Bile Reflux Gastritis in Patients with Chronic Heartburn: Prevalence, Pathophysiology, and Clinical Relevance

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Abstract

Chronic heartburn is a prevalent gastrointestinal complaint traditionally attributed to acid-mediated gastroesophageal reflux disease (GERD). However, increasing evidence suggests that non-acid components, particularly duodenogastric bile reflux, play a significant yet under-recognized role in the pathogenesis of persistent upper gastrointestinal symptoms. Bile reflux gastritis, characterized by the retrograde flow of bile acids and duodenal contents into the stomach, has been increasingly identified in patients with chronic heartburn, especially those who demonstrate suboptimal response to conventional acid-suppressive therapy. Despite its clinical relevance, the true prevalence of bile reflux gastritis in this population remains uncertain due to diagnostic limitations and overlapping clinical and histopathological features with other forms of gastritis.

This review aims to comprehensively evaluate the prevalence, underlying pathophysiological mechanisms, and clinical significance of bile reflux gastritis in patients presenting with chronic heartburn. It explores the complex interaction between gastric and esophageal mucosal injury induced by bile acids, pancreatic enzymes, and gastric acid, emphasizing the concept of mixed reflux. Particular attention is given to the disruption of gastroduodenal motility, pyloric incompetence, and alterations in gastric emptying that facilitate bile reflux. Furthermore, the review highlights the challenges associated with diagnosing bile reflux gastritis, including the limitations of endoscopy, histology, and ambulatory reflux monitoring techniques.

Clinically, bile reflux gastritis may contribute to persistent dyspeptic symptoms, refractory heartburn, and mucosal damage that extends beyond the stomach to the esophagus. The condition has also been implicated in the development of complications such as intestinal metaplasia and Barrett's esophagus, underscoring its potential long-term significance. Therapeutic strategies remain challenging, as standard proton pump inhibitors do not adequately address bile-mediated injury, necessitating consideration of alternative medical and surgical approaches.

In conclusion, bile reflux gastritis represents an important but often overlooked contributor to chronic heartburn. Improved recognition, diagnostic precision, and targeted management strategies are essential to optimize outcomes in affected patients and to address an important gap in current gastroenterological practice.

Keywords: *Bile Reflux Gastritis, Chronic Heartburn*

Introduction

Chronic heartburn is one of the most common gastrointestinal symptoms encountered in clinical practice and is most frequently attributed to gastroesophageal reflux disease (GERD), a condition traditionally driven by gastric acid exposure to the esophageal mucosa. However, a substantial subset of patients continues to experience persistent symptoms despite optimal acid-suppressive therapy, particularly with proton pump inhibitors (PPIs). This clinical scenario, often termed refractory GERD, has prompted increasing interest in alternative and complementary mechanisms of mucosal injury beyond acid reflux alone. Among these, bile reflux—resulting in bile reflux gastritis—has emerged as a significant yet underappreciated contributor to upper gastrointestinal symptomatology, particularly in patients with chronic heartburn. [1–3]

Bile reflux gastritis is characterized by the retrograde flow of duodenal contents, including bile acids, pancreatic enzymes, and intestinal secretions, into the stomach, leading to mucosal irritation and inflammation. Under physiological conditions, coordinated gastroduodenal motility and an intact pyloric sphincter prevent such reflux. However, disruption of these mechanisms—whether due to motility disorders, surgical alterations, or functional abnormalities—can facilitate the backflow of bile into the gastric lumen. This process not only damages the gastric mucosa but may also extend proximally, contributing to esophageal injury when combined with gastric reflux, thereby creating a complex entity often referred to as mixed (acid and bile) reflux. [4–6]

The clinical relevance of bile reflux gastritis in patients with chronic heartburn lies in its potential to explain persistent or atypical symptoms that are poorly responsive to conventional GERD therapies. Unlike acid-mediated injury, bile-induced mucosal damage involves distinct biochemical and cellular mechanisms, including disruption of epithelial barriers, induction of oxidative stress, and promotion of inflammatory pathways. Moreover, bile acids have been implicated in the pathogenesis of more serious complications, such as intestinal metaplasia and Barrett's esophagus, raising concerns about their long-term impact on gastrointestinal health. [7–9]

Despite its importance, bile reflux gastritis remains inadequately characterized in terms of prevalence, largely due to diagnostic challenges. Currently available tools, including endoscopy, histopathological examination, and ambulatory reflux monitoring techniques such as impedance-pH monitoring and Bilitec systems, have limitations in accurately detecting and quantifying bile reflux. Additionally, there is significant overlap between the clinical and histological features of bile reflux gastritis and other forms of gastritis, further complicating diagnosis and leading to underrecognition in routine practice. [10–12]

The aim of this review is to provide a comprehensive and integrated analysis of bile reflux gastritis in patients with chronic heartburn, with a focus on its prevalence, underlying pathophysiological mechanisms, and clinical implications. By synthesizing current evidence from gastroenterology, hepatology, and motility research, this article seeks to highlight the role of bile reflux as a key factor in refractory upper gastrointestinal symptoms. Furthermore, it addresses existing gaps in knowledge, particularly regarding diagnostic standardization and optimal management strategies, thereby underscoring the need for improved clinical awareness and future research in this evolving field. [13–15]

Epidemiology and Prevalence of Bile Reflux Gastritis

The true prevalence of bile reflux gastritis in patients with chronic heartburn remains difficult to establish due to the absence of standardized diagnostic criteria and the limitations of currently available diagnostic modalities. However, accumulating evidence suggests that bile reflux is not uncommon, particularly among patients with persistent or refractory gastroesophageal symptoms. Studies utilizing impedance-pH monitoring and Bilitec technology have demonstrated that a significant proportion of patients with chronic heartburn exhibit mixed reflux, involving both gastric acid and duodenal contents. Estimates indicate that bile reflux may be present in approximately 10–20% of patients with typical GERD symptoms, with higher rates reported in those who do not respond adequately to proton pump inhibitor therapy. [16–18]

In patients with refractory GERD, the prevalence of bile reflux appears to be substantially higher.

Several clinical investigations have shown that up to 30–40% of patients with persistent heartburn despite PPI therapy have evidence of non-acid or weakly acidic reflux, a component of which includes bile acids. This subgroup represents a diagnostically challenging population in whom traditional acid suppression fails to address the underlying pathophysiology. Furthermore, the coexistence of bile reflux gastritis in these patients suggests that duodenogastric reflux may play a central role in symptom persistence and mucosal injury. [19–21]

Geographical and demographic variations in the prevalence of bile reflux gastritis have also been observed, although data remain limited. Higher prevalence rates have been reported in regions with increased incidence of Helicobacter pylori infection and gastric motility disorders, suggesting potential interactions between infectious, inflammatory, and functional factors. Additionally, bile reflux is more commonly identified in older populations, possibly reflecting age-related changes in gastric motility and pyloric function. Gender differences are less although some studies suggest a slight predominance in males, particularly in post-surgical cohorts. [22–24]

Post-surgical patients represent a well-recognized group with a markedly increased risk of bile reflux gastritis. Procedures such as partial gastrectomy, pyloroplasty, and cholecystectomy can disrupt normal anatomical and physiological barriers, facilitating the retrograde flow of bile into the stomach. In such populations, the prevalence of bile reflux gastritis may exceed 50%, and symptoms often include epigastric pain, nausea, and persistent heartburn. Importantly, these patients provide valuable insights into the pathophysiological consequences of bile exposure on the gastric and esophageal mucosa. [25–27]

Despite these observations, it is important to emphasize that the reported prevalence of bile reflux gastritis varies widely across studies, largely due to differences in diagnostic definitions and methodologies. Endoscopic findings such as bile pooling and mucosal erythema are subjective and lack specificity, while histological features overlap with other forms of gastritis. Advanced techniques such as Bilitec monitoring, although more specific for bile detection, are not widely available and have technical limitations. As a result, bile reflux gastritis remains underdiagnosed in routine clinical practice, and its true epidemiological burden is likely underestimated. [28–30]

Pathophysiology of Duodenogastric (Bile) Reflux

Duodenogastric reflux represents the core mechanism underlying bile reflux gastritis and involves the retrograde passage of duodenal contents—such as bile acids, pancreatic enzymes, and intestinal secretions—into the stomach. Although transient reflux may occur physiologically, particularly in the postprandial period, it is usually limited and effectively cleared without causing mucosal damage. Pathological bile reflux arises when this balance is disrupted, leading to prolonged exposure of the gastric mucosa to injurious duodenal components and subsequent inflammation. [31,32]

A central factor in this process is dysfunction of the pyloric sphincter, which normally acts as a mechanical barrier preventing the backflow of duodenal contents. Impairment of pyloric function may result from motility disorders, neurohormonal dysregulation, or structural alterations, particularly following gastric or biliary surgery. Additionally, abnormalities in gastric and duodenal motility—such as delayed gastric emptying or increased duodenal pressure—further facilitate reflux. These disturbances are commonly observed in conditions like diabetes mellitus and post-vagotomy states, highlighting the multifactorial nature of bile reflux pathogenesis. [33]

Bile acids play a pivotal role in mediating mucosal injury. They disrupt the gastric epithelial barrier by solubilizing membrane lipids, increasing mucosal permeability, and promoting hydrogen ion back-diffusion. The extent of injury is influenced by the chemical composition of bile acids and the intragastric pH. Conjugated bile acids tend to exert greater toxicity in acidic environments, whereas unconjugated bile acids are more damaging at neutral pH, emphasizing the dynamic interaction between acid and bile in gastric injury. [34,35]

Beyond their direct cytotoxic effects, bile acids trigger inflammatory and molecular pathways that contribute to sustained mucosal damage. These include the generation of reactive oxygen species, activation of inflammatory signaling pathways such as nuclear factor-kappa B, and increased production

of pro-inflammatory cytokines. Chronic exposure may lead to epithelial apoptosis, impaired regeneration, and progressive mucosal changes, potentially predisposing to intestinal metaplasia and other premalignant conditions. [36]

Importantly, bile reflux rarely occurs in isolation in patients with chronic heartburn. Instead, it frequently coexists with acid reflux, resulting in mixed reflux that has a synergistic deleterious effect on both gastric and esophageal mucosa. Acidic conditions enhance bile acid solubility and penetration, while bile components may impair mucosal defense and prolong acid exposure. This interaction provides a mechanistic explanation for persistent symptoms in patients who do not respond adequately to acid suppression alone. [37]

In parallel, impairment of gastric mucosal defense mechanisms further exacerbates injury. Normally, protective factors such as mucus secretion, bicarbonate production, epithelial integrity, and mucosal blood flow maintain gastric homeostasis. In the setting of chronic bile exposure, these defense systems become compromised, leading to increased vulnerability to inflammation and structural damage. The cumulative effect of these processes ultimately results in the histological and clinical features characteristic of bile reflux gastritis. [38]

Interaction Between Bile Reflux and Gastroesophageal Reflux Disease (Mixed Reflux Concept)

The relationship between bile reflux and gastroesophageal reflux disease (GERD) is complex and increasingly recognized as clinically significant, particularly in patients with chronic or refractory heartburn. While GERD has traditionally been attributed to gastric acid exposure, it is now evident that duodenal contents, including bile acids, frequently contribute to reflux episodes. This has led to the concept of mixed reflux, in which both acid and bile act synergistically to produce mucosal injury and symptom generation. Importantly, bile reflux rarely occurs in isolation in patients with chronic heartburn, underscoring the need for an integrated understanding of reflux pathophysiology. [39,40]

Mechanistically, bile reflux can extend beyond the stomach into the esophagus, particularly when lower esophageal sphincter (LES) dysfunction is present. In such cases, duodenogastroesophageal reflux occurs, exposing the esophageal mucosa to a combination of gastric acid and bile acids. This mixed exposure has been shown to be more injurious than acid alone, as bile acids can disrupt epithelial integrity, enhance acid-mediated damage, and impair mucosal repair processes. Experimental and clinical studies have demonstrated that the combination of bile and acid leads to increased inflammation, deeper tissue injury, and greater risk of complications compared to isolated acid reflux. [41]

The physicochemical interaction between bile acids and gastric acid further amplifies mucosal damage. Acidic conditions increase the solubility and lipophilicity of bile acids, facilitating their penetration into epithelial cells. Once the mucosa, bile acids induce mitochondrial dysfunction, oxidative stress, and activation of inflammatory pathways. This not only contributes to symptom persistence but also explains why some patients experience severe mucosal injury despite relatively controlled acid exposure, particularly those on proton pump inhibitor therapy. [42]

Clinically, the presence of bile in refluxate has been associated with more severe forms of GERD, including erosive esophagitis and Barrett's esophagus. Patients with mixed reflux often present with more persistent and treatment-resistant symptoms, such as chronic heartburn, regurgitation, and epigastric discomfort. Moreover, bile reflux has been implicated in the progression from non-erosive reflux disease to more advanced pathological states, suggesting a role in disease evolution and severity. [43]

From a diagnostic perspective, distinguishing between acid reflux and mixed reflux remains challenging. Standard pH monitoring is limited to detecting acid exposure and cannot identify non-acidic components such as bile. Advanced techniques, including impedance-pH monitoring, allow for the detection of non-acid reflux events, while Bilitec monitoring specifically measures bilirubin as a surrogate for bile reflux. However, these tools are not widely available and have technical limitations, contributing to the underdiagnosis of mixed reflux in routine clinical practice. [44]

Therapeutically, the recognition of mixed reflux has important implications. Proton pump inhibitors, while effective in reducing gastric acid secretion, do not address bile reflux and may even alter gastric

pH in a way that increases bile toxicity. As a result, patients with significant bile reflux may continue to experience symptoms despite adequate acid suppression. This highlights the need for alternative or adjunctive treatments, such as prokinetic agents, mucosal protectants, or surgical interventions, in selected cases. Understanding the interplay between bile and acid reflux is therefore essential for optimizing management strategies in patients with chronic heartburn. [45]

Risk Factors and Predisposing Conditions

The development of bile reflux gastritis in patients with chronic heartburn is influenced by a range of structural, functional, and clinical factors that disrupt the normal coordination of gastroduodenal physiology. One of the most important predisposing mechanisms is impairment of pyloric sphincter function, which allows retrograde flow of duodenal contents into the stomach. This dysfunction may arise from intrinsic motility disorders or as a consequence of surgical interventions that alter the anatomical integrity of the pyloric region, thereby compromising its barrier role. [46]

Gastric and duodenal motility disorders represent another critical group of risk factors. Delayed gastric emptying, commonly observed in conditions such as diabetes mellitus and functional dyspepsia, increases intragastric volume and pressure, promoting reflux of duodenal contents. Similarly, abnormal duodenal motility or increased duodenal can facilitate the backward movement of bile into the stomach. These motility disturbances are often subtle but play a central role in the pathogenesis of bile reflux, particularly in patients without prior surgical history. [47]

Post-surgical states are among the most well-established risk factors for bile reflux gastritis. Procedures such as partial gastrectomy, pyloroplasty, and cholecystectomy can significantly alter normal gastrointestinal anatomy and physiology. In particular, disruption of the pyloric barrier or changes in bile flow dynamics can predispose patients to persistent duodenogastric reflux. These patients frequently present with chronic epigastric symptoms and heartburn, providing a clear clinical model for understanding bile-mediated mucosal injury. [48]

Lifestyle-related factors may also contribute to the development or exacerbation of bile reflux. Diets high in الدهون, smoking, and alcohol consumption have been associated with impaired gastric motility and increased reflux episodes. Additionally, obesity may play an indirect role by increasing intra-abdominal pressure, thereby promoting both gastric and duodenal reflux. Although these factors are more commonly linked to acid reflux, their contribution to bile reflux should not be underestimated, particularly in patients with overlapping risk profiles. [49]

Certain medications can predispose individuals to bile reflux by affecting gastrointestinal motility or sphincter function. Drugs such as anticholinergics, calcium channel blockers, and opioids may delay gastric emptying or reduce pyloric tone, facilitating duodenogastric reflux. Long-term use of proton pump inhibitors, while effective in reducing acid secretion, may alter gastric pH and potentially influence bile composition and activity, thereby modifying the pattern of mucosal injury in susceptible individuals. [50]

Finally, underlying inflammatory and infectious conditions may contribute to bile reflux gastritis through indirect mechanisms. For example, Helicobacter pylori infection can alter gastric motility and acid secretion, potentially influencing the dynamics of bile reflux. Additionally, chronic gastritis of any etiology may weaken mucosa mechanisms, making the stomach more susceptible to injury from refluxed bile. These interactions highlight the multifactorial nature of bile reflux gastritis and the importance of considering a broad range of predisposing conditions in affected patients. [51]

Clinical Presentation in Patients with Chronic Heartburn

The clinical presentation of bile reflux gastritis in patients with chronic heartburn is often nonspecific and overlaps significantly with classical gastroesophageal reflux disease (GERD), making differentiation challenging in routine practice. The most common symptom remains persistent heartburn, which may be described as a burning retrosternal sensation; however, in patients with bile reflux, this symptom is frequently more resistant to standard acid-suppressive therapy. In addition to heartburn, patients often report epigastric pain or discomfort, suggesting concomitant gastric involvement rather than isolated esophageal disease. [52,53]

Regurgitation is another prominent symptom, but unlike acid reflux, bile reflux may be associated with a bitter or bilious taste in the mouth, particularly in the early morning or after meals. Some patients describe yellow-green fluid regurgitation, which can be a clinical clue pointing toward duodenogastric involvement. Nausea and occasional vomiting, especially of bile-stained material, may also occur and are more suggestive of bile reflux gastritis than typical GERD. These features, although not universally present, can help raise clinical suspicion in appropriate settings. [54]

Dyspeptic symptoms are frequently observed in patients with bile reflux gastritis and may include postprandial fullness, early satiety, bloating, and upper abdominal discomfort. These manifestations reflect underlying gastric mucosal irritation and motility disturbances. In many cases, such symptoms coexist with heartburn, contributing to a complex clinical picture that may be misclassified as functional dyspepsia or refractory GERD. This overlap further complicates diagnosis and often delays appropriate management. [55]

An important clinical characteristic of bile reflux–associated heartburn is its poor response to proton pump inhibitors. While PPIs effectively suppress gastric acid production, they do not prevent the reflux of bile or other duodenal contents. As a result, patients may continue to experience symptoms despite adequate acid suppression, leading to repeated treatment escalations without significant benefit. This therapeutic failure should prompt consideration of alternative mechanisms, including bile reflux, particularly in patients with long-standing or severe symptoms. [56]

In more advanced cases, chronic exposure to bile acids may result in mucosal injury extending beyond the stomach to involve the esophagus. This can manifest as complications such as erosive esophagitis or even Barrett's esophagus, which may be asymptomatic or present with worsening reflux symptoms. Alarm features, including weight loss, anemia, or persistent vomiting, are less common but warrant further investigation to exclude significant structural disease or malignancy. [57]

Overall, the clinical presentation of bile reflux gastritis in patients with chronic heartburn is heterogeneous and often indistinguishable from acid-mediated disorders based on symptoms alone. A high index of suspicion is therefore required, particularly in patients with refractory symptoms, prominent dyspepsia, or atypical features such as bilious regurgitation. Recognizing these patterns is essential for guiding further diagnostic evaluation and optimizing patient management. [58]

Endoscopic Features of Bile Reflux Gastritis

Endoscopy remains a primary diagnostic tool in the evaluation of patients with chronic heartburn, although its role in identifying bile reflux gastritis is largely supportive rather than definitive. The most commonly described endoscopic finding is the presence of bile pooling within the gastric lumen, often appearing as a yellow-green fluid layer. This finding, particularly when observed in a fasting patient, raises suspicion for duodenogastric reflux; however, it lacks specificity, as transient bile reflux can occur in otherwise healthy individuals. [59]

Mucosal changes associated with bile reflux gastritis are typically characterized by erythema, edema, and a diffusely inflamed appearance of the gastric mucosa, especially in the antral region. In some cases, the mucosa may appear friable or exhibit superficial erosions. These findings reflect underlying chemical injury rather than acid-mediated damage and are often described as reactive or chemical gastritis on correlation with histology. Despite these features, distinguishing bile-induced injury from other forms of gastritis based solely on endoscopic appearance remains challenging. [60]

Another notable feature is the potential extension of mucosal injury toward the proximal stomach and even the distal esophagus in cases of mixed reflux. Endoscopic evidence of esophagitis in conjunction with bile staining may suggest the presence of duodenogastroesophageal reflux. However, the severity of esophageal involvement does not always correlate directly with visible bile, and many patients with significant symptoms may have minimal or even normal endoscopic findings, further complicating interpretation. [61]

It is also important to recognize that endoscopic findings in bile reflux gastritis are often subtle and nonspecific. Unlike peptic ulcer disease or severe erosive esophagitis, there are no pathognomonic features that definitively establish the diagnosis. As a result, endoscopy should be interpreted in

conjunction with clinical presentation and, when necessary, adjunctive diagnostic modalities. Biopsy is frequently performed to support the diagnosis, although histological findings may overlap with other types of gastritis. [62]

In clinical practice, the main value of endoscopy lies in excluding alternative or coexisting pathology, such as peptic ulcers, malignancy, or Helicobacter pylori–associated gastritis. Additionally, it provides an opportunity to assess the extent of mucosal injury and to obtain tissue samples for histopathological evaluation. While the visualization of bile and reactive mucosal changes can support the diagnosis of bile reflux gastritis, a comprehensive approach integrating clinical, endoscopic, and functional data remains essential for accurate diagnosis and management. [63]

Histopathological Characteristics

Histopathological examination plays an important supportive role in the diagnosis of bile reflux gastritis, although it is not entirely specific and must be interpreted in the appropriate clinical context. The characteristic pattern is often described as reactive (chemical) gastropathy, reflecting mucosal injury caused by irritants such as bile acids rather than infectious or autoimmune processes. This distinction is important, as it guides both diagnosis and management, particularly in patients with chronic heartburn and inconclusive endoscopic findings. [64]

One of the hallmark histological features is foveolar hyperplasia, which represents elongation and tortuosity of the gastric pits. This is typically accompanied by a reduction in inflammatory cell infiltrate compared to other forms of gastritis, such as Helicobacter pylori–associated gastritis. The relative paucity of inflammatory cells, despite evident epithelial injury, is a key feature that supports the diagnosis of chemical gastropathy and helps differentiate it from chronic inflammatory conditions. [65]

Additional findings include edema of the lamina propria, vascular congestion, and smooth muscle proliferation extending into the mucosal layer. Surface epithelial damage is also commonly observed, with evidence of mucin depletion and cellular degeneration. These changes reflect ongoing injury and impaired mucosal mechanisms due to repeated exposure to bile acids and other duodenal contents. In some cases, regenerative epithelial changes may be present, indicating attempts at mucosal repair. [66]

In more advanced or chronic cases, histopathological alterations may progress to include intestinal metaplasia, a condition in which gastric epithelium is replaced by intestinal-type cells. This finding is clinically significant, as it is considered a premalignant change and may increase the risk of gastric or esophageal neoplasia, particularly when combined with other risk factors such as chronic inflammation or persistent reflux. The role of bile acids in promoting such changes has been supported by both experimental and clinical studies. [67]

Despite these characteristic features, it is important to acknowledge that histological findings in bile reflux gastritis are not pathognomonic. Similar patterns may be observed in patients exposed to other chemical irritants, including nonsteroidal anti-inflammatory drugs. Therefore, histopathology should not be used in isolation but rather integrated with clinical history, endoscopic findings, and, when available, functional diagnostic studies. This combined approach enhances diagnostic accuracy and helps avoid misclassification of gastritis subtypes in patients with chronic heartburn. [68]

Diagnostic Modalities

Accurate diagnosis of bile reflux gastritis in patients with chronic heartburn remains challenging due to the lack of a single definitive diagnostic test. Instead, a combination of clinical evaluation, endoscopy, histopathology, and functional studies is typically required. While symptom assessment provides initial clues, it is insufficient to distinguish bile reflux from acid-mediated disease, particularly given the significant overlap in presentation. Therefore, objective diagnostic modalities play a crucial role in identifying bile involvement and guiding management. [69]

Upper gastrointestinal endoscopy is often the first-line investigation, primarily used to assess mucosal integrity and exclude alternative diagnoses. Findings such as bile pooling and reactive mucosal changes may suggest bile reflux, but they are not specific. Histopathological examination of biopsy samples can support the diagnosis by demonstrating features of reactive gastropathy; however, these findings must be interpreted in conjunction with clinical and endoscopic data. Neither endoscopy nor histology alone

can reliably confirm bile reflux. [70]

Ambulatory pH monitoring has traditionally been used to evaluate acid reflux but has important limitations in this context, as it does not detect non-acidic components such as bile. As a result, patients with persistent symptoms despite normal acid exposure may still have significant reflux of duodenal contents. This limitation has led to the development of combined impedance-pH monitoring, which allows for the detection of both acid and non-acid reflux episodes by measuring changes in electrical resistance within the esophagus. This technique provides a more comprehensive assessment of reflux patterns and is particularly useful in patients with refractory symptoms. [71]

Bilitec monitoring represents a more specific method for detecting bile reflux by measuring bilirubin absorbance in the upper gastrointestinal tract. It provides quantitative data on bile exposure and has been used in research settings to establish the role of bile in reflux disease. However, its clinical application is limited by technical challenges, including interference from gastric contents and dietary factors, as well as limited availability in routine practice. Despite these limitations, it remains an important tool in specialized centers and research studies. [72]

Other adjunctive diagnostic approaches include gastric scintigraphy and aspiration techniques to assess duodenogastric reflux, although these are less commonly used. In clinical practice, the diagnosis is often made based on a combination of suggestive findings rather than a single confirmatory test. A high index of suspicion is particularly important in patients with chronic heartburn who do not respond to standard acid suppression therapy, as this subgroup is more likely to have a significant bile reflux component. [73]

Overall, the diagnosis of bile reflux gastritis requires an integrated approach that combines clinical judgment with targeted investigations. The limitations of current diagnostic tools highlight the need for improved and standardized methods to accurately identify bile reflux and differentiate it from other causes of upper gastrointestinal symptoms. Such advancements would significantly enhance the ability to tailor treatment strategies and improve outcomes in affected patients. [74]

Conclusion

Bile reflux gastritis represents an underrecognized yet clinically significant contributor to chronic heartburn, particularly in patients who fail to respond adequately to conventional acid-suppressive therapy. Its pathogenesis involves complex interactions between impaired gastroduodenal motility, pyloric dysfunction, and the injurious effects of bile acids on the gastric and esophageal mucosa. The frequent coexistence of bile and acid reflux further complicates the clinical picture, often leading to persistent symptoms and increased risk of mucosal damage. Despite advances in diagnostic techniques, the identification of bile reflux remains challenging due to the lack of standardized and widely accessible tools. Consequently, a high index of suspicion and a comprehensive, integrated diagnostic approach are essential. Improved recognition of this condition is critical for guiding appropriate management strategies, which may require therapies beyond acid suppression. Future research should focus on refining diagnostic modalities and developing targeted treatments to address this important gap in gastroenterological care.

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