amebic appendicitis is relatively uncommon, with an incidence of 0.5% to 2.3% in endemic areas[21,22]. However, its association with fulminant necrotizing colitis, as observed in our patient, is even rarer, requiring a high index of suspicion for timely diagnosis.

CONCLUSION

Intestinal amebiasis, caused by *Entamoeba histolytica*, is an endemic parasitic infection in our region. Although it is often asymptomatic, it has the potential to become severe and invasive, posing a life-threatening risk. One of its most frequent manifestations is lower GI bleeding, which, when presenting as an initial symptom, poses a diagnostic challenge due to its wide range of possible etiologies. However, a detailed and thorough medical history, an evaluation of risk factors, and a high index of suspicion guide the selection of appropriate diagnostic studies and facilitate a definitive diagnosis.

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Case report

Type II Abernethy malformation in an adult: case report

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Abstract

Background: Abernethy malformations are vascular developmental anomalies characterized by hypoplasia or agenesis of the portal vein. These malformations have a variable clinical presentation due to associated complications and are often diagnosed incidentally through imaging studies, primarily in pediatric patients. **Case Summary:** We report the case of a 39-year-old female patient who presented with spider telangiectasias. Laboratory tests revealed pancytopenia and elevated liver transaminases. Given the complexity of the case, autoimmune diseases and portal vein thrombosis were ruled out through autoantibody testing and Doppler ultrasound. Incidentally, triphasic computed tomography of the abdomen revealed splenomegaly, an aneurysm of the inferior segmental artery of the left kidney, splenorenal collaterals, and portal vein hypoplasia consistent with Abernethy malformation type II. **Conclusions:** Abernethy malformation is rare in adults and was an incidental finding in this case. Although dermatological signs contributed to its detection, the relationship between the hemangioma and this condition, as well as its role as a potential physical sign, remains unclear.

Keywords

Vascular malformations, congenital anomalies, case study.

INTRODUCTION

Congenital extrahepatic portosystemic shunts, also known as Abernethy malformations, are vascular developmental anomalies characterized by hypoplasia or agenesis of the portal vein and diversion of portomesenteric blood flow to a systemic vein before reaching the portal bifurcation[1]. This condition was first described by John Abernethy in 1793[2]. According to Morgan and Superina[3], Abernethy malformations are classified into two main types: type I, characterized by complete absence of the portal vein with total diversion of portal blood to the inferior vena cava, and type II, involving portal hypoplasia with partial diversion of blood flow to the inferior vena cava through extrahepatic connections.

According to Franchi and colleagues[4], diagnosing this condition presents a significant challenge due to its varied clinical presentation, which may include hepatic tumors, hepatopulmonary syndrome, pulmonary arterial hypertension, portosystemic encephalopathy, heart failure, and glomerulonephritis. However, the diagnosis can also be an incidental finding. Baiges and colleagues[5] reported 66 cases of Abernethy malformation, 80% of which were diagnosed incidentally. Doppler ultrasound is the initial diagnostic tool for detection[6]. Other vascular malformations may coexist, although they are frequently underdiag-

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nosed[7]. Additionally, further laboratory testing is often required, depending on the patient's clinical presentation, including arterial ammonia levels, brain magnetic resonance imaging (MRI), electroencephalography, or liver biopsy[8].

The objective of this article is to report the case of a 39-year-old female patient who sought medical consultation for a dermatological concern and was found to have abnormal laboratory results. Follow-up assessments, including imaging studies, revealed incidental findings of multiple portosystemic shunts with portal hypoplasia consistent with a type II Abernethy malformation, accompanied by alterations in renal vasculature.

CASE DESCRIPTION

This case concerns a 39-year-old female patient from Azuay, Ecuador, who presented with telangiectasias as her primary reason for consultation. Her medical history included a pyogenic granuloma in the oral cavity and slow-healing lesions on her left foot. She had menarche at age 11, gravidity (G): 1, parity (P): 1, and one living child (LC): 1. She experienced pregnancy at age 15, with a vaginal delivery complicated by severe immediate postpartum hemorrhage. Prior to the pregnancy, her menstrual cycles were regular; however, she developed amenorrhea afterward.

On physical examination, erythematous skin lesions were observed on the palms, anterior chest, and face (**Figure 1**), which were confirmed as hemangiomas by biopsy. Additionally, there was a residual pyogenic granuloma lesion on the lower lip that disappeared upon digital pressure and was associated with mild tenderness on palpation. The patient displayed a complete absence of axillary and pubic hair.

Laboratory tests revealed pancytopenia and elevated liver transaminases: aspartate aminotransferase (AST) at 147 U/L (reference range: 0.0–32.0 U/L) and alanine aminotransferase (ALT) at 149 U/L (reference range: 0.0–35.0 U/L). Additionally, elevated alpha-fetoprotein levels were detected at 9.5 IU/ml (reference range: 0.0–5.8 IU/ml), prompting further imaging studies.

An abdominal ultrasound revealed hepatomegaly with a slightly heterogeneous size, increased echogenicity, and splenomegaly measuring 15 x 6.4 cm. A subsequent 3D reconstruction abdominal angiography (**Figure 2**) showed that the proximal third of the portal vein measured approximately 8.6 mm, with hypoplasia of the portal hilum and its branches. Multiple shunts were observed connecting the splenic and superior mesenteric veins to the inferior vena cava, along with a splenorenal shunt measuring approximately 10 mm. Additionally, tortuous collateral veins extended to the short gastric and splenorenal veins. The liver displayed parenchymal density changes and Glisson's capsule irregularities consistent with chronic liver disease, as well as dilated venous vessels at the lower pole of the left kidney. Based on these findings, Abernethy malformation was diagnosed as an incidental finding via computed tomography, and a lower segmental renal artery aneurysm was identified through Doppler color ultrasound (**Figure 3**).

Other conditions, such as systemic lupus erythematosus (negative antinuclear antibodies and anti-DNA antibodies), antiphospholipid syndrome (anticardiolipin IgG: 4.3 [reference value: <12 = negative], anticardiolipin IgM: 3.2 [<12 = negative], negative lupus anticoagulant, anti-β2 glycoprotein IgG: 3.1 U/mL [<12 U/mL = negative], anti-β2 glycoprotein IgM: 4.5 U/mL [reference value: <12 U/mL = negative]), and portal vein thrombosis (ruled out through hepatic Doppler ultrasound and thrombophilia screening) were excluded.

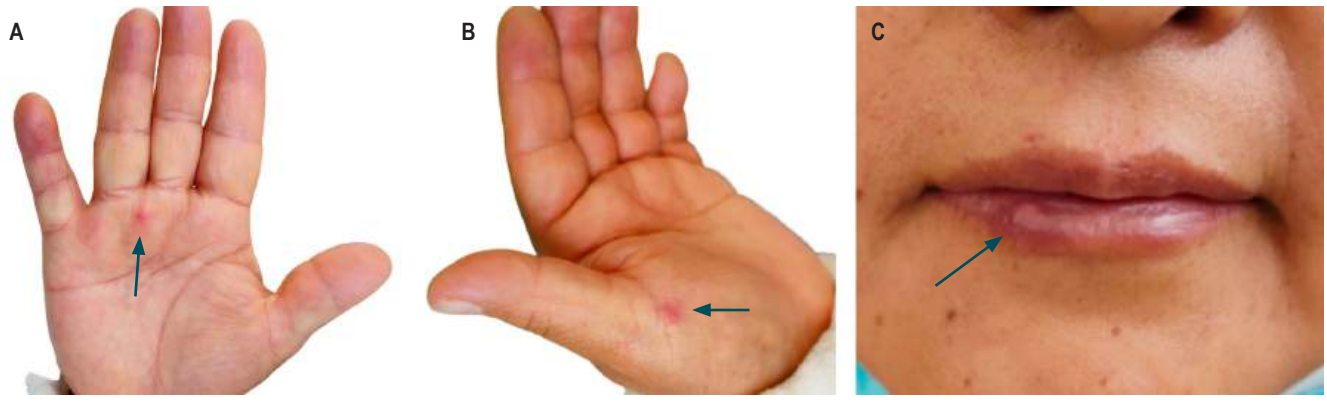


Figure 1. Cutaneous Lesions. **A.** Telangiectasia over erythematous skin in the middle of the Right palmar digital pad (arrow). **B.** Telangiectasia over erythematous skin in the left thenar eminence (arrow). **C.** Erythematous papule residual from the pyogenic granuloma on the lower lip (arrow). Author's File.

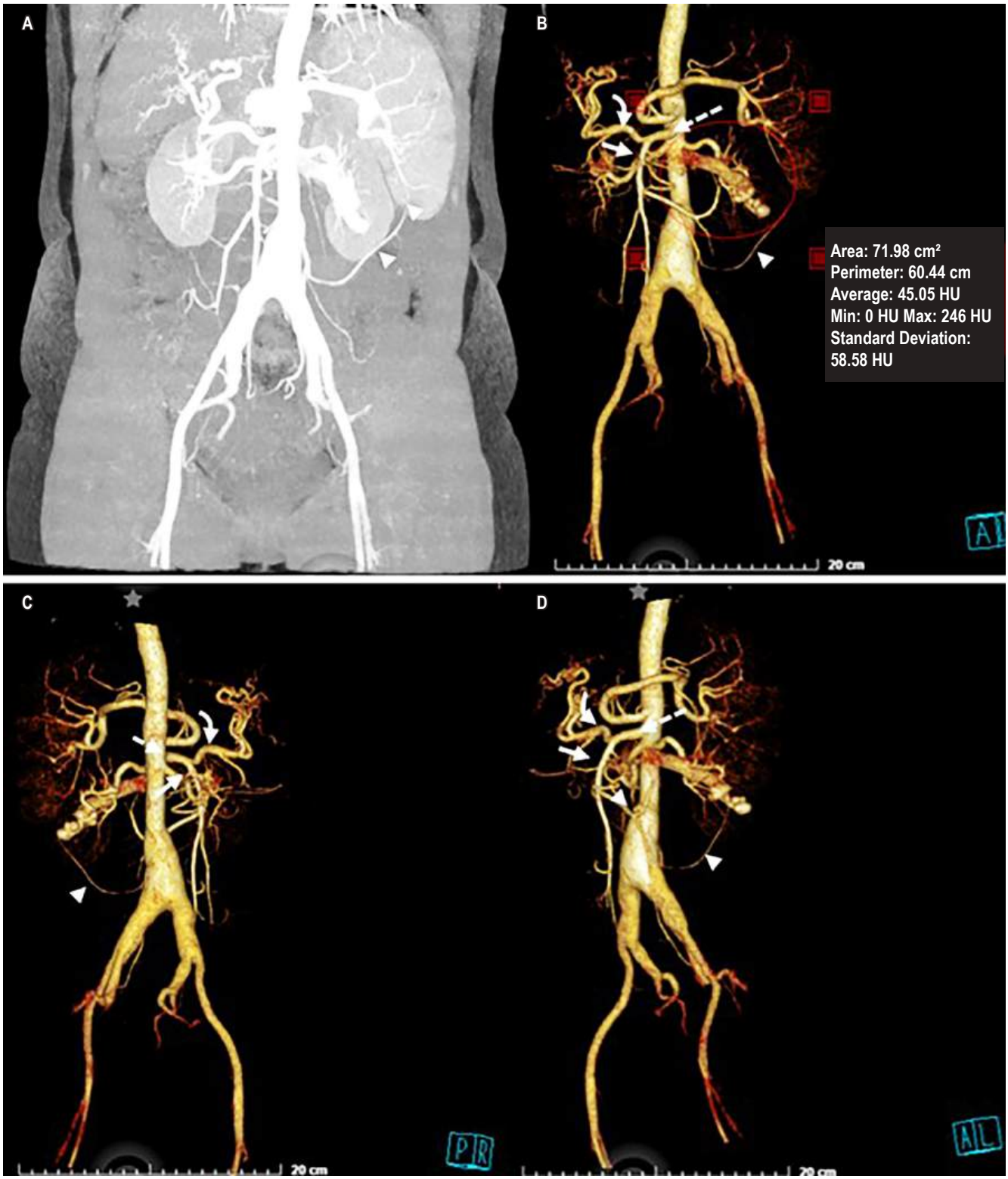


Figure 2. A. Abdominal angiography. **B.** 3D reconstruction, anterior view. **C.** Posterior view. **D.** Anterolateral view. The images show the junction of the superior mesenteric vein (straight arrow) and the splenic vein (curved arrow) draining directly into the superior vena cava (dashed arrow), along with a shunt connecting the splenic and superior mesenteric veins to the inferior vena cava. This shunt extends toward the left hypochondrium, descends near the lower renal pole, and reconnects with the inferior vena cava (arrowheads). Author's File.

Protein C and antithrombin II deficiencies were detected, prompting investigations for factor V Leiden mutation and G20210A prothrombin gene mutation, both of which yielded negative results, attributing the deficiencies to the patient's liver disease. Hormonal evaluation showed the following results: thyroid-stimulating hormone (TSH): 2.84 μIU/mL (reference range: 0.27–4.20 μIU/mL), free T_3: 1.8 pg/mL (reference range: 2.0–4.4 pg/mL), free T_4: 0.23 ng/dL (reference range: 0.93–1.70 ng/dL), prolactin: 3.4 ng/mL (reference range: 4.79–23.30 ng/mL), and morning cortisol: 3.2 μg/dL (reference range: 6.2–19.4 μg/dL), indicating hypopituitarism.

The patient experienced one episode of syncope and was later hospitalized due to a chronic subdural hematoma and subarachnoid hemorrhage, as evidenced by cranial computed tomography (**Figure 4**). She subsequently developed respiratory decompensation and was admitted to the intensive care unit due to bacterial hospital-acquired pneumonia. Later, a pleural effusion was detected, necessitating chest tube drainage, after which she remained hospitalized until stabilization.

Clinical follow-up of the non-traumatic chronic subdural hematoma was conducted due to the bleeding risk, and the patient showed favorable progress with reversal of the condition. At present, the patient has cirrhosis classified as Child-Pugh A and is being treated for hypopituitarism with hormone replacement therapy: 100 μg/day of levothyroxine and 5 mg/day of prednisone, with regular monitoring of blood hormone levels. A surgical resolution for the Abernethy malformation was offered, but the patient declined, as she remains stable at this time.

DISCUSSION

This report presents a case of type II Abernethy malformation diagnosed incidentally at the age of 39 during a dermatological consultation. Blood tests revealed pancytopenia, elevated liver transaminases, and elevated alpha-fetoprotein levels, prompting the need for imaging studies. These studies showed portal system hypoplasia with multiple portosystemic shunts and morphological alterations of the left kidney's inferior segmental artery. Despite the patient having received care within the national health system on multiple occasions, the malformations had not been previously detected due to a lack of clinical suspicion, as the patient did not present symptoms typically associated with this condition.

This malformation likely originates between the fourth and eighth weeks of gestation due to excessive regression

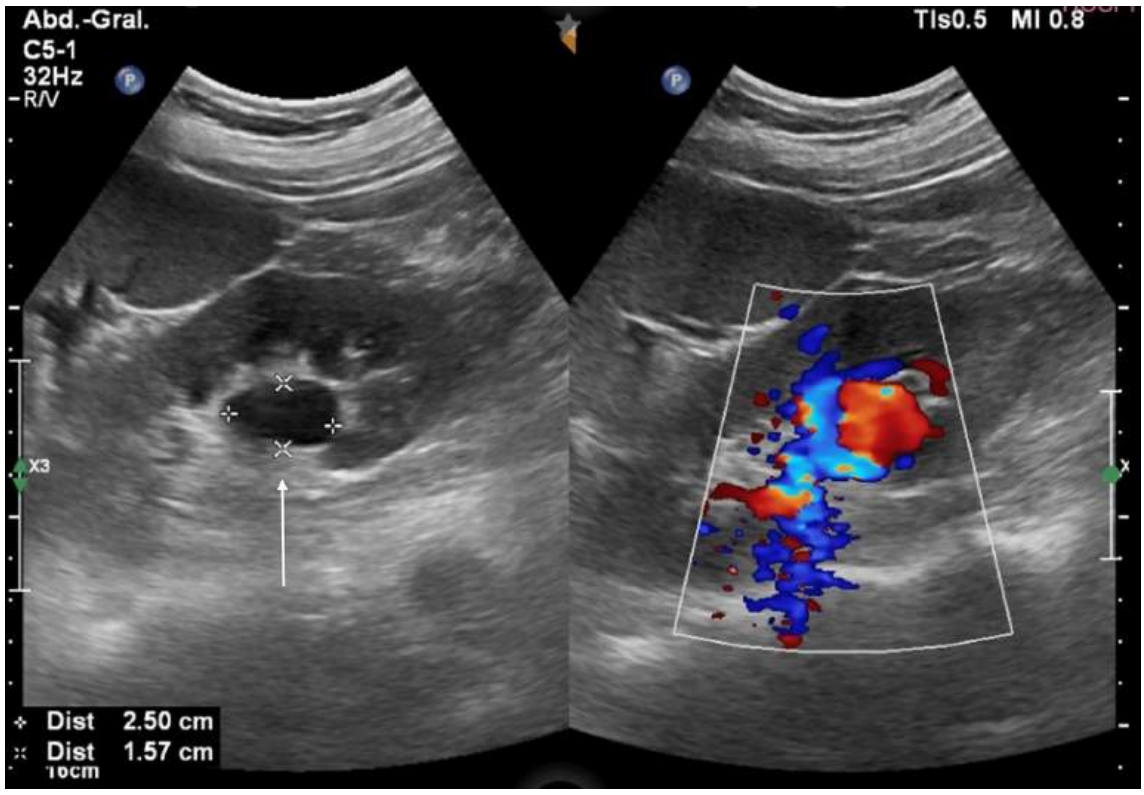


Figure 3. Color Doppler Ultrasound. Aneurysmal dilation of the inferior segmental artery with a yin-yang pattern measuring approximately 25 x 15 mm at the lower pole of the left kidney (arrow). Author's File.

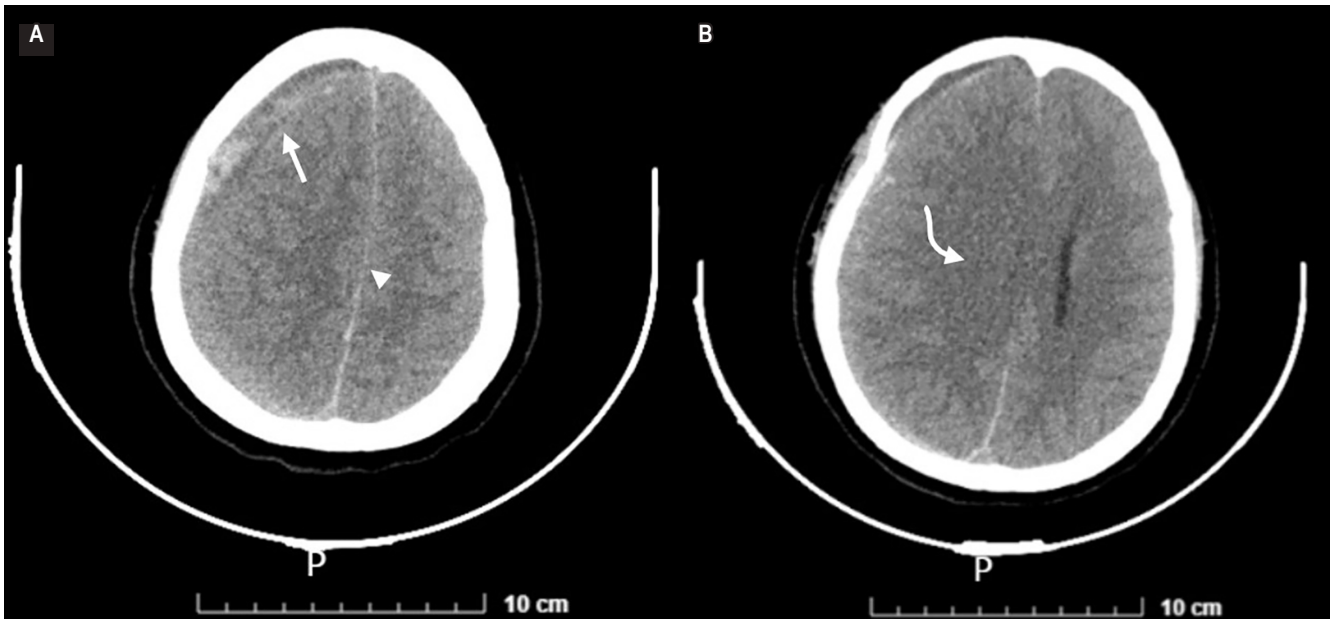


Figure 4. Cranial Computed Tomography. **A.** Chronic right subdural hematoma (arrow), with a 12 mm midline shift (arrowhead). **B.** Ventricular involvement (curved arrow). Author's File.

of the periduodenal vitelline veins, leading to the absence of the portal vein and diversion of blood flow into the systemic circulation[9]. It results from incomplete vascular remodeling between the symmetrical embryonic hepatoperihepatic circulations and the asymmetrical fetal system[10]. Another possible origin is agenesis of the ductus venosus, which predisposes the umbilical vein's oxygenated blood to bypass the liver and flow directly to the heart via persistent abnormal vessels, resulting in abnormal shunting and hypoplasia of the portal system[11].

Abernethy malformation is a rare and underdiagnosed condition, with few reported cases. From its first description in 1793 until 2021, 323 cases have been documented, with type I malformation being more prevalent than type II[12]. Approximately 70% of diagnosed cases occur in patients under 18 years of age[13], with an estimated global incidence of 2.5 cases per year[14]. In Ecuador, a case involving a 6-year-old child was reported in 2017[15].

In this case, the dermatological concern was spider veins consistent with hemangioma, a physical sign previously reported by Kothari[16] in two pediatric cases. This finding led to an incidental imaging diagnosis via computed tomography (CT). Subsequently, the patient experienced an episode of syncope, a symptom also described by Lin and colleagues[17] in two reported cases. Other documented clinical presentations of Abernethy malformation include cholestasis, precocious puberty, and growth restriction[18].

In our patient, venous hypoplasia was detected via ultrasound and diagnosed incidentally through 3D reconstruction angiography. El-Medany and colleagues[19] reported cardiological presentations as the reason for consultation in their cases and used magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound for diagnosis.

The complexity and rarity of this condition initially led to a clinical suspicion of portal vein thrombosis, as seen in the case of type I Abernethy malformation reported by Tamiru and colleagues[20], since the portal vein may appear poorly visualized in imaging studies, as occurred in both cases. Differential diagnoses, such as systemic lupus erythematosus and antiphospholipid syndrome, were also considered.

In this case, splenorenal collaterals, an aneurysm of the inferior segmental artery of the left kidney, and a shunt connecting the splenic and superior mesenteric veins to the inferior vena cava were identified. Therefore, other arteriovenous malformations must also be detected, similar to the case reported by Păcurar and colleagues[21], which involved type Ib Abernethy malformation with a hepatic artery originating from the superior mesenteric artery, hepatic veins forming a short common trunk before draining into the inferior vena cava, and a supernumerary right renal artery arising from the aorta.

The Morgan and Superina classification system[3] was used; however, other authors categorize Abernethy malformations into three types. Kobayashi and colleagues[22] des-

cribed types A, B, and C based on the location of portal blood drainage into the inferior vena cava, renal vein, or inferior mesenteric vein, respectively. Kanazawa and colleagues[23] classified hypoplasia according to its severity, as observed on angiography, into mild, moderate, or severe types.

Shunt closure can be performed via surgical ligation or endovascular balloon occlusion. However, conservative management may be appropriate for asymptomatic patients or those with incidental diagnoses[24]. Surgery is indicated in children with clinically significant disease, as spontaneous closure after the age of two years is unlikely, and complications can be severe[25]. The theoretical risk of portal vein thrombosis can be mitigated with anticoagulants such as heparin, although due to clinical heterogeneity, treatment must be individualized[26].

Early surgical intervention in pediatric cases leads to partial or complete regression of tumorous lesions, if present. Therefore, increased awareness of less common clinical presentations of portosystemic shunts is essential for early diagnosis[18], which can reduce complications and associated morbidity, improve the patient's quality of life, and optimize public healthcare system expenditures.

CONCLUSIONS

Abernethy malformation is rare in adult patients and, in this case, was an incidental diagnosis. The dermatological signs guided its discovery; however, although other cases of patients with Abernethy malformation and hemangioma have been reported, there is insufficient evidence to recommend this clinical feature as a reliable physical sign. This is further complicated by the existence of other conditions with similar clinical or imaging presentations. For these reasons, we encourage future researchers in this specific area to investigate whether a causal relationship exists and to provide a pathophysiological explanation, as well as to identify other vascular anomalies that may coexist in patients with extrahepatic portosystemic venous shunts.

Informed Consent and Patient Perspective

Written informed consent was obtained from the patient to publish her data anonymously. The patient reports an understanding of her condition and its severity and is currently willing to adhere to the planned clinical follow-up.

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Conflict of Interest

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Authorship Statement

All authors contributed to the collection, analysis, and interpretation of the data, as well as to the design and drafting of the content, and they approved the final version to be published.

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Case report

Jejunal Adenocarcinoma: A Report of Two Cases

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Abstract

Introduction: Adenocarcinomas of the small intestine are a rare cause of gastrointestinal neoplasms. Their incidence increases with age and has recently been reported to be on the rise, likely due to the implementation of advanced diagnostic tests. Nevertheless, they remain a diagnostic challenge, leading to delayed care, especially in patients with advanced disease, which limits treatment options and worsens prognosis. **Case Report:** This article presents two cases of patients diagnosed with jejunal adenocarcinoma. Both patients exhibited nonspecific symptoms and imaging and endoscopic evidence of small intestinal lesions. They were treated with minimally invasive surgery, and the diagnosis was confirmed histopathologically. The first patient experienced tumor recurrence at three years, presenting with advanced-stage disease. The second case involved hepatic and cervical lymph node metastases identified at the time of diagnosis. **Discussion and Conclusions:** Despite the atypical presentation and advanced stage at diagnosis, both patients received surgical and systemic oncological treatment. However, further studies are needed to assess the potential implementation of new diagnostic and therapeutic strategies aimed at improving clinical outcomes.

Keywords

Jejunum, adenocarcinoma, double-balloon enteroscopy, lymph nodes, neoplasm metastasis.

INTRODUCTION

Small intestine neoplasms are a rare clinical entity, accounting for approximately 5% of all gastrointestinal tumors[1,2]. Their incidence varies geographically, but the typical age of presentation is between 55 and 65 years, with a higher prevalence observed in male and Black populations[3]. There are four histological subtypes of small intestine malignancies, with adenocarcinomas and neuroendocrine tumors comprising over 50% of diagnosed cases. In recent years, an increase in the incidence of these tumors has been noted, likely attributable to advancements and greater accessibility in diagnostic tools; however, few studies have comprehensively described the true epidemiology of this disease[1,4,5].

Diagnosing small intestine adenocarcinoma poses a significant challenge for clinicians due to the variability and non-specificity of symptoms, which may present as abdominal pain, weight loss, occult gastrointestinal bleeding, or intestinal obstruction, among others. Surgical resection with negative margins and lymphadenectomy remains the cornerstone of treatment, offering favorable oncological outcomes in early-stage cases, with 5-year survival rates exceeding 85%[6–8]. Nonetheless, due to low clinical suspicion, non-specific symptomatology, the limitations of con-

ventional endoscopic examinations in visualizing lesions, and inconclusive imaging studies, over 60% of patients are diagnosed at an advanced stage. Additionally, there are significant gaps in knowledge regarding the efficacy of adjuvant therapies for these patients, with much of the available data extrapolated from colorectal cancer studies. This report presents two cases of small intestine adenocarcinoma, detailing their management and outcomes[1,2,5,9].

CASE DESCRIPTION

Case 1

This case involves a 67-year-old male patient presenting with a three-month history of progressive dyspeptic symptoms and vomiting. Initial diagnostic studies, including upper gastrointestinal endoscopy, colonoscopy, liver, pancreas, and biliary tract ultrasound, as well as magnetic resonance cholangiopancreatography, revealed no findings to explain the clinical presentation. However, a contrast-enhanced abdominal CT scan showed thickening of the jejunal walls over an extended segment, suggestive of an inflammatory or neoplastic process, without the detection of a discrete mass. An enteroscopy was performed, which identified an exophytic, concentric, and lumen-stenosing lesion located one meter distal to the ligament of Treitz in the mid-jejunum. Biopsies of the lesion confirmed the presence of jejunal adenocarcinoma (**Figure 1**).

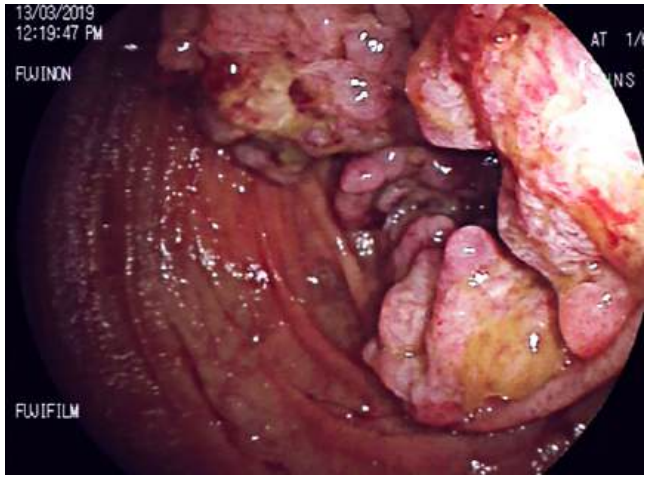


Figure 1. Enteroscopic image showing an infiltrative lesion in the proximal jejunum. Source: Medical record of Case 1.

The patient subsequently underwent laparoscopic surgery performed by the Gastrointestinal Surgery and Digestive Endoscopy Service. A solid, tumor-like lesion was identified 40 cm distal to the ligament of Treitz, accompanied by marked edema, retrograde dilation of the proximal bowel loops, and multiple mesenteric adenopathies near the mesojejunum. A segmental jejunal resection with primary end-to-end anastomosis and lymphadenectomy was performed. Pathological analysis confirmed a well-differentiated jejunal adenocarcinoma infiltrating the serosa, with negative margins, no lymphatic or vascular invasion, and 0/9 lymph nodes positive for malignancy. The tumor was staged as pT4N0M0 with no microsatellite instability.

Given the stage IIA classification, the Clinical Oncology team recommended surveillance only. However, the patient did not attend follow-up visits and returned three years later with imaging findings consistent with peritoneal carcinomatosis (omental cake) on contrast-enhanced abdominal CT. A positron emission tomography (PET) scan revealed multiple hypermetabolic peritoneal lesions suggestive of carcinomatosis, without hypermetabolic foci in the liver or distant extra-abdominal sites. A new staging laparoscopy demonstrated a peritoneal cancer index (PCI) of 17, with peritoneal involvement, moderate ascites, and nodular lesions in the small bowel mesentery, left diaphragmatic dome, and omentum. Multiple biopsies were taken, and histopathological and immunohistochemical analysis confirmed metastatic adenocarcinoma (**Figure 2**).



Figure 2. PET scan showing multiple areas of peritoneal involvement, with no other hypermetabolic foci. Source: Medical record of Case 1.

The patient is currently clinically stable, with an Eastern Cooperative Oncology Group (ECOG) performance sta-

tus of 0. He is receiving treatment for metastatic disease with a XELOX regimen combined with bevacizumab. The oncology team will assess the response to treatment to determine the feasibility and indication for cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC).

Case 2

This case involves a 58-year-old female patient with a history of hypertension and non-insulin-dependent diabetes. She presented with a two-year history of progressively worsening diffuse abdominal pain. In the four months leading up to her initial consultation, significant weight loss, normocytic anemia, and changes in bowel habits were noted. An upper gastrointestinal endoscopy and colonoscopy were performed but failed to identify the cause of her clinical presentation. A contrast-enhanced thoracoabdominal CT scan revealed diffuse, irregular, concentric thickening of the walls of a short jejunal segment, measuring 1.7 cm in thickness, with heterogeneous density. Additionally, a necrotic-centered mass was observed in the adjacent mesentery, along with lesions suggestive of metastases in the right ovary, left adrenal gland, and hepatic segments II, IV, and VIII.

The patient underwent enteroscopy, which identified an ulcerated exophytic lesion with fibrin coverage and circumferential involvement, narrowing the jejunal lumen by 50%, located 100 centimeters distal to the pylorus. The lesion was marked with India ink, and biopsies were taken (**Figure 3**).



Figure 3. Enteroscopic image showing an infiltrative lesion 1 meter distal to the ligament of Treitz. Source: Medical record of Case 2.

Histopathological analysis confirmed jejunal adenocarcinoma. Based on these findings, the Gastrointestinal Surgery and Endoscopy team performed a laparoscopic resection with end-to-end jejunal anastomosis, lymphadenectomy, omentectomy, and palliative right oophorectomy due to the risk of obstruction and persistent bleeding. The final pathology report identified a moderately differentiated jejunal adenocarcinoma with clear resection margins, serosal and adjacent fat involvement, and the presence of perineural and vascular invasion, with 0 out of 13 lymph nodes testing positive for malignancy. The omental and ovarian tissue samples were negative for malignancy, and there was no evidence of microsatellite instability.

The Clinical Oncology team recommended palliative surgery for jejunal adenocarcinoma. However, histopathological analysis found no evidence of malignancy in the mesenteric root lymph nodes, ovarian tissue, or peritoneal fluid. As a result, follow-up of the hepatic lesions with magnetic resonance imaging (MRI) was indicated, along with initiation of the FOLFOX chemotherapy regimen. During clinical follow-up, the patient developed a right supraclavicular adenopathy. Histopathological and immunohistochemical analysis confirmed mucinous adenocarcinoma of intestinal origin, with positive markers for CKAE1/AE3, CK20, CDX2, MUC1, and MUC2, and negative markers for CK7, PAX8, and MUC5AC. The patient is currently awaiting evaluation of her response to the initiated therapy to determine the most appropriate second-line treatment options.

DISCUSSION

Small intestine tumors have historically accounted for less than 5% of all gastrointestinal tract tumors, despite the small intestine being the longest segment of the digestive system. Some authors suggest that the low incidence in this location may be due to specific physiological characteristics, including rapid intestinal transit, the consistency of the chyme, which may reduce mucosal trauma, the segment's unique bacterial flora, and the protective role of the mucosal barrier with its high IgA concentration[1,3,10,11]. There are several histological subtypes of small intestine tumors, with adenocarcinoma being the most prevalent, accounting for 30% to 50% of cases, depending on the cohort analyzed. Neuroendocrine tumors rank second, followed by stromal tumors such as gastrointestinal stromal tumors (GIST), sarcomas, and lymphomas[3,4].

In a recently published study by Yao and colleagues in 2021, the U.S. population cancer database, which spans over 40 years, was reviewed to determine the prevalence of various histological types of small intestine tumors. The study reported a substantial increase in the diagnosis of neuroendocrine tumors, particularly those located in the duodenum, without corresponding changes in mortality

rates. This finding suggests either overdiagnosis or improvements in diagnostic and therapeutic processes. Notably, significant variations were also observed in the prevalence of sarcomas, GISTs, and lymphomas, accompanied by a marked reduction in mortality rates. This decline is likely attributable to the introduction of imatinib for the treatment of sarcomas and GISTs and rituximab for lymphomas. Lastly, an increase in the incidence of adenocarcinomas has also been documented, though without significant changes in mortality rates. This suggests that diagnoses are still being made at advanced stages of the disease, when the prognosis is poor[1].

Due to their location, jejunal and ileal adenocarcinomas are challenging to diagnose. Among the most common symptoms are recurrent episodes of gastrointestinal bleeding, with findings of bleeding stigmata during upper gastrointestinal endoscopy and colonoscopy, though without identification of a clear bleeding source, as well as diffuse abdominal pain. In more advanced stages of the disease, symptoms typical of other gastrointestinal neoplasms, such as weight loss, intestinal obstruction, and perforation with peritonitis, may also appear[8]. A retrospective study conducted at the University of Texas found that the most common site for small intestine adenocarcinoma was the duodenum (52% of cases), followed by the jejunum (25%) and the ileum (13%), with a median age of presentation of 55 years and a higher prevalence in men (61%). The epidemiological findings were consistent with the expected age of presentation for this condition[12].

The diagnostic process includes identifying non-specific gastrointestinal symptoms, as previously described, and employing diagnostic tools such as direct visualization via video capsule endoscopy or single- or double-balloon enteroscopy, with the latter method being preferred due to its capacity for biopsy collection and immunohistological analysis. Imaging studies offer improved sensitivity and specificity in locally advanced and metastatic stages. To date, no tumor markers provide reliable characterization of this condition, although there are reports of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) being used[2,8,12,13].

According to the 2022 National Comprehensive Cancer Network (NCCN) guidelines, treatment strategies for early and locally advanced stages include segmental resection with lymphadenectomy and margins of 5 to 10 cm. Due to the rarity of this condition, chemotherapy regimens are extrapolated from treatments for colonic adenocarcinomas. For adjuvant treatment of lesions classified as T3N0M0 or higher, 5-fluorouracil/leucovorin is recommended, while for metastatic or inoperable stages, FOLFOX, CAPEOX, or capecitabine are advised, with immunotherapy options such as bevacizumab or nivolumab depending on the tumor profile. Follow-up is conducted similarly to that for other gastrointestinal adenocarcinomas, with particular emphasis on the first two years, during which the risk of recurrence is highest[3,8,14].

In this case report, both patients underwent histological confirmation of their diagnosis via preoperative enteroscopy and received segmental resection with optimal lymphadenectomy in accordance with clinical guidelines. The first patient did not receive adjuvant therapy, while the second received palliative adjuvant chemotherapy due to the advanced stage of the disease. Despite the significant difference in initial staging, both patients experienced disease progression and have a poor survival prognosis, particularly when compared to the significant advances achieved in the management of other gastrointestinal tract malignancies, such as rectal adenocarcinoma[1,2,9,12].

CONCLUSIONS

Small intestine neoplasms pose a significant diagnostic challenge for healthcare teams due to their low incidence, nonspecific early symptoms, limited evidence on therapeutic approaches, and the difficulty of obtaining histopathological confirmation. Although recent publications have reported an increase in the diagnosis and potential overdiagnosis of neuroendocrine tumors, the epidemiology of adenocarcinomas—particularly those of the duodenum and jejunum—remains relevant, as their incidence has risen over time without improvements in survival outcomes despite the introduction of new treatment strategies[2,6,8].

The evidence regarding the treatment, staging, and follow-up of jejunal adenocarcinoma is limited due to the rarity of this disease. However, as with other gastrointestinal tumors, international guidelines recommend preventive strategies that include a healthy, fiber-rich diet, the consumption of at least 2 liters of water daily, a low intake of saturated fats, and regular exercise, defined as at least three sessions per week.

Jejunal adenocarcinoma remains a lethal condition, typically diagnosed at locally advanced or metastatic stages. Histopathological confirmation depends on obtaining tissue samples from anatomically challenging locations and often requires enteroscopy, which is not widely available, or staging laparoscopy, which is more invasive. Adjuvant and neoadjuvant therapy regimens are extrapolated from treatments for colonic and rectal neoplasms. The histopathological classification system and the limited understanding of lymphatic mapping to date hinder improvements in disease-free survival and overall survival rates[15–17].

The management and treatment of jejunal adenocarcinoma require a multidisciplinary team with expertise to facilitate early diagnostic suspicion and optimize surgical treatment, which is crucial to improving the low survival rates associated with this increasingly recognized condition according to the scarce evidence available in the literature[1,11].

Conflict of Interest

None of the authors have any conflicts of interest related to the planning, production, or writing of this article. It is also clarified that artificial intelligence was not used in any of the aforementioned stages of this article.

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Case report

Phlegmonous Gastritis in a Cirrhotic Patient with a Gastrointestinal Stromal Tumor

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Abstract

Phlegmonous gastritis is a rare disease with high mortality, developing from a pyogenic infection originating from gastric cancer or ulcers. Identified risk factors include immunosuppressive therapy and endoscopic procedures. Early diagnosis and intensive medical treatment are crucial, although emergency surgery may be required in some cases. We present the case of a 63-year-old woman with a history of liver cirrhosis and a gastrointestinal stromal tumor (GIST), who was admitted to the emergency department with secondary bacterial peritonitis following phlegmonous gastritis. In the subsequent days, the patient experienced a poor clinical course and a fatal outcome.

Keywords

Gastritis, liver cirrhosis, peritonitis, gastrointestinal bleeding.

INTRODUCTION

Phlegmonous gastritis is a rare and often fatal form of acute gastritis, with a mortality rate approaching 50%. It is characterized by a pyogenic infection of the gastric submucosa and muscularis propria, typically sparing the mucosal layer[1–5].

This condition is most commonly associated with *Streptococcus pyogenes*, though other microorganisms such as *Staphylococcus spp., Klebsiella pneumoniae, Escherichia coli, Haemophilus influenzae, Proteus,* and *Clostridium spp.* have also been implicated[4,6]. Clinical presentation is typically non-specific and includes abdominal pain, fever, nausea, vomiting, and signs of systemic infection[3].

We present the case of a 63-year-old woman with hepatic cirrhosis and a gastric gastrointestinal stromal tumor (GIST) who developed secondary bacterial peritonitis associated with phlegmonous gastritis, with *S. pyogenes* isolated in ascitic fluid and blood cultures.

CASE REPORT

The patient was a 63-year-old woman with hepatic cirrhosis due to metabolic dysfunction-associated steatotic liver disease (MASLD), previously classified as Child-Pugh B, without any history of acute decompensation. She presented to the emergency department with severe abdominal pain, rated at 9/10 in intensity. An upper digestive endoscopy performed three weeks earlier (**Figure 1**) revealed three medium-sized esophageal varices and a 23 x 26 mm ulcerated subepithelial lesion located in the gastric fundus.

Endoscopic ultrasound identified endosonographic features consistent with a gastric GIST (**Figure 2**). Fourteen days prior to admission, she experienced abdominal pain and ascites, followed by episodes of fever and disorientation five days before her arrival at the hospital.

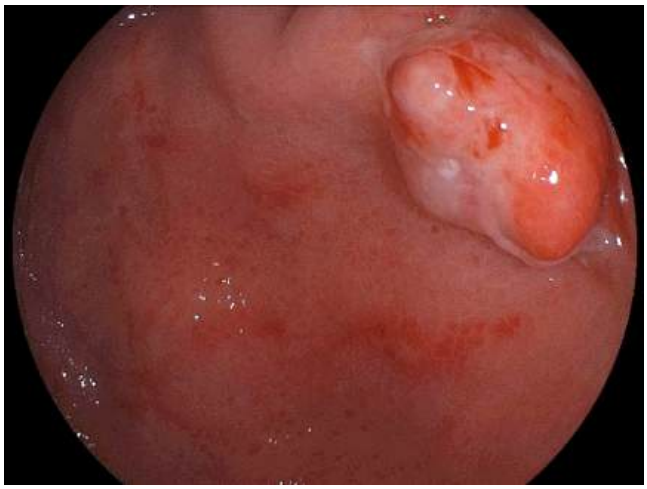


Figure 1. Upper digestive endoscopy showing an ulcerated gastric subepithelial lesion. Source: Gastroenterology Department, Hospital Cayetano Heredia.

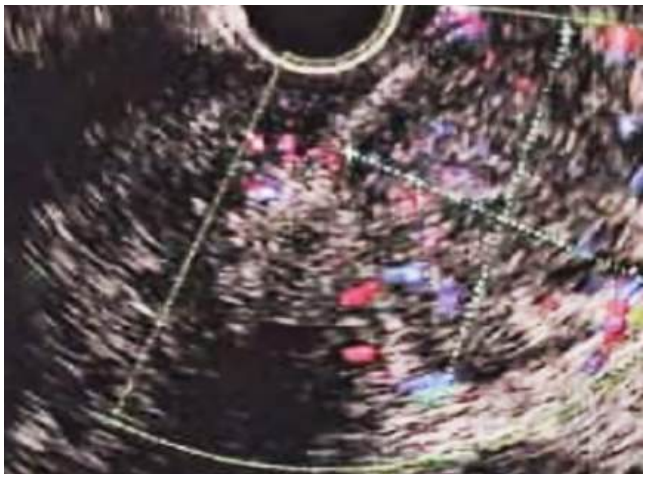


Figure 2. Endoscopic ultrasound showing a heterogeneous lesion in the fourth echolayer, measuring 23 x 26 mm, consistent with a GIST. Source: Gastroenterology Department, Hospital Cayetano Heredia.

On admission, the patient presented with tachycardia, normal blood pressure, and jaundice. Abdominal evaluation revealed shifting dullness and tenderness in the epigastric and mesogastric regions. Laboratory tests showed leukocytosis (14.61 cells/mm^3) with a left shift, thrombocytopenia, mildly elevated transaminases, elevated C-reactive protein (192 mg/L), and severe hypoalbuminemia (2.3 g/dL). Analysis of the ascitic fluid met Runyon's criteria[7], with protein levels of 2 g/dL, glucose at 47 mg/dL, and lactate dehydrogenase levels exceeding the upper limit of serum reference values, confirming a diagnosis of secondary bacterial peritonitis. Treatment with meropenem was initiated.

An abdominal computed tomography (CT) scan (**Figure 3**) revealed thickening of the gastric wall up to 13 mm, with peripheral mucosal and serosal enhancement and heterogeneous content within the thickened wall, without evidence of pneumatosis. A few days later, *S. pyogenes* was isolated in both the ascitic fluid and blood cultures. The final diagnosis was phlegmonous gastritis secondary to an ulcerated and infected gastric GIST. Broad-spectrum antibiotic therapy was continued; however, the patient's clinical course worsened, and she died five days after admission.

DISCUSSION

Phlegmonous gastritis is a form of acute gastritis caused by the invasion of the gastric wall by pyogenic organisms[8]. The diffuse type is more frequently reported than the localized (antral) type, the latter having a mortality rate of up to 54%[4,9–11].

It is essential to distinguish among three closely related nosological entities: gastric emphysema, phlegmonous gastritis, and emphysematous gastritis. Gastric emphysema refers to the presence of gas within the gastric wall following mucosal disruption and typically has a favorable prognosis[12], such as after endoscopic therapy. Phlegmonous gastritis involves the invasion of the gastric wall by pyogenic organisms, without the presence of gas in the gastric wall. In contrast, emphysematous gastritis is a rare, severe form of phlegmonous gastritis, characterized by suppurative inflammation of the gastric wall with gas present[8,10], and it frequently progresses to perforation[13]. Primary cases are often associated with an ulcer or neoplastic lesion, as in our case. However, secondary cases can arise from systemic infections, and in some instances, no identifiable origin is found (idiopathic cases)[14].

There are multiple risk factors, including conditions associated with immunosuppressive states (viral infections, diabetes *mellitus*, autoimmune diseases, chronic kidney disease, hepatic cirrhosis, leukemia, alcoholism, chemotherapy-induced neutropenia, malnutrition, chronic corticosteroid use) and those directly related to the stomach (mucosal injury, cancer, therapeutic endoscopic procedures). Our patient presented with Child-Pugh C cirrhosis during this hospitalization (previously Child-Pugh B) and an ulcerated gastric GIST larger than 2 cm, as well as a recent endoscopic ultrasound performed in the preceding days[3,5].

The clinical presentation is non-specific but often involves sepsis, upper abdominal pain, peritonitis, and purulent

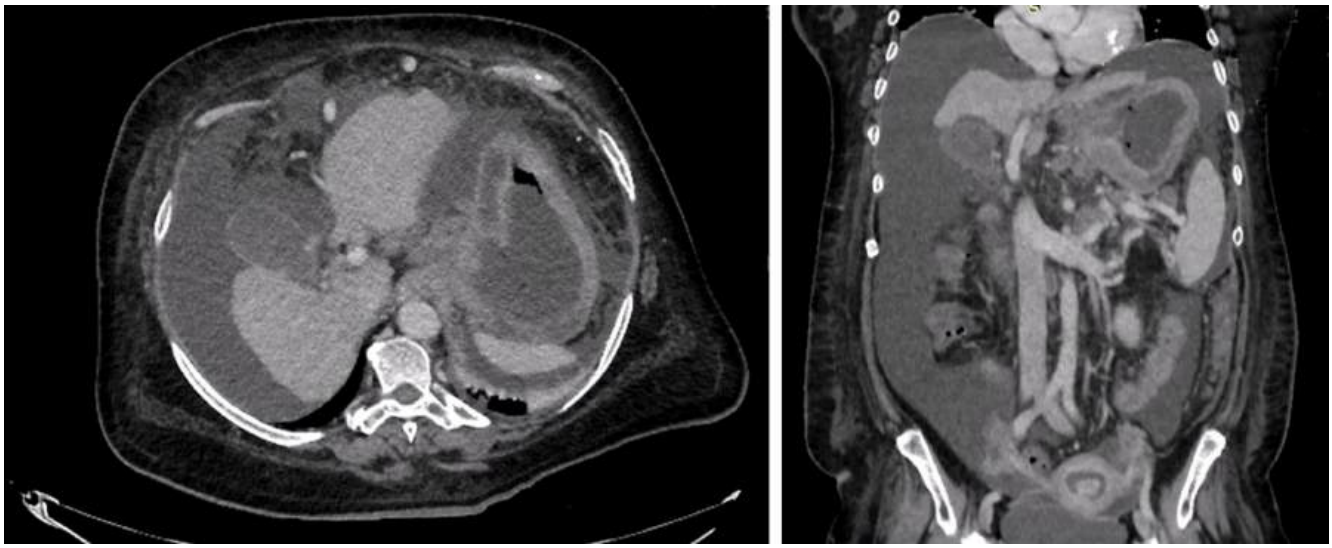


Figure 3. Abdominal computed tomography showing gastric wall thickening with peripheral mural enhancement. Source: Gastroenterology Department, Hospital Cayetano Heredia.

ascites[1]. Other manifestations include nausea, vomiting, and hematemesis. Since it poses a diagnostic challenge, computed tomography (CT) is a valuable tool, with key findings including gastric wall thickening and abscesses[4,15,16].

Upper gastrointestinal endoscopy may reveal mucosal erythema and edema, while endoscopic ultrasound is the most effective diagnostic test, as it allows for the identification of submucosal edema and thickening. Rapid initiation of antibiotic therapy after diagnosis—or even in cases of high clinical suspicion—is recommended, as delayed treatment is associated with a high mortality rate, approaching 92%[6,14].

The frequency of ascites or secondary bacterial peritonitis in phlegmonous gastritis is unknown. Severe cases may have unfavorable outcomes due to perforation[17]. In such situations, urgent surgical intervention is necessary, and studies have reported a significantly lower mortality rate following surgery[14,18].

Our patient did not initially undergo surgical treatment due to the absence of signs of perforation and the potential postoperative complications in a patient with Child-Pugh C cirrhosis. Subsequently, as her clinical condition deteriorated, her family declined surgical intervention. In such cases, we believe that treatment decisions should be individualized for each patient.

CONCLUSIONS

Phlegmonous gastritis is a rare condition with a high mortality rate, necessitating a high index of diagnostic suspicion. Computed tomography and endoscopic ultrasound are crucial for early diagnosis. Early antibiotic therapy is associated with a better prognosis. Surgical management should be considered in cases of poor clinical evolution, diffuse forms of the disease, or perforation.

Conflict of Interest

The authors declare no conflicts of interest.

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Case report

Dieulafoy's Lesion: A Case Report with an Atypical Anatomical Variation

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Abstract

Dieulafoy's lesion is a rare and potentially life-threatening cause of gastrointestinal bleeding, resulting from vascular injury due to submucosal erosion that penetrates through the mucosa. It can lead to gastrointestinal hemorrhage with severe complications. This condition accounts for 1%–2% of gastrointestinal bleeding cases, most commonly occurring in the gastric fundus, and it typically affects individuals over 50 years of age with multiple comorbidities. This report describes a rare etiology of gastrointestinal bleeding associated with a thrombectomy and an atypical anatomical location.

Keywords

Dieulafoy's lesion, gastrointestinal bleeding, angiodysplasia, hemorrhagic shock.

INTRODUCTION

Dieulafoy's lesion is a rare but potentially life-threatening clinical entity first described in 1884 by Gallard, who, during the autopsies of two patients with massive gastrointestinal hemorrhage, identified what he termed *miliary aneurysms of the stomach*. It was not until 1897 that the French surgeon Paul Georges Dieulafoy noted that these lesions could progress into gastric ulcers, referring to them as *exulceratio simplex*[(1)]. Dieulafoy's lesion accounts for approximately 5% of gastrointestinal hemorrhages in adults[(2)]. These lesions are typically described as a form of angiodysplasia involving the submucosal exposure of a blood vessel within the gastrointestinal tract, which can erode over time and lead to severe bleeding. Most lesions (70%) occur proximally within the stomach, with the remaining distributed across the duodenum (15%), esophagus (8%), colon (2%), and anus (1%)[(3)]. The condition is associated with high mortality rates, reaching up to 80% in cases where early detection is not achieved[(4)].

We present the case of a male patient who, following thrombectomy for grade IV thrombosed hemorrhoids, experienced massive gastrointestinal hemorrhage accompanied by hemodynamic instability. Endoscopy and colonoscopy were performed, with the latter revealing an actively bleeding Dieulafoy's lesion. Hemostasis was achieved

through sclerotherapy with adrenaline and the placement of a hemostatic clip on the affected vessel.

CLINICAL CASE

The patient is a 69-year-old male with no prior comorbidities who was recently hospitalized for rectal bleeding. A colonoscopy revealed diverticulosis in the descending-sigmoid colon and inflamed, thrombosed grade IV hemorrhoids. During his hospital stay, a thrombectomy of three hemorrhoidal bundles was performed, and the patient was discharged following satisfactory clinical progress.

Five days after discharge, the patient presented to the emergency department with a two-hour history of rectal bleeding, accompanied by diaphoresis and a syncopal episode. Upon admission, vital signs indicated bradycardia (heart rate [HR]: 52 beats per minute [bpm]) and hypotension (blood pressure [BP]: 85/50 mm Hg with a mean arterial pressure [MAP] of 61 mm Hg). Physical examination revealed mucocutaneous pallor and moderate active bleeding upon digital rectal examination. Suspecting hemorrhagic shock of lower gastrointestinal origin, the patient was managed with an 80 mg bolus of omeprazole, followed by a continuous infusion at 8 mg/hour, along with fluid resuscitation using crystalloids. Initial laboratory findings were as follows: hemoglobin (7.4 g/dL), platelet count (371,000/µL), serum creatinine (1.2 mg/dL), blood urea nitrogen (24 mg/dL), lactate (2.3 mg/dL), prothrombin time (12.1 seconds), partial thromboplastin time (21.6 seconds), and international normalized ratio (1.17). The patient was transferred to the intensive care unit (ICU), where two units of red blood cells were transfused. Endoscopy, colonoscopy, and an abdominal-pelvic angiography were requested. The angiography of the abdomen and pelvis revealed findings consistent with arterial atheromatosis but showed no evidence of aortic syndrome or other abnormalities.

After 48 hours, upper gastrointestinal endoscopy and colonoscopy were performed. The endoscopy showed Forrest IIB and III gastric ulcers that required adrenaline sclerotherapy, as well as erosive duodenitis. The colonoscopy revealed grade IV internal hemorrhoids, a thrombectomy scar on the right anterior hemorrhoidal site, and an actively bleeding Dieulafoy's lesion (**Figure 1**). A hemostatic clip was applied to the base of the vessel to prevent further bleeding (**Figure 2**).

The patient maintained hemodynamic stability 48 hours post-procedure, with stable vital signs and no recurrence of bleeding. Therefore, outpatient management was deemed appropriate. An outpatient follow-up appointment with colorectal surgery and general surgery was scheduled, and the patient has remained under continuous follow-up with no recurrence of gastrointestinal symptoms since discharge.

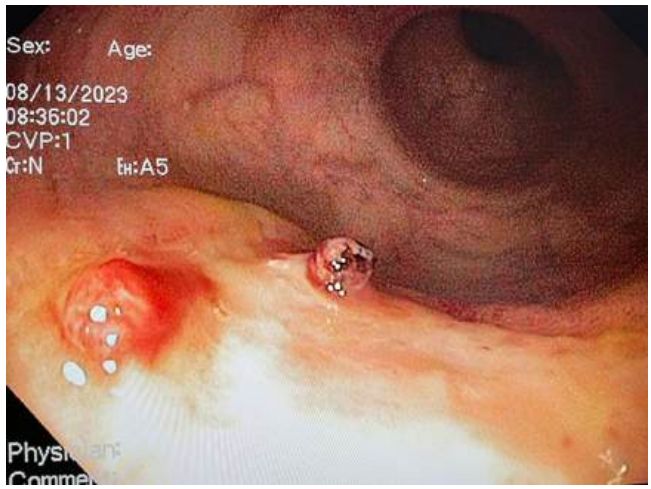


Figure 1. Colonoscopy showing the exposed vessel. Courtesy of Dr. Gilberto Jaramillo.

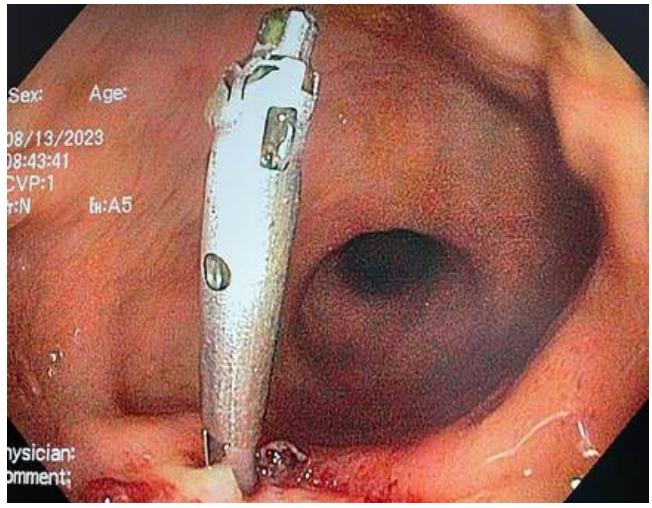


Figure 2. Hemostatic clip placed on the Dieulafoy's lesion. Courtesy of Dr. Gilberto Jaramillo.

DISCUSSION

Dieulafoy's lesion poses a significant diagnostic challenge in patients with gastrointestinal bleeding due to its rare etiology and high mortality rate. In this case, the lesion presented in an unusual location—the rectum—following a surgical procedure. Rectal location is uncommon and can be mistaken for vascular anomalies such as arteriovenous malformations or aneurysms[5]. Diagnosis must be meticulous, as in the absence of active bleeding, these lesions may be confused with other findings, such as polyps, or the culprit vessel may appear intact without erosion or ulceration[6]. The vessel may also only become visible during active bleeding or may be obscured by a clot after a prior bleeding episode[7]. Endoscopic criteria for diagnosing Dieulafoy's lesion include: active arterial bleeding with micropulsatile

flow and small mucosal defects (<3 mm) without mucosal ulceration or erosion; visible protrusion of the vessel; and the presence of clotted blood at the mucosal junction[8].

The diagnostic yield of endoscopy for Dieulafoy's lesion is approximately 70% in gastric lesions, which are the most common presentation. In some studies, this rate dropped to 49%, with up to 33% of patients requiring a second endoscopic procedure[9]. In a study evaluating rectal Dieulafoy's lesions, colonoscopy failed to diagnose 9% of patients, and surgical intervention was necessary in some cases to confirm the diagnosis[10]. Although there is no consensus on the optimal treatment approach for Dieulafoy's lesion, endoscopic management remains the first-line treatment, supported by thermal therapies, regional epinephrine injection, and mechanical methods. The use of hemostatic clips has proven to be an effective and simple technique for preventing massive bleeding and rebleeding[11]. Other diagnostic methods, such as computed tomography angiography or contrast-enhanced magnetic resonance imaging, are rarely employed for detecting rectal lesions and are typically reserved for cases in which colonoscopy fails to establish a diagnosis[12].

Surgical intervention is often the definitive method to achieve hemostasis, particularly when previous approaches fail and the patient remains hemodynamically unstable. Studies indicate that 3% to 16% of patients require surgery, primarily due to recurrent bleeding episodes following endoscopic therapy[13].

CONCLUSION

Dieulafoy's lesion is a rare condition, and rectal location is an even less common anatomical site. However, it should be considered in patients presenting with massive gastrointestinal bleeding, particularly due to the often-intermittent nature of the bleeding, which can limit diagnostic investigations. A high index of suspicion is essential, especially in patients with a history of surgical interventions, as illustrated by this case. There are no clear guidelines on the optimal therapy for rectal lesions; however, endoscopic intervention combined with argon plasma coagulation or epinephrine injection is considered the standard treatment. The use of hemostatic clips has proven to be an effective adjunct therapy in cases of hemodynamic instability, as observed in our patient. Surgical intervention should be reserved for refractory cases where all previous therapeutic approaches have failed. Given the rarity of this condition, future research opportunities remain open, including the creation of a population-based registry to systematically organize data on patients with Dieulafoy's lesion.

Conflict of Interest

The authors declare no potential conflicts of interest related to the research, authorship, or publication of this article.

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Consent for Publication

Written consent from the patients was not obtained, as this report does not include identifiable patient data.

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Case report

Intestinal Perforation Associated with Chicken Bone Ingestion: A Case Report

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Abstract

Introduction: Intestinal perforations caused by foreign bodies are rare, occurring in less than 20% of cases. The clinical presentation is nonspecific and can mimic other surgical pathologies, making diagnosis often intraoperative. Treatment for such cases is surgical. **Objective:** To describe the case of an elderly female patient presenting with acute abdomen, where an incidental finding of a foreign body was identified through abdominal computed tomography, revealing a chicken bone that perforated an intestinal loop. **Discussion:** Foreign bodies in the gastrointestinal tract often go unnoticed in many individuals as they typically do not cause symptoms. When complications arise, the symptoms are nonspecific, and the diagnosis is usually made during surgery. Therefore, thorough history-taking, a high index of suspicion in certain patients, and timely management are critical. **Conclusion:** Intestinal perforation caused by foreign bodies is uncommon. Diagnostic suspicion is crucial, and surgical treatment is an important approach in managing these complications.

Keywords

Intestinal perforation, peritonitis, abdominal pain, general surgery, mortality.

INTRODUCTION

Foreign body ingestion is a common occurrence across healthcare services, with pediatric patients being disproportionately affected[(1)]. In most cases (80%–90%), foreign bodies that pass through the gastrointestinal tract do not cause any harm; however, some patients experience complications such as bleeding, ulceration, mucosal erosion, local scarring, or perforation[(2)].

The clinical presentation of intestinal perforations is typically acute and rapidly progressive, necessitating urgent surgical intervention. The foreign bodies most frequently associated with this complication include fish bones, chicken bones, toothpicks, and dentures, among others[(2,3)]. In terms of management, patients without clinical deterioration are often placed on watchful waiting. However, in approximately 10%–20% of cases where complications arise, endoscopic intervention is required, while 1% of patients require urgent surgical procedures[(1)].

This case report describes an elderly female patient who presented to the emergency department with acute abdominal pain and underwent surgery, during which an

incidental foreign body was identified as the cause of intestinal perforation. The objective of this report is to highlight how foreign body ingestion can lead to significant clinical deterioration in some patients.

CASE DESCRIPTION

The patient was a 72-year-old female with a medical history of arterial hypertension and breast cancer, presenting with a four-day history of generalized abdominal pain accompanied by distension and nausea. An external abdominal ultrasound had revealed a renal cyst and cholelithiasis. Due to persistent symptoms, she was admitted to the emergency department. Upon initial assessment, she presented with generalized abdominal pain, predominantly in the mesogastrium, and significant abdominal distension.

Laboratory tests revealed hypocalcemia, elevated nitrogenous waste levels, hypoglycemia, moderate hypokalemia, and arterial blood gases indicative of metabolic acidosis. Radiographic and contrast-enhanced abdominal and pelvic CT scans showed signs of hollow intestinal loop rupture, free fluid, and inflammatory changes in the peritoneum. Additionally, the imaging revealed a linear hyperdense structure in the left adnexal region and sigmoid colon, along with a right cortical renal cyst and cholelithiasis (**Figure 1**).

The patient was evaluated by the surgical team, who decided to perform an urgent exploratory laparotomy. Intraoperatively, diffuse peritonitis involving all four abdominal quadrants was observed (with 1600 mL of purulent fluid), as well as evidence of rectal perforation caused by a foreign body (a chicken bone) (**Figure 2**). A partial colectomy and colostomy were performed, and the foreign body was removed (**Figure 3**). Postoperatively, the patient required intensive care unit (ICU) monitoring and was administered a broad-spectrum antibiotic regimen for one week.

DISCUSSION

Foreign body ingestion is generally not a clinical concern, but in some cases, it can lead to significant complications. A direct relationship has been reported between the size of the foreign body and the location of the complication. Specifically, objects thicker than 2 cm and longer than 6 cm rarely pass through the gastrointestinal tract[4]. It is important to note that not all foreign bodies are visible using certain radiological studies; for instance, wooden splinters and some plant thorns are not detectable on standard X-rays.

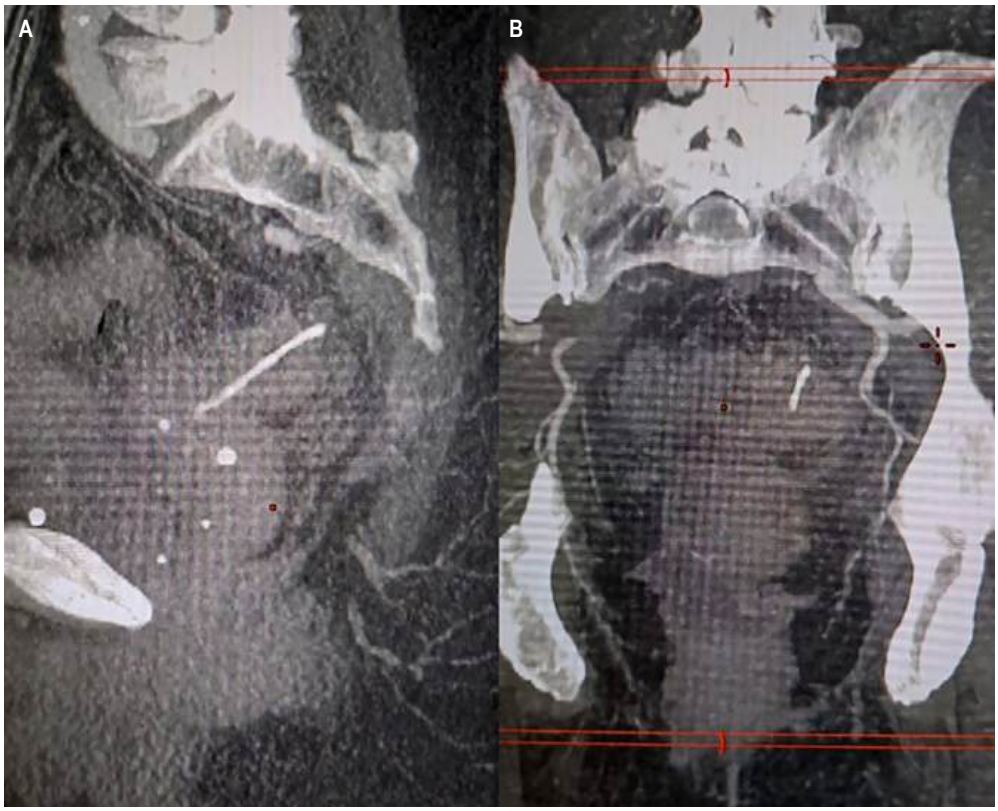


Figure 1. Abdominal and pelvic CT scan showing signs of hollow intestinal loop rupture, free fluid, inflammatory changes in the peritoneum, and a linear hyperdense structure in the left adnexal region and sigmoid colon. Image courtesy of the Radiology Department, Fundación Cardiovascular de Colombia. Bucaramanga, Colombia.

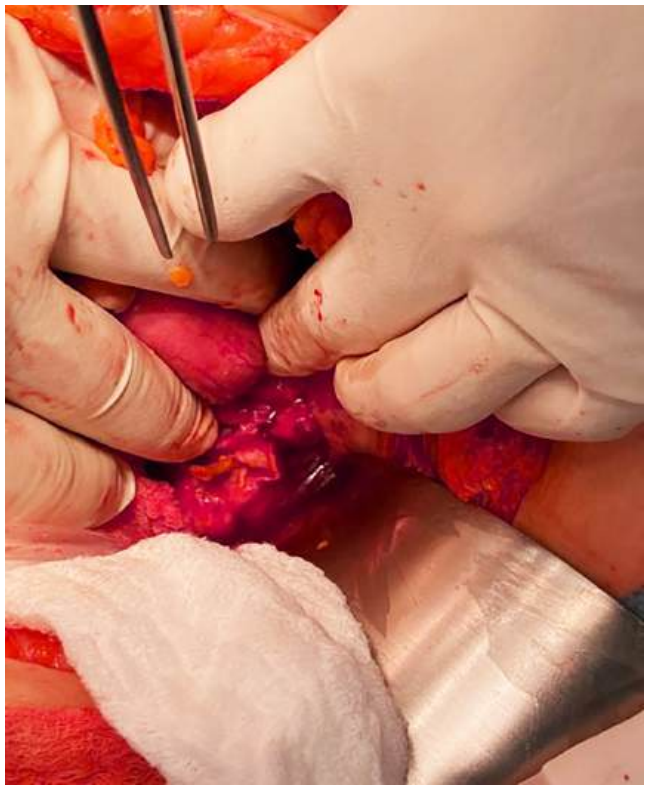


Figure 2. Intraoperative finding of mid-rectal perforation caused by a foreign body (chicken bone). Image courtesy of the Surgery Department, Fundación Cardiovascular de Colombia. Bucaramanga, Colombia.

Certain conditions, such as stenotic lesions, fistulas, or diverticula, increase the risk of complications associated with foreign body ingestion. In cases involving chicken bone ingestion—considered a sharp object—the rate of gastrointestinal tract complications has been estimated to be as high as 35%[1].

Preoperative diagnosis of perforations is rare, as their clinical presentation can be non-specific, especially in cases of peritonitis, abscesses, enterovesical fistulas, obstructions, or hemorrhages, all of which can mimic other surgical pathologies. Common symptoms in such cases, as well as in other reported patients, include abdominal pain and distension lasting several days[5]. The most frequent sites of perforation are the distal ileum, cecum, and left colon. Contrast-enhanced computed tomography (CT) is one of the recommended diagnostic methods for such cases, as reported in the literature, as it can detect small objects such as bones[6–8]. Additionally, for cases in which bones have not passed the proximal duodenum, endoscopy is advised[9].

Surgical treatment should be individualized. In patients without hemodynamic involvement, conservative management may be effective; however, in patients presenting with acute abdomen due to intestinal perforation, surgical resection is the optimal approach[10].

CONCLUSIONS

Foreign bodies that enter the gastrointestinal system generally do not cause any clinical implications for patients. However, larger objects can cause complications in various parts of the digestive system. One such complication is intestinal perforation, which can occur due to the narrowing and angulation of the gastrointestinal tract. In these cases, surgical intervention involving colonic resection is necessary.



Figure 3. A. Partial colectomy specimen and extracted foreign body. **B.** Extracted chicken bone, measuring 5 cm in length. Source: Surgery Department, Fundación Cardiovascular de Colombia. Bucaramanga, Colombia.

Ethical Responsibilities

This study was conducted in accordance with the prevailing guidelines for clinical research and received prior approval from the institution's scientific committee. Informed consent and authorization were obtained from the patient. The guidelines established in Resolution 008430 of 1993 by the Colombian Ministry of Health and the Declaration of Helsinki, first issued in 1964 and last updated in October 2013, were followed. The recommendations of good clinical practice guidelines for clinical research and the fundamental ethical principles of respect for persons, beneficence, and justice outlined in the Belmont Report were adhered to.

Protection of Human and Animal Subjects

The authors declare that no experiments were conducted on humans or animals for this study.

Conflict of Interest

The authors declare no conflicts of interest.

Funding Sources

This study was self-funded by the authors.

Use of Artificial Intelligence

The authors declare that no artificial intelligence (AI) technologies, such as large language models, chatbots, or image generators, were used in the preparation of this work.

Author Contributions

JCSR, GCP, and EFMH participated in the study design, research protocol planning, data collection, patient case analysis, and manuscript preparation. JDCS and EDGG contributed to the study design, research protocol planning, and manuscript revisions.

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Letter to the editor

Commentary on "Information Needs of Patients with Cirrhosis of the Liver and Quality of Life"

Deydania Gimna Pastor-Baraco.[1*]

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Dear Editor,

After reviewing with great interest the recent article by Yepes-Barreto and colleagues (2024)[1], which highlights the prioritized information needs of patients with cirrhosis and the actual use of certain support services to estimate their relationship with quality of life using the SF-36 version 2 survey, I would like to offer some observations and constructive suggestions.

Firstly, the SF-36 version 2 scale is a generic, non-disease-specific questionnaire applied to collective groups to outline a health status profile[2]. However, there are specific instruments tailored to certain pathologies, such as the Chronic Liver Disease Questionnaire (CLDQ). The CLDQ is the first disease-specific tool designed to evaluate health-related quality of life (HRQoL) in relation to the progression or severity of chronic liver disease, such as cirrhosis, using coherent, comprehensible, and concise questions[3]. The CLDQ has undergone transcultural adaptation and validation in various languages, including Spanish, demonstrating its feasibility, reproducibility, ease of adaptation, and fairness[4]. A study by Janani and colleagues (2018) demonstrated that disease severity and related complications impact HRQoL[5]. Consequently, the combination of a generic scale with a disease-specific tool is sometimes used to address and detect significant clinical changes resulting from interventions[6].

Secondly, the study by Yepes-Barreto and colleagues (2024) used telephone interviews, which pose a higher likelihood of response bias, particularly among patients with lower educational levels[7] and those over the age of 75[8].

Thirdly, the same study identified the selection of three support services by patients based on their preferences. However, a more precise assessment of support needs in patients with cirrhosis is available through the first Support Needs Assessment Tool for Cirrhosis (SNAC). This 39-item, disease-specific instrument measures the type and extent of perceived support needs, promoting patient-centered care and facilitating timely referrals to various multidisciplinary support services[9].

In conclusion, the study by Yepes-Barreto and colleagues (2024) offers valuable insights into the information needs and support services for patients with liver cirrhosis. However, the inclusion of more specific assessment tools, such as the CLDQ and SNAC, along with data collection methods that minimize bias, could significantly enhance the quality and applicability of the findings. I commend the authors for their efforts and hope these observations prove useful for future research in this important field.

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Response to the letter to the editor: Commentary on "Information Needs of Patients with Cirrhosis of the Liver and Quality of Life"

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As noted in your letter, there are both generic and disease-specific tools available for measuring health-related quality of life (HRQoL). The SF-36 version 2 scale was selected for the study due to its accessibility, widespread use, and extensive validation in various languages, including Spanish. It has proven to be effective in different clinical settings. In contrast, the Liver Disease Quality of Life Instrument (LDQOL), though specifically designed for patients with cirrhosis, is more limited in its application. Moreover, while the LDQOL has been validated in Spanish, the validation was conducted in a European population, which means its results may not be directly generalizable to our study population[(1)].

It is also important to note that the questions included in the LDQOL are designed to detect changes in quality of life related to symptoms of advanced liver disease. However, our cohort primarily consisted of patients with compensated cirrhosis, for whom the SF-36 version 2 is more likely to capture variations in quality of life.

Lastly, we believe the suggestion to use a tool like the Support Needs Assessment for Cirrhosis (SNAC) is highly relevant, as it could have provided a more precise and structured assessment of the support service needs of this population. It is important to mention that although the data collection for the study was carried out in 2021, the research protocol was designed and submitted for approval to the Ethics Committee of Universidad de Cartagena in early 2020, at a time when information on the SNAC was not yet available. We sincerely appreciate your comments and will take them into account for future research in this area.

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Determinants of quality of life in women with liver cirrhosis

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Dear Editor,

We read with great interest the article by Yepes-Barreto and colleagues[(1)], which aimed to explore the association between quality of life and sexual function in female patients with liver cirrhosis through the use of questionnaires and clinical assessments. We believe that this study is highly relevant for improving the care of women with liver cirrhosis. However, we would like to share some comments regarding the variables employed. We were struck by the omission of certain sociodemographic variables in the analysis, as these are cited in several studies as significant factors contributing to reduced quality of life in cirrhotic patients. For instance, in the study by Teshome and colleagues, low educational attainment, lack of access to health insurance, and residence in rural areas were identified as factors that diminish patients' quality of life[(2)]. Similarly, other studies have assessed economic stability-related variables. In the study by Pradhan and colleagues, unemployment and low income were found to negatively impact patients' quality of life[(3)]. Additionally, research by Souza and colleagues established a relationship between low household income and poor quality of life in these patients, reporting a statistically significant value of $p = 0.03$, underscoring the importance of this variable in the assessment of quality of life[(4)].

It is also important to highlight the availability of disease-specific questionnaires, such as the Liver Disease Quality of Life (LDQOL) 1.0 instrument. This tool incorporates the SF-36 questionnaire and adds 12 disease-specific scales, providing a more comprehensive assessment of liver disease-related quality of life. This instrument has been validated in countries such as Brazil, where it demonstrated strong reliability in studies involving cirrhotic patients[(5)]. Notably, this tool has also been employed in Colombia to assess the quality of life of liver transplant patients, yielding significant findings when comparing pre- and post-transplant outcomes[(6)].

Based on the literature review, we conclude that studies should include sociodemographic factors to enhance their findings, as these variables act as confounding factors that indirectly affect patients' quality of life, particularly in low-resource settings. We also recommend the future adaptation of liver cirrhosis-specific questionnaires to obtain a more detailed analysis of quality-of-life outcomes.

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Response to the letter to the editor

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Dear Editor,

In response to the letter to the editor regarding our article Quality of Life and Sexual Function in Women with Liver Cirrhosis in Colombia[(1)], we would like to state the following: Female sex has consistently been identified in various studies and geographic regions as a negative predictor of quality of life in patients with liver cirrhosis. The observations made about the absence of certain sociodemographic data (educational level, place of origin, and health insurance coverage) in the analysis of these patients' quality of life are valid. In this regard, we would like to clarify that all patients were beneficiaries of the Colombian Mandatory Health Plan (affiliated with a Health Promoting Entity [EPS in Spanish]) and resided in the urban area of Cartagena. Therefore, due to the homogeneity of this information across the sample, these variables were subsequently excluded from the analysis.

Unfortunately, information on educational level was not collected during patient interviews, and a reliable source to obtain this data afterward was not found, which is why it was not included in the study. Although we were unable to quantify the patients' income, we did gather socioeconomic stratum data (ranging from 1 to 6) through the Social Program Beneficiary Identification System (SISBEN), which classifies patients based on income and living conditions. Eighty percent of the patients belonged to strata 1, 2, and 3, which are considered low-income groups.

Regarding the use of the SF-36 version 2 scale, it was selected for the study due to its accessibility, widespread use, and extensive validation in multiple languages, including Spanish, which has proven its utility in various clinical settings. Conversely, although the Liver Disease Quality of Life Instrument (LDQOL) was specifically designed for patients with cirrhosis, its application is more limited, and the fact that it has been used in studies conducted in Colombia and Brazil does not necessarily imply that the survey underwent a validation process prior to its use in those contexts.

We sincerely appreciate your comments and will take them into account for future research in this area.

Sincerely,

The authors

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