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A COMPREHENSIVE REVIEW OF CLASSIFICATION, RISK FACTORS, AND PATHOPHYSIOLOGY OF GASTRITIS

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Abstract:
Background: Gastritis is a multifaceted condition characterized by inflammation of the gastric mucosa, with a wide array of etiologies, risk factors, and pathophysiology. **Aim:** This review aims to provide an in-depth exploration of the pathophysiology, classification, and risk factors for gastritis, drawing from recent research and clinical insights. **Method:** The PubMed and Google Scholar Search Engines were the primary databases used for the search process, with articles collected from 1960 to 2024. **Conclusion:** The risk factors for gastritis are diverse, including infectious agents like H. pylori, irritants, and lifestyle habits such as diet and alcohol. The ABCD classification assesses H. pylori levels and pepsinogen to aid in early detection and management, which is crucial for preventing serious complications, such as gastric cancer. Diagnostic methods, both invasive and non-invasive, are essential for accurately identifying autoimmune and bacterial gastritis, thereby enhancing patient care.

Keywords: Gastritis, Pathophysiology, Etiologies, Classification, Diagnostic Approaches and Risk factors.

INTRODUCTION

Gastritis is a complex condition characterized by inflammation of the gastric mucosa, which can manifest in various forms, including autoimmune gastritis and chronic atrophic gastritis. Autoimmune gastritis is characterized by the destruction of parietal cells, resulting in impaired gastric acid secretion and vitamin B12 malabsorption, which often leads to pernicious anemia. [1,2] This condition is associated with circulating autoantibodies to gastric H+/K+ATPase, which are critical for acidification of gastric juice. Chronic atrophic gastritis (CAG) represents a severe form of gastritis where there is significant loss of gastric mucosa and glandular structures, potentially leading to gastric cancer if left untreated.[3] The relationship between CAG and gastric cancer is well-established, as chronic inflammation and atrophy are precursors to malignancy. [4] Helicobacter pylori (HP) infection is a major contributor to chronic gastritis, with long-standing infections increasing the risk of high-grade dysplasia and coincident carcinoma.
The bacterium induces chronic inflammation, which can progress to atrophic gastritis and subsequently to cancer. [4,5] In addition to HP, other infectious factors also play a role in the etiology of gastritis. These include various pathogens that can irritate the gastric lining, contributing to inflammation. Furthermore, chemical factors, such as exposure to irritants, can lead to gastritis by damaging the gastric mucosa. Chronic inflammation, primarily driven by HP, is a critical risk factor for the progression of gastritis to more severe conditions, including gastric cancer [6]. Non-steroidal anti-inflammatory agents (NSAIDs) are particularly noteworthy, as they are associated with the development of reactive gastropathy. However, their role is considered less significant compared to HP. [7] Lifestyle factors also contribute significantly to the risk of developing gastritis. Diet has been statistically linked to the incidence of gastritis, with a significance level of $\rho = 0.004$, indicating a strong relationship. Additionally, smoking is recognized as a risk factor, with a statistical significance of $\rho = 0.013$, further emphasizing the impact of lifestyle choices on gastric health.

Alcohol consumption and stress are also implicated, as they can exacerbate gastric inflammation and compromise the immune response. [8] Diagnosis of gastritis can be challenging due to the asymptomatic nature of early stages and the variability in symptoms. Methods such as endoscopy, histology, and serological tests are employed to identify the condition; however, they often do not correlate well with one another. [9] The ABCD scheme of gastritis classification (autoimmune, bacterial, chemical reactive, and other forms) is commonly used to aid in diagnosis and treatment planning. Understanding the multifactorial nature of gastritis, including its etiology, symptoms, and potential complications, is essential for effective management and prevention of associated risks, such as gastric cancer.

ABCD CLASSIFICATION OF GASTRITIS

The ABCD classification of gastritis is a systematic approach that categorizes different types of gastritis based on the presence of Helicobacter pylori (H. pylori) infection and serum pepsinogen levels. This classification is crucial for assessing gastric cancer risk and guiding clinical management.
The classification consists of four groups:
Group A: Autoimmune Gastritis. This type is characterized by an autoimmune response that affects the gastric mucosa, leading to chronic inflammation and potential complications such as gastric cancer. It is essential to identify this group as it requires specific management strategies.
Group B: Bacterial Gastritis This group includes individuals who test positive for H. pylori but negative for pepsinogen, indicating that chronic atrophic gastritis (CAG) is either absent or mild. The presence of H. pylori is significant as it is a major risk factor for various gastric diseases, including ulcers and gastric cancer.
Group C: Chronic Atrophic Gastritis (CAG) Individuals in this group are positive for both H. pylori and pepsinogen, indicating a more severe form of gastritis characterized by the loss of gastric glandular cells. This condition is often associated with an increased risk of gastric cancer, making its identification critical for early intervention.
Group D: Severe CAG with Intestinal Metaplasia. This group consists of subjects who are negative for H. pylori but positive for pepsinogen, suggesting extensive gastric atrophy and intestinal metaplasia. This condition is also linked to a heightened risk of gastric cancer, emphasizing the need for careful monitoring and management.
The assessment of pepsinogen levels plays a vital role in this classification. Serum pepsinogen levels are used to evaluate gastric mucosal health and the severity of atrophic gastritis. A low pepsinogen I level or a low pepsinogen I/II ratio can indicate significant gastric atrophy, which is a precursor to gastric cancer. [9,10]
Table (1): ABC method classification of gastritis: according to the serology of H. pylori antibody and pepsinogen (PG) status; The occurrence of gastric cancer rises progressively and notably from A to D. [10]

		H. pylori Antibody titer	
		-ve	+ve
pepsinogen status	Normal	Group A	Group B
	Atrophic	Group D	Group C

PATHOPHYSIOLOGY OF GASTRITIS

Gastritis encompasses a range of inflammatory conditions that affect the gastric mucosa, each with distinct pathophysiological mechanisms. Autoimmune gastritis (AIG) is characterized by a complex interplay of immune responses that lead to the destruction of gastric parietal cells, primarily targeting the H+/K+-ATPase autoantigen. This autoimmune condition is closely associated with pernicious anemia, in which the immune system mistakenly attacks the body's own tissues, leading to impaired gastric acid secretion and subsequent nutritional deficiencies. The pathophysiology of AIG involves the activation of pathogenic CD4+ T cells that recognize the parietal cell autoantigen, H/K ATPase.
These T cells play a crucial role in orchestrating the immune response, which can lead to inflammation and damage to the gastric mucosa. The presence of autoantibodies against parietal cells and intrinsic factor further complicates the disease, as these antibodies can contribute to the destruction of gastric cells and correlate with the severity of gastritis. In AIG, the immune response is initiated by the recognition of the H/K ATPase, which is expressed on the surface of gastric parietal cells. This recognition triggers a cascade of immune events, including the recruitment of CD4+CD25+ T regulatory cells that attempt to modulate the immune response. However, the regulation is often insufficient, leading to a predominance of pathogenic T cell activity. The cytokine milieu produced by these T cells, which includes a mix of TH1 and TH2 cytokines, further exacerbates the inflammatory response, resulting in chronic gastritis characterized by lymphocytic infiltration and loss of parietal cells. Diagnostic methods such as the complement fixation test and

immunofluorescent methods have been employed to detect the presence of autoantibodies in patients with AIG. These tests reveal the immune response associated with the disease and help in understanding the underlying autoimmune mechanisms. Additionally, skin tests using gastric mucosa extracts have shown positive reactions in certain cases, indicating an immune response relevant to the pathophysiology of AIG. [11-13]

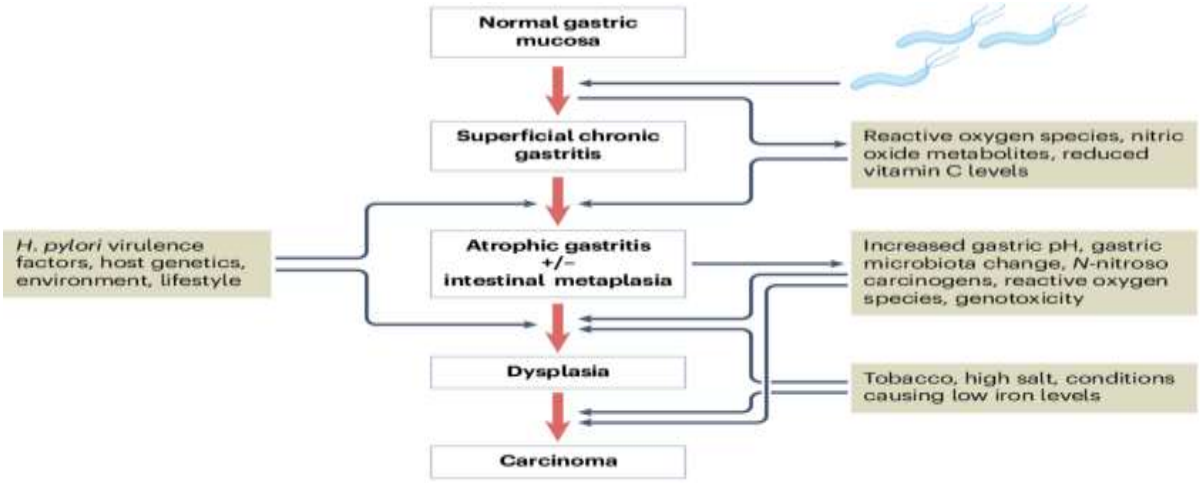

FIGURE (2): PATHOGENESIS OF GASTRIC CARCINOMA [14]

Bacterial gastritis, primarily caused by Helicobacter pylori (H. pylori), is a significant health concern due to its association with various gastro-duodenal diseases and its potential to lead to more severe conditions such as gastric cancer. The pathophysiology of this condition involves a complex interplay between the bacterium and the host's immune response. H. pylori is a gram-negative bacterium that colonizes the gastric mucosa, where it thrives in the acidic environment of the stomach, largely due to its urease enzyme, which neutralizes gastric acid. This adaptation allows H. pylori to persist and induce chronic inflammation, characterized by the recruitment of leukocytes to the gastric mucosa. This leukocyte infiltration is a hallmark of the inflammatory response in bacterial gastritis, leading to increased gastritis scores, which serve as a measurable indication of the severity of inflammation. The inflammatory response is further exacerbated by the production of proinflammatory factors, such as monochloramine, which is derived from both leukocytes and H. pylori itself. This factor plays a crucial role in the pathophysiology of H. pylori-associated diseases, contributing to the ongoing cycle of inflammation and tissue damage.

The interaction between H. pylori and the host immune system is mediated by various virulence factors, including CagA and BabA, which enhance bacterial adherence and modulate the inflammatory response.[15,16] Chronic infection with H. pylori can lead to multifocal atrophic gastritis, characterized by significant changes in the gastric mucosa, including loss of gastric acid secretory capacity. This progression is associated with an increased risk of developing gastric cancer, as the chronic inflammation and atrophy create a conducive environment for malignant transformation. The WHO has classified H. pylori as a class 1 carcinogen, underscoring its significant role in the pathophysiology of gastric diseases. [7,9] Moreover, the genetic diversity of H. pylori enables it to adapt to various stress conditions, leading to the emergence of drug-resistant strains that complicate eradication efforts and contribute to the persistence of gastritis. [16]

Chronic Atrophic Gastritis (CAG) is a progressive disease characterized by the degeneration of the gastric mucosa, which plays a crucial role in its pathophysiology. The condition is primarily driven by chronic inflammation, often triggered by Helicobacter pylori infection, leading to the replacement of normal gastric glandular structures with connective tissue or metaplastic atrophy. This inflammatory process results in atrophic changes, which refer to the reduction in the size and function of the gastric mucosa, significantly impairing gastric acid secretion and intrinsic factor production. The pathophysiological progression of CAG includes metaplastic changes, where the gastric epithelium transforms into a different type, indicating a worsening of the condition. These metaplastic changes are often accompanied by dysplasia, a pathological alteration that raises the risk of progression to gastric cancer. In fact, studies have shown that a significant percentage of patients with CAG exhibit dysplastic changes, highlighting the potential for malignant transformation. Chronic inflammation is a key factor in the development of gastric mucosal atrophy and is associated with various environmental and genetic factors. The presence of H. pylori is particularly

notable, as its eradication has been debated regarding its effectiveness in reversing atrophic changes in the stomach. While some studies suggest that H. pylori eradication may improve gastric atrophy in the corpus, it does not appear to have the same effect in the antrum. Additionally, lifestyle factors such as smoking and dietary habits can further exacerbate the condition, contributing to the deterioration of the gastric mucosa. Intestinal metaplasia (IM) is another critical phase in the progression of CAG, where the gastric mucosa undergoes significant changes that can lead to the development of gastric adenocarcinoma. The presence of IM indicates a higher risk for cancer development, particularly in the context of chronic atrophic gastritis [17-20]

DIAGNOSTIC APPROACHES

As mentioned earlier, gastritis often involves assessing the presence of Helicobacter pylori (H. pylori) and measuring pepsinogen levels. H. pylori is a significant contributor to bacterial gastritis, and its detection is crucial for effective management of the condition. Various diagnostic methods are available, each with its strengths and limitations. Histological examination of gastric biopsy samples is considered the gold standard for diagnosing H. pylori infection and assessing the status of the gastric mucosa, including inflammation and premalignant changes. This invasive method is complemented by the rapid urease test (RUT), which is often the initial test of choice due to its low cost, rapid results, and simplicity. RUT can provide semi-quantitative grading of gastritis activity, which is beneficial for understanding the severity of the condition. Non-invasive tests, such as the urea breath test and stool antigen test, are also effective for diagnosing active H. pylori infection. The 13C/14C-urea breath tests are particularly reliable and are recommended for post-treatment monitoring. These tests are advantageous in primary care settings where invasive procedures may not be feasible.

Serologic testing for IgG and IgA antibodies offers another non-invasive approach, although it primarily indicates exposure rather than active infection. The combined use of IgG and IgA ELISAs can enhance diagnostic accuracy, making it a valuable tool for identifying H. pylori infection. However, the role of serology in routine diagnosis remains somewhat questionable, as it is more suited for epidemiological purposes. In addition to H. pylori detection, measuring pepsinogen levels can provide insights into gastric mucosal health. Low pepsinogen levels may indicate atrophic gastritis, which is often associated with autoimmune gastritis. This dual approach—assessing H. pylori status alongside pepsinogen levels—can help differentiate between autoimmune and bacterial gastritis, guiding appropriate treatment strategies. [21-23] Furthermore, one of the primary diagnostic tools for autoimmune gastritis is the complement fixation test, which assesses the presence of autoimmune antibodies in patients with gastric diseases. This test, in conjunction with the immunofluorescent method, has yielded positive reactions in patients, demonstrating its utility in diagnosing autoimmune conditions associated with gastritis. Additionally, serological markers such as anti-parietal cell antibodies are crucial for confirming the diagnosis of CAG, as they provide specific insights into the autoimmune response. [12,24]

Endoscopic diagnosis is essential for identifying changes in the gastric mucosa associated with gastritis, particularly through the detection of specific findings such as corpus-dominant atrophy. This type of atrophy is indicative of autoimmune gastritis, which has distinct clinical and pathophysiological implications compared to other forms of gastritis, such as those associated with Helicobacter pylori (H. pylori) infection. The endoscopic examination can reveal various abnormalities, including erosion, ulcerations, and other specific patterns that correlate with the presence of gastritis. For instance, the identification of erosion during endoscopy not only highlights the severity of the mucosal damage but also aligns with pathological findings, thereby reinforcing the diagnosis. Furthermore, the presence of H. pylori is a significant factor that correlates with these endoscopic abnormalities, emphasizing its relevance in the management of gastritis. [25,26]

CONCLUSION

The risk factors for gastritis are diverse, including infectious agents like H. pylori, irritants, and lifestyle habits such as diet and alcohol. The ABCD classification assesses H. pylori levels and pepsinogen to aid in early detection and management, which is crucial for preventing serious complications, such as gastric cancer. Diagnostic methods, both invasive and non-invasive, are essential for accurately identifying autoimmune and bacterial gastritis, thereby enhancing patient care.

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AUTHOR CONTRIBUTIONS

The corresponding author assisted the first author in working on the original manuscript, and each author gave their final approval before the work was submitted to a journal for publication. Each co-author helped with editing, gathering literature, and creating tables and figures.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ETHICAL APPROVAL

Not Applicable

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