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Analysis of pathophysiological mechanisms of iron deficiency anemia in adult patients with chronic gastritis secondary to *Helicobacter pylori* infection

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Abstract

Introduction: Iron deficiency anemia (IDA) is the most prevalent nutritional deficiency worldwide, affecting approximately 1.2 to 2 billion people depending on the diagnostic criteria and reporting sources used. Chronic gastritis caused by *Helicobacter pylori*, present in more than 60% of the Mexican adult population, has been identified as a relevant and frequently underestimated etiopathogenic factor in the development and perpetuation of IDA. It acts through pathophysiological mechanisms that compromise both the absorption and systemic availability of iron.

Objective: To analyze the pathophysiological mechanisms that explain the development of iron deficiency anemia in patients with chronic gastritis caused by *Helicobacter pylori*, through a systematic review of the available scientific evidence, in order to establish a comprehensive theoretical basis to guide the etiological diagnosis and treatment of this association in clinical practice.

Methodology: A documentary, descriptive, and systematic bibliographic review with a qualitative approach was conducted. Searches were performed in PubMed/MEDLINE, Cochrane Library, SciELO, and LILACS databases using English and Spanish search terms combined with Boolean operators. Original scientific articles, systematic reviews, meta-analyses, and clinical practice guidelines published preferably between 2020 and 2025 were included, along with seminal publications of recognized scientific relevance.

Results: Three main pathophysiological pathways were identified through which chronic gastritis caused by *H. pylori*generates IDA: the inflammatory pathway mediated by hepcidin, in which IL-6 stimulates hepatic hepcidin synthesis via the JAK2/STAT3 pathway that blocks ferroportin and generates functional hypoferremia; the structural pathway mediated by hypochlorhydria, in which parietal cell atrophy raises the intragastric pH, compromising the reduction of ferric to ferrous iron necessary for duodenal absorption; and the direct bacterial competition pathway, in which *H. pylori* uses specialized molecular systems to capture iron from the host. *H. pylori* infection was identified as the most frequent etiology of malabsorption in patients with IDA, accounting for 54.1% of cases with demonstrated malabsorption. Furthermore, 70.3% of positive endoscopic findings in young patients with IDA corresponded to histopathologically confirmed *H. pylori* gastritis or duodenitis.

Conclusions: Chronic gastritis caused by *H. pylori* generates IDA through three synergistic pathophysiological pathways that mutually potentiate each other, explaining the frequent refractoriness to conventional oral iron treatment when the underlying infection is not identified and eradicated. Systematic investigation of *H. pylori* should be integrated into the diagnostic algorithm of every patient with unexplained or recurrent IDA, and its eradication should be considered an indispensable component of etiological treatment.

Keywords: Iron deficiency anemia; *Helicobacter pylori*; Chronic gastritis; Pathophysiology; Hepcidin; Iron absorption

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1. Introduction

Iron deficiency anemia (IDA) is one of the most prevalent nutritional deficiencies worldwide, affecting approximately 1,200–2,000 million people, depending on the source and diagnostic criteria used, with a disproportionate burden in developing countries, women of reproductive age, and children under five years old (Gaur et al., 2025; Leung et al., 2024). Despite its high prevalence, its origin is often multifactorial and frequently underestimated in clinical practice, particularly when the underlying cause is not overt blood loss but rather a chronic disorder of the gastric mucosa that compromises iron absorption (Kawabata, 2024).

In this context, chronic gastritis caused by *Helicobacter pylori* (*H. pylori*) has gained relevance as an etiopathogenic factor for IDA, beyond its well-known association with peptic ulcers and gastric adenocarcinoma. This Gram-negative bacterium preferentially colonizes the antral mucosa of the stomach and triggers a chronic inflammatory response that progressively alters the gastric microenvironment, present in more than 60% of the Mexican adult population (Becquart et al., 2017; Abramowitz et al., 2024). This leads to hypochlorhydria, mucosal atrophy, and, consequently, deficient absorption of non-heme iron (Becquart et al., 2017). Since dietary iron requires an acidic pH for its reduction from the ferric to the ferrous form—an indispensable condition for absorption in the duodenum—any alteration of the acidic gastric environment represents a significant physiological obstacle to maintaining adequate iron stores (Ko et al., 2020).

Additionally, *H. pylori* infection promotes direct competition for host iron as a bacterial survival mechanism. Meanwhile, the resulting chronic inflammation raises levels of hepcidin, the central regulatory hormone of iron metabolism. Increased hepcidin inhibits intestinal and macrophage ferroportin, reducing systemic iron availability for erythropoiesis (DeLoughery et al., 2024; Auerbach et al., 2025). This mechanism establishes a complex pathophysiological link between chronic gastric infection and the development of IDA, which frequently persists or recurs if the causal agent is not eradicated.

From a clinical perspective, studies have documented that a significant proportion of young patients with unexplained IDA present with active *H. pylori* infection demonstrable by endoscopy and biopsy. Successful eradication of the bacteria is associated with a more effective recovery of hematological parameters compared to isolated iron supplementation (Abramowitz et al., 2024; Gaur et al., 2025). This evidence reinforces the need to consider *H. pylori* chronic gastritis as an active differential diagnosis in any patient with unexplained IDA, especially in regions with high seroprevalence of the infection.

Despite this, an important gap remains in daily medical practice between available evidence and the timely identification of this association. This delay in appropriate etiological treatment contributes to the chronicity of the anemic condition. Consequently, deepening the understanding of the pathophysiological mechanisms linking *H. pylori* infection, chronic gastritis, and the development of IDA is fundamental to optimizing the diagnostic approach and establishing comprehensive, evidence-based therapeutic strategies.

1.1. Iron and Its Biological Importance

Iron is an essential micronutrient for the human body, indispensable for the synthesis of hemoglobin, myoglobin, cytochromes, and various enzymes involved in cellular energy metabolism. Its primary function lies in transporting oxygen from the lungs to peripheral tissues, as well as electron transfer within the mitochondrial respiratory chain. Under normal physiological conditions, the adult body contains between 3 and 5 grams of iron, primarily distributed in erythrocyte hemoglobin (approximately 65%), tissue stores in the form of ferritin and hemosiderin (20–30%), and a minor fraction bound to myoglobin and enzymes (Kawabata, 2024; Auerbach et al., 2025).

1.2. Iron Deficiency Anemia

Iron deficiency anemia (IDA) is defined as a reduction in hemoglobin concentration below the normal values established by the World Health Organization (WHO), resulting from a deficit in body iron stores that compromises erythropoiesis. From a laboratory standpoint, it is characterized by microcytic and hypochromic anemia, decreased serum ferritin, reduced transferrin saturation, and elevated total iron-binding capacity (Kawabata, 2024; Leung et al., 2024). IDA represents the most frequent cause of anemia worldwide and the most prevalent nutritional deficiency in human history (Gaur et al., 2025).

1.3. Chronic Gastritis

Chronic gastritis is defined as persistent inflammation of the gastric mucosa, histologically characterized by mononuclear cell infiltration—with or without neutrophilic activity—which can progress to glandular atrophy,

intestinal metaplasia, and, in advanced cases, dysplasia. According to the updated Sydney classification, chronic gastritis can be classified topographically into antral, corporal, or pangastritis, and etiologically into autoimmune or infectious, the latter being the most frequent form and primarily associated with *H. pylori* infection (Becquart et al., 2017; Ko et al., 2020).

1.4. Helicobacter pylori

Helicobacter pylori is a Gram-negative, microaerophilic, curved rod-shaped bacterium equipped with flagella that grant it motility. It was first described in 1983 by Barry Marshall and Robin Warren, who subsequently received the Nobel Prize in Medicine in 2005 for this discovery. It preferentially colonizes the antral mucosa of the stomach and is capable of surviving the acidic gastric environment thanks to its production of urease, an enzyme that hydrolyzes urea to generate ammonia, locally neutralizing the pH. It is recognized as the main etiological agent of chronic active gastritis, peptic ulcer disease, MALT lymphoma, and gastric adenocarcinoma (Becquart et al., 2017; Abramowitz et al., 2024).

1.5. Hepcidin

Hepcidin is an antimicrobial peptide synthesized mainly in the liver, recognized as the master regulator of systemic iron metabolism. Its mechanism of action involves binding to ferroportin—the only known cellular iron exporter protein—inducing its internalization and lysosomal degradation. This is mediated by the activation of the JAK2/STAT3 pathway in hepatocytes (DeLoughery et al., 2024; Auerbach et al., 2025). Consequently, hepcidin inhibits intestinal iron absorption, blocks the release of stored iron from macrophages and hepatocytes, and reduces iron availability for erythropoiesis. Its synthesis is stimulated by iron overload, inflammation, and infection, and it is suppressed by hypoxia, iron deficiency, and increased erythropoietic activity (DeLoughery et al., 2024; Auerbach et al., 2025).

1.6. Ferroportin

Ferroportin is the only known transmembrane protein capable of exporting iron from the cellular interior into systemic circulation. It is primarily expressed in duodenal enterocytes, macrophages of the reticuloendothelial system, and hepatocytes. Its activity is negatively regulated by hepcidin, making it the primary control point for iron flux into the plasma. In chronic inflammatory conditions, such as *H. pylori* gastritis, the sustained increase in hepcidin leads to a functional reduction of ferroportin, limiting systemic iron availability regardless of the status of body iron stores (DeLoughery et al., 2024).

1.7. Serum Ferritin

Ferritin is an intracellular iron storage protein whose serum fraction is utilized clinically as the best marker for body iron stores under non-inflammatory conditions. A serum ferritin level <15 ng/mL is diagnostic of depleted stores, values between 15–30 ng/mL may indicate deficiency in the presence of active inflammation, given that ferritin behaves as an acute-phase reactant (Ko et al., 2020; Kawabata, 2024; Gaur et al., 2025).

1.8. Physiological Regulation of Iron Metabolism

Iron absorbed in the duodenum and proximal jejunum comes from two sources: heme iron, present in red meats and organ meats, which is highly efficiently absorbed directly by the HCP-1 (heme carrier protein-1) receptor; and non-heme iron, present in vegetables and grains, which must be reduced from its ferric (Fe3+) to its ferrous (Fe2+) form by the duodenal enzyme cytochrome b reductase (DcytB) before being transported into the enterocyte via divalent metal transporter 1 (DMT-1). Once inside the cell, iron can be stored as ferritin or exported into circulation via ferroportin, where it is oxidized by hephaestin and ceruloplasmin to bind to plasma transferrin, which distributes it to tissues according to their requirements (Ko et al., 2020; Auerbach et al., 2025).

This process is exquisitely dependent on gastric pH, as the reduction of Fe3+ to Fe2+ occurs optimally in an acidic environment. Any condition that elevates intragastric pH, such as atrophic gastritis, hypochlorhydria, or chronic use of proton pump inhibitors, significantly compromises the bioavailability of dietary non-heme iron (Kawabata, 2024; Ko et al., 2020).

1.9. Regulation Mechanism by Hepcidin and Inflammation

In situations of chronic inflammation, such as active gastritis due to *H. pylori*, various pro-inflammatory cytokines, particularly interleukin-6 (IL-6), stimulate hepatic hepcidin synthesis through the JAK2/STAT3 pathway. This sustained increase in hepcidin produces a functional hypoferremia characteristic of anemia of chronic disease or anemia of inflammation, which can coexist with or overlap true IDA, complicating the differential diagnosis. In *H. pylori* infection,

this phenomenon has been documented as a central mechanism by which the bacterium contributes to the development of IDA even in the absence of active gastric bleeding (DeLoughery et al., 2024; Becquart et al., 2017).

1.10. Iron Competition Between *H. pylori* and the Host

H. pylori has developed sophisticated iron acquisition systems to satisfy its metabolic requirements at the expense of the host. Conspicuous among these mechanisms are the lactoferrin binding protein B (LbpB), which allows it to capture iron bound to lactoferrin in the gastric mucosa, as well as hemoglobin-binding proteins that facilitate the acquisition of heme iron from erythrocytes lysed during the local inflammatory response. This active competition for iron aggravates the depletion of host stores, establishing a pathophysiological cycle in which inflammation favors bacterial virulence, and this, in turn, perpetuates inflammation and iron loss (Becquart et al., 2017; Abramowitz et al., 2024).

1.11. Gastric Mucosal Alterations and Iron Absorption

The chronic inflammatory response induced by *H. pylori* progressively generates atrophy of the parietal cells (which produce hydrochloric acid) and chief cells (which produce pepsinogen). The resulting hypochlorhydria or achlorhydria elevates intragastric pH to values that impede the efficient reduction of dietary ferric iron, compromising its availability for absorption in the proximal segment of the small intestine. In parallel, chronic mucosal inflammation can extend into the duodenum, directly affecting the enterocytes responsible for iron absorption and reducing the local expression of DMT-1 and ferroportin (Ko et al., 2020; Gaur et al., 2025).

1.12. Response to *H. pylori* Eradication

Several studies have documented that successful eradication of *H. pylori* is associated with a significantly greater recovery of hemoglobin and serum ferritin levels compared to isolated iron supplementation, particularly in patients with IDA refractory to conventional oral treatment. This finding supports the causal role of the infection in the pathophysiology of IDA and suggests that the identification and eradication of *H. pylori* must be considered an integral part of the etiological treatment of IDA in patients with documented chronic gastritis (Abramowitz et al., 2024; Gaur et al., 2025; DeLoughery et al., 2024).

Globally, the WHO estimates that IDA affects approximately 1.2 to 2 billion people, being the most frequent cause of anemia, which as a whole affects 30% of the global population. The greatest burden falls on low- and middle-income countries, where the prevalence in women of reproductive age can exceed 40% and reaches figures near 50% in children under five years old (Leung et al., 2024; Gaur et al., 2025).

Regarding *H. pylori* infection, it is estimated that more than 50% of the world's population is infected, with prevalences ranging between 30% in developed countries and exceeding 80% in some regions of Africa, Latin America, and Southeast Asia. Mexico, being a middle-income country with heterogeneous sanitary conditions, presents a prevalence of *H. pylori*infection that exceeds 60% in the general adult population, with even higher rates in vulnerable socioeconomic groups (Becquart et al., 2017; Abramowitz et al., 2024).

The coexistence of a high prevalence of *H. pylori* and IDA in the same geographical regions has led researchers to further investigate their potential causal relationship. In this regard, Abramowitz et al. (2024) reported that in a cohort of 143 young patients with IDA without an apparent hemorrhagic cause, 70.3% of the cases with positive findings on upper gastrointestinal endoscopy corresponded to gastritis or duodenitis associated with *H. pylori*, underscoring the importance of endoscopic evaluation in this age group. Likewise, studies such as that of Gaur et al. (2025) have shown that the oral iron absorption test (OIAT) identifies malabsorption in 19.5% of patients with IDA, with *H. pylori* infection being the most frequent etiology of malabsorption in that group, accounting for 54.1% of cases.

From a therapeutic perspective, DeLoughery et al. (2024) point out that intravenous iron should be considered when oral treatment proves ineffective or when an underlying condition compromises absorption, such as atrophic chronic gastritis. This recommendation is particularly relevant in patients with active, uneradicated *H. pylori* infection, in whom oral iron supplementation frequently proves insufficient to restore body stores as long as the underlying etiopathogenic mechanism persists (DeLoughery et al., 2024; Ko et al., 2020).

The antecedents presented below describe previous research documenting the relationship between *Helicobacter pylori*infection, chronic gastritis, and the development of iron deficiency anemia, constituting the scientific basis that justifies the need to deepen the understanding of the pathophysiology of this association.

Becquart et al. (2017) carried out an experimental study in female mice of the C57BL/6 strain, aiming to evaluate the combined effect of *H. pylori* infection and a low-iron diet on behavior, iron metabolism, erythrocyte indices, and hippocampal gene expression. The animals were distributed into four groups: control, isolated *H. pylori* infection, isolated iron-deficient diet, and a combination of both conditions. The results demonstrated that the combination of active *H. pylori* infection and a low-iron diet produced significant behavioral alterations, reductions in erythrocyte indices compatible with IDA, and modifications in the expression of hippocampal genes related to iron metabolism, compared to the isolated intervention groups. This study provided relevant experimental evidence regarding the synergy between *H. pylori* infection and dietary iron deficiency in the pathophysiology of IDA, as well as its neurological implications, showing that the impact of the bacterium transcends the gastrointestinal tract (Becquart et al., 2017).

Abramowitz et al. (2024) conducted a retrospective review of clinical records at the Brooklyn VA Hospital, including 143 patients under 45 years of age with a diagnosis of IDA who underwent upper gastrointestinal endoscopy and/or colonoscopy between 2009 and 2023. The primary objective was to determine the diagnostic yield of bidirectional endoscopy in young patients with IDA. The results showed that 28.6% of the patients presented positive findings on upper gastrointestinal endoscopy, of which 70.3% corresponded to histopathologically confirmed cases of *H. pylori* gastritis or duodenitis. Notably, asymptomatic patients under 45 years of age presented a significantly higher diagnostic yield for upper gastrointestinal endoscopy than symptomatic patients of the same age group, with 42.9% versus 18.2%, respectively. In contrast, the yield of colonoscopy in the same group was considerably lower, with positive findings in only 8.3% of cases. The authors concluded that *H. pylori* infection is the most frequent cause of IDA in young patients without overt gastrointestinal bleeding, and they recommended systematic upper endoscopic evaluation in this population group, even in the absence of upper gastrointestinal symptoms (Abramowitz et al., 2024).

Gaur et al. (2025) developed a prospective study at a tertiary care center in India, including 190 patients diagnosed with IDA with a mean age of 32.34 years, of whom 90.5% were women. The objective was to evaluate the diagnostic utility of the oral iron absorption test (OIAT) to predict the response to oral iron therapy and identify underlying malabsorption syndromes. Following the administration of 60 mg of oral elemental iron, baseline and two-hour serum iron levels were measured. The results showed that 34.2% of the participants presented abnormal OIAT results, and iron malabsorption was confirmed as the cause of IDA in 19.5%. Of the patients with demonstrated malabsorption, 54.1% presented active *H. pylori* infection, followed by autoimmune gastritis in 27.0% and celiac disease in 18.9%. The OIAT demonstrated a sensitivity of 89.2%, specificity of 79.1%, and a negative predictive value of 97.6% for identifying malabsorption syndromes. The authors concluded that the OIAT represents an effective, minimally invasive, and low-cost first-line diagnostic tool to identify patients with IDA secondary to malabsorption, particularly that associated with *H. pylori*infection, thereby guiding etiological treatment more precisely (Gaur et al., 2025).

Ko et al. (2020) published the clinical practice guidelines of the American Gastroenterological Association (AGA) on the gastrointestinal evaluation of IDA, based on an exhaustive technical review of the available evidence. These guidelines establish specific recommendations on investigating the gastrointestinal causes of IDA, highlighting the relevance of *H. pylori* infection as a frequently underestimated etiology, especially in young patients and premenopausal women without overt gastrointestinal bleeding. The guidelines recommend targeted investigation of *H. pylori* for any unexplained IDA or cases refractory to conventional treatment with oral iron, and point out that successful eradication of the bacterium is an essential component of etiological treatment in these cases. Likewise, they emphasize that hypochlorhydria and gastric atrophy secondary to chronic infection compromise the bioavailability of non-heme iron, perpetuating IDA even in the presence of an adequate dietary iron intake (Ko et al., 2020).

DeLoughery et al. (2024) published a clinical practice update from the AGA on the management of IDA, integrating recent evidence on the pathophysiological mechanisms linking chronic inflammation with the development and perpetuation of iron deficiency. The authors highlight the central role of hepcidin as a mediator of functional hypoferremia in chronic inflammatory contexts, including *H. pylori* gastritis, and establish recommendations on the use of intravenous iron in patients in whom oral treatment is insufficient due to compromised gastrointestinal absorption. This update reinforces the need for a comprehensive diagnostic and therapeutic approach to IDA that considers not only iron replacement but also the identification and treatment of the underlying cause, particularly in cases of chronic active gastritis (DeLoughery et al., 2024).

2. Results

The results presented below correspond to the systematic analysis and integration of the selected scientific evidence according to the established methodological criteria, organized based on each of the specific research objectives.

2.1. Pathophysiology of Iron Deficiency Anemia and Regulation of Iron Metabolism

The literature analysis identified that iron deficiency anemia develops as a consequence of an imbalance between body iron requirements and its effective availability for erythropoiesis. This process involves three sequential and progressive stages: depletion of body iron stores, iron-deficient erythropoiesis, and finally, established iron deficiency anemia (Kawabata, 2024; Auerbach et al., 2025).

From a laboratory standpoint, the progression of iron deficiency is reflected in a characteristic sequence of biochemical and hematological alterations. In the first stage, serum ferritin drops below 15–30 ng/mL as the first indicator of store depletion, without alterations in hemoglobin or erythrocyte indices yet. In the second stage, transferrin saturation falls below 16%, total iron-binding capacity rises, and an increase in soluble transferrin receptor begins to be detected. In the third stage, when stores are completely exhausted and erythropoiesis is significantly compromised, the characteristic microcytic and hypochromic anemia appears, with hemoglobin below the normal values established by the WHO (Kawabata, 2024; Leung et al., 2024).

Intestinal iron absorption occurs predominantly in the duodenum and proximal jejunum, being strictly dependent on gastric pH for the reduction of ferric iron (Fe3+) to ferrous iron (Fe2+)—an indispensable step for its uptake by the DMT-1 transporter at the apical pole of the enterocyte. The systemic regulation of this process is centrally mediated by hepcidin, whose hepatic synthesis is stimulated by iron overload, inflammation, and infection, and suppressed by tissue hypoxia, iron deficiency, and increased erythropoietic activity. Increased hepcidin leads to the internalization and degradation of ferroportin in enterocytes, macrophages, and hepatocytes, thereby reducing the flux of iron into the systemic circulation (Ko et al., 2020; DeLoughery et al., 2024).

Table 1 Laboratory parameters across stages of iron deficiency

Parameter	Depletion of Stores	Iron-Deficient Erythropoiesis	Established Iron Deficiency Anemia
Serum Ferritin (ng/mL)	<15–30	<15	<15
Transferrin Saturation (%)	Normal	<16	<16
TIBC (µg/dL)	Normal or ↑	↑	↑
Hemoglobin (g/dL)	Normal	Normal or mild ↓	<12 women / <13 men
MCV (fL)	Normal	Normal or mild ↓	<80
Soluble Transferrin Receptor	Normal	↑	↑

Source: Prepared by the author based on Kawabata (2024) and Leung et al. (2024). MCV: mean corpuscular volume; TIBC: total iron-binding capacity. ↑ = elevated; ↓ = decreased.

2.2. Mechanisms of Gastric Mucosal Damage by *H. pylori* and Its Impact on Iron Absorption

The analysis of the included studies demonstrated that *H. pylori* compromises iron absorption through progressive structural and functional alterations of the gastric mucosa, the magnitude of which is proportional to the duration of the infection and the degree of accumulated histological damage (Becquart et al., 2017; Ko et al., 2020).

In the experimental study by Becquart et al. (2017) conducted in female C57BL/6 mice, it was shown that active *H. pylori*infection combined with a low-iron diet produced significant reductions in erythrocyte indices, including hemoglobin, hematocrit, and mean corpuscular volume, compared to the isolated intervention groups. This finding evidenced that *H. pylori* infection acts as a potentiation factor for iron deficiency, amplifying the effect of insufficient intake on the hematological status of the organism.

From a histopathological viewpoint, chronic *H. pylori* infection follows a progressive sequence of damage known as the Correa cascade, which comprises: chronic active gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia, and, in advanced cases, gastric adenocarcinoma. In the stages of atrophic gastritis, the progressive destruction of hydrochloric acid-producing parietal cells generates hypochlorhydria or achlorhydria, a condition that raises the intragastric pH above 4, severely compromising the reduction of dietary ferric iron to its absorbable ferrous form. In parallel, the reduction in intrinsic factor production by atrophic parietal cells may be associated with vitamin B12

deficiency, a condition that can coexist with IDA and contribute to a mixed anemia presentation (Ko et al., 2020; DeLoughery et al., 2024).

In the study by Abramowitz et al. (2024), which included 143 young patients with IDA, it was found that 28.6% presented positive findings on upper gastrointestinal endoscopy, of which 70.3% corresponded to histopathologically confirmed *H. pylori* gastritis or duodenitis. This data reflects that the gastric mucosal lesion induced by *H. pylori* is detectable and quantifiable in a significant proportion of young patients with IDA without an apparent hemorrhagic cause, underscoring the importance of endoscopic evaluation in this age group.

Table 2 Endoscopic and histopathological findings in young patients with iron deficiency anemia

Finding	**Frequency (%)**
Positive findings on upper gastrointestinal endoscopy (EGD)	28.6%
H. pylori gastritis/duodenitis (out of the positive findings)	70.3%
Positive findings on colonoscopy	8.3%
Asymptomatic patients with positive findings on EGD	42.9%
Symptomatic patients with positive findings on EGD	18.2%

Source: Prepared by the author based on Abramowitz et al. (2024). EGD: esophagogastroduodenoscopy. Note: The term 'duonitits' from the original text has been corrected to 'duodenitis'.

2.3. Role of Hepcidin and Ferroportin in Chronic Inflammation by *H. pylori*

The results of the bibliographic analysis evidenced that the hepcidin-ferroportin pathway constitutes the central pathophysiological mechanism linking chronic inflammation induced by *H. pylori* with reduced systemic iron availability, independently of the status of body iron stores (DeLoughery et al., 2024; Auerbach et al., 2025).

The chronic inflammatory response generated by *H. pylori* infection stimulates the production of various pro-inflammatory cytokines, among which interleukin-6 (IL-6) stands out as the primary inducer of hepatic hepcidin synthesis through the activation of the JAK2/STAT3 pathway. The sustained increase in hepcidin causes the internalization and lysosomal degradation of ferroportin in duodenal enterocytes, reticuloendothelial system macrophages, and hepatocytes, effectively blocking iron release into the systemic circulation from all its sources: intestinal absorption, macrophage stores, and hepatic stores (DeLoughery et al., 2024).

This phenomenon generates a characteristic functional hypoferremia, where body iron stores may be partially preserved but iron is unavailable for erythropoiesis due to ferroportin blockade. This condition can overlap or be confused with anemia of chronic disease or anemia of inflammation, complicating the differential diagnosis and misdirecting treatment exclusively toward oral iron supplementation without addressing the underlying cause of elevated hepcidin (Kawabata, 2024; Ko et al., 2020).

From a clinical perspective, Gaur et al. (2025) demonstrated that in 19.5% of the patients with IDA studied using the oral iron absorption test, an underlying malabsorption syndrome exists as the root cause, with *H. pylori* infection being the most frequent etiology, responsible for 54.1% of these cases. The oral iron absorption test showed a sensitivity of 89.2%, a specificity of 79.1%, and a negative predictive value of 97.6%, constituting an effective diagnostic tool to identify patients in whom the mechanism of IDA involves alterations in iron absorption or bioavailability mediated, among other factors, by hepcidin elevation (Gaur et al., 2025).

Table 3 Malabsorption etiologies identified via oral iron absorption test (OIAT) in patients with iron deficiency anemia

Malabsorption Etiology	**Frequency (%)**
Helicobacter pylori infection	54.1%
Autoimmune gastritis	27.0%
Celiac disease	18.9%
Total with demonstrated malabsorption	19.5% of the total patient cohort

Source: Prepared by the author based on Gaur et al. (2025). The percentages for specific etiologies correspond to the subgroup with demonstrated malabsorption (19.5% of the total cohort).

2.4. Mechanisms of Direct Bacterial Competition for Host Iron

The analysis of the available scientific evidence allowed the identification that *H. pylori* has developed a sophisticated set of host iron acquisition mechanisms, which actively contribute to the depletion of body stores and the development of IDA, independently of the indirect effects mediated by inflammation and hypochlorhydria (Becquart et al., 2017; Abramowitz et al., 2024).

Among the main mechanisms of direct bacterial competition for iron identified in the literature are the following: first, the production of lactoferrin-binding protein B (LbpB), which allows the bacterium to capture iron bound to lactoferrin present in gastric mucosal secretions; second, the expression of hemoglobin-binding proteins that facilitate the acquisition of heme iron from erythrocytes lysed during the local inflammatory response; third, the production of siderophores, low molecular mass molecules with high affinity for iron that enable its uptake from the gastric microenvironment; and fourth, the expression of the FeoB transport system, which allows the direct uptake of ferrous iron from the gastric environment, favored by the local microenvironment generated by the bacterium's own metabolic activity (Becquart et al., 2017).

The study by Becquart et al. (2017) experimentally demonstrated that active *H. pylori* infection modifies the expression of genes related to iron metabolism in the hippocampus of mice, showing that the impact of bacterial competition for iron transcends the gastrointestinal tract and can generate systemic effects that include neurological and behavioral alterations. This finding takes on special relevance in the context of the pediatric population, where iron deficiency during critical stages of neurological development can have irreversible consequences on cognition and learning.

2.5. Impact of *H. pylori* Eradication on Hematological Parameters

The results of the literature analysis consistently evidenced that successful eradication of *H. pylori* is associated with a significantly greater recovery of hematological parameters compared to isolated oral iron supplementation, particularly in patients with IDA refractory to conventional treatment (Abramowitz et al., 2024; DeLoughery et al., 2024; Ko et al., 2020).

DeLoughery et al. (2024) establish in the AGA clinical practice update that intravenous iron should be considered when oral treatment is ineffective or when an underlying condition compromises gastrointestinal absorption, such as *H. pylori*-induced chronic atrophic gastritis. This recommendation implies explicit recognition by one of the most influential gastroenterological societies worldwide that uneradicated *H. pylori* infection constitutes a real and frequent cause of refractoriness to oral iron treatment in IDA.

Ko et al. (2020) point out in the AGA clinical practice guidelines that *H. pylori* investigation should form part of the diagnostic algorithm for unexplained IDA, and that successful eradication of the bacterium must be considered an integral part of etiological treatment in all cases where active infection is documented. This recommendation has direct implications for clinical practice, given that eradication treatment with antibiotics and a proton pump inhibitor is accessible, short-term, and carries a high success rate when properly applied.

Gaur et al. (2025) demonstrated that the oral iron absorption test, by early identifying patients with malabsorption secondary to *H. pylori*, allows treatment to be directed toward bacterial eradication as a first-line therapy, with a subsequent favorable impact on the recovery of hematological parameters and a reduction in the need for prolonged iron supplementation.

Table 4 Diagnostic performance of the oral iron absorption test (OIAT) for identifying malabsorption in patients with iron deficiency anemia

Diagnostic Parameter	Value
Sensitivity	89.2%
Specificity	79.1%
Positive Predictive Value (PPV)	Not reported
Negative Predictive Value (NPV)	97.6%
Patients with abnormal OIAT	34.2%
Patients with confirmed malabsorption	19.5%

Source: Prepared by the author based on Gaur et al. (2025). OIAT: Oral Iron Absorption Test. PPV: Positive Predictive Value; NPV: Negative Predictive Value. Note: The incorrect acronym 'PAHO' from the original text has been updated to the correct term OIAT.

2.6. Integrated Pathophysiological Model

The integration of the analyzed evidence allowed the construction of a pathophysiological model that coherently and systematically explains the relationship between chronic gastritis due to *H. pylori* and the development of IDA through three main pathways that act synergistically and mutually potentiate each other (Becquart et al., 2017; Ko et al., 2020; DeLoughery et al., 2024; Auerbach et al., 2025).

- **The inflammatory pathway mediated by hepcidin:** Chronic infection by *H. pylori* stimulates the production of IL-6 and other pro-inflammatory cytokines that activate hepatic hepcidin synthesis via the JAK2/STAT3 pathway. This blocks ferroportin in enterocytes, macrophages, and hepatocytes, generating a functional hypoferremia that compromises erythropoiesis regardless of the state of body iron stores.
- **The structural pathway mediated by hypochlorhydria:** Progressive atrophy of parietal cells secondary to chronic inflammation elevates intragastric pH, preventing the reduction of ferric iron to ferrous iron and compromising its duodenal absorption. This has a greater impact on non-heme iron of plant origin, which represents the main dietary iron source in low-resource populations.
- **The direct bacterial competition pathway:** *H. pylori* utilizes its own iron acquisition systems—including LbpB, hemoglobin-binding proteins, siderophores, and the FeoB system—to capture iron from the gastric microenvironment at the expense of the host, contributing directly to the depletion of body iron stores and worsening the deficiency state.

The synergistic interaction of these three pathways explains why IDA associated with *H. pylori* chronic gastritis is frequently refractory to conventional oral iron treatment and tends to recur after its discontinuation if the underlying bacterial infection is not identified and eradicated. This integrated model further points out that the most effective therapeutic intervention point in this context is *H. pylori* eradication, which simultaneously interrupts the three described pathophysiological pathways, progressively restoring gastric mucosal integrity, normalizing intragastric pH, reducing hepcidin production, and eliminating bacterial competition for host iron (Ko et al., 2020; DeLoughery et al., 2024; Gaur et al., 2025).

3. Discussion

The results obtained in this study through a systematic review of the available scientific evidence confirm that chronic gastritis caused by *Helicobacter pylori* represents a relevant and frequently underestimated etiopathogenic factor in the development and perpetuation of iron deficiency anemia. It acts through three main pathophysiological pathways that mutually potentiate each other: the inflammatory pathway mediated by hepcidin, the structural pathway mediated by hypochlorhydria, and the direct bacterial competition pathway for host iron. These findings are consistent with recent scientific literature and reinforce the need to integrate *H. pylori* investigation into the standard diagnostic algorithm for unexplained IDA or cases refractory to conventional treatment.

3.1. On the Pathophysiology of Iron Deficiency Anemia and the Role of Gastric pH

One of the most relevant findings of this review is the confirmation of the central role of gastric pH in regulating non-heme iron absorption. As pointed out by Ko et al. (2020) and Kawabata (2024), reducing ferric to ferrous iron is an indispensable step for its uptake by the DMT-1 transporter at the apical pole of the duodenal enterocyte. This process occurs optimally in an acidic environment and is severely compromised when the intragastric pH exceeds 4. This finding is particularly relevant in the context of chronic gastritis caused by *H. pylori*, given that progressive parietal cell atrophy generates hypochlorhydria that can develop silently over years, obscuring the connection between both conditions for both the patient and the treating physician.

In this regard, the results of the present study are congruent with those of DeLoughery et al. (2024), who highlight in the AGA clinical practice update that atrophic gastritis secondary to *H. pylori* should be considered a frequent cause of suboptimal response to oral IDA treatment. They recommend evaluating intravenous iron in patients for whom oral supplementation is insufficient due to compromised gastrointestinal absorption. However, it is important to note that while intravenous iron treatment is effective for replenishing body stores, it does not resolve the root cause of malabsorption if the *H. pylori* infection is not eradicated, implying a real risk of IDA recurrence after parenteral treatment is discontinued (DeLoughery et al., 2024; Ko et al., 2020).

3.2. On the Role of Hepcidin as a Central Mediator of Functional Hypoferremia

The results of this review confirm that hepcidin represents the primary molecular mediator linking chronic inflammation induced by *H. pylori* with reduced systemic iron availability. This finding is consistent with that reported

by Auerbach et al. (2025), who detail the mechanism by which IL-6 produced in response to bacterial infection activates the JAK2/STAT3 pathway in hepatocytes, stimulating hepcidin synthesis and the subsequent blockade of ferroportin in enterocytes, macrophages, and hepatocytes. The clinical consequence of this mechanism is a functional hypoferremia that can coexist with partially preserved body iron stores, creating a scenario that can be confused with anemia of chronic disease and lead to inappropriate treatment (Kawabata, 2024; DeLoughery et al., 2024).

The distinction between true iron deficiency anemia and anemia of inflammation/disease is fundamental, given that the clinical treatment diverges radically: true IDA responds directly to iron supplementation and *H. pylori* eradication, whereas anemia of chronic disease requires controlling the underlying inflammatory process itself (Kawabata, 2024).

In this context, the finding by Gaur et al. (2025) is particularly relevant, demonstrating that the oral iron absorption test identified malabsorption in 34.2% of the patients with IDA studied, with *H. pylori* infection being the most frequent etiology at 54.1% of cases. This result suggests that a significant proportion of patients with IDA who are managed empirically with oral iron in primary care could have an underlying, identifiable, and treatable cause that is not being systematically investigated. The high sensitivity (89.2%) and high negative predictive value (97.6%) of the OIAT reported by these authors position this test as an effective, accessible, and minimally invasive first-line diagnostic tool for identifying patients with IDA secondary to *H. pylori*-mediated malabsorption (Gaur et al., 2025).

However, it is important to contrast this finding with the perspective of Ko et al. (2020), who acknowledge that implementing additional diagnostic tests in primary care can be limited by factors such as accessibility, cost, and infrastructure availability, particularly in low- and middle-income regions where the burden of IDA is highest. This tension between available evidence and real-world healthcare system limitations represents one of the main challenges in translating scientific findings into daily clinical practice, highlighting the need to develop diagnostic algorithms adapted to the context and resources available at each level of care (Ko et al., 2020; DeLoughery et al., 2024).

3.3. On the Mechanisms of Direct Bacterial Competition for Iron

The results of the scientific evidence analysis showed that *H. pylori* does not act solely through indirect pathways on iron metabolism via inflammation and hypochlorhydria, but also competes actively and directly for host iron using specific molecular systems. The experimental study by Becquart et al. (2017) provided foundational evidence in this regard, demonstrating that active *H. pylori* infection in mice on a low-iron diet produced significantly greater hematological and neurological alterations than those observed in the isolated intervention groups. This suggests a synergistic effect between direct bacterial competition for iron and insufficient dietary iron intake.

This finding is especially relevant in the context of Latin American populations, where the coexistence of a high prevalence of *H. pylori* infection, diets dominated by low-bioavailability non-heme iron, and socioeconomic conditions that limit access to animal-derived heme iron sources creates a scenario of particular vulnerability for the development of severe IDA and its consequences on cognitive development and productive capacity (Becquart et al., 2017; Leung et al., 2024). In this sense, the results of the present review differ from those reported in some previous studies that attributed IDA in these populations exclusively to dietary factors, underestimating the role of chronic bacterial infection as an independent etiopatogenic determinant (Gaur et al., 2025).

3.4. On the Impact of *H. pylori* Eradication on Hematological Recovery

One of the most relevant findings with major clinical implications in this review is the accumulated evidence regarding the favorable impact of *H. pylori* eradication on the recovery of hematological parameters in patients with IDA. The results of the analysis are consistent in pointing out that successful eradication of the bacterium—by simultaneously interrupting the three described pathophysiological pathways—leads to a more complete and durable recovery of hemoglobin and serum ferritin levels compared to isolated oral iron supplementation, particularly in patients with refractory or recurrent IDA (Ko et al., 2020; DeLoughery et al., 2024; Abramowitz et al., 2024).

In agreement with these findings, Abramowitz et al. (2024) reported that in 70.3% of young patients with IDA and positive endoscopic findings, the underlying diagnosis was histopathologically confirmed *H. pylori* gastritis or duodenitis, reinforcing the recommendation to consider endoscopic evaluation in young patients with unexplained IDA. These results align with the recommendations of Ko et al. (2020) and DeLoughery et al. (2024), who state that the investigation and eradication of *H. pylori* must be an integral part of the therapeutic approach to IDA in all cases where active infection is documented, given that eradication antibiotic treatment is accessible, short-term, and carries a high success rate when properly applied.

Nevertheless, it is important to recognize that the available evidence on the impact of *H. pylori* eradication on hematological recovery comes predominantly from observational studies and narrative reviews, with a limited availability of high-methodological-quality randomized clinical trials evaluating this association prospectively and under controlled conditions. This limitation in the current evidence represents an opportunity for future research to strengthen clinical recommendations with a more robust level of evidence (Gaur et al., 2025; DeLoughery et al., 2024).

3.5. On the Limitations of the Present Investigation

This study presents some limitations that must be honestly and transparently acknowledged. First, as a systematic bibliographic review with a qualitative-descriptive design, the results obtained depend on the quality and availability of the primary studies included, making it impossible to generate original data to complement or contrast the analyzed evidence. Second, the methodological variability among the included studies, which range from experimental research in animal models to narrative reviews and clinical practice guidelines, limits the possibility of making direct comparisons between their results.

Third, the absolute majority of primary papers evaluated were restricted to populations within highly developed nations or Asian regions, meaning primary datasets from Latin American contexts were noticeably limited. This lack of regional studies restricts direct extrapolation to the Mexican population, where unique epidemiological, dietary, and socioeconomic conditions significantly influence clinical presentations (Becquart et al., 2017; Abramowitz et al., 2024).

These limitations signal the need to develop primary research within the Latin American and Mexican context to characterize more precisely the prevalence, mechanisms, and clinical impact of the association between *H. pylori* chronic gastritis and IDA in our population, generating local evidence that complements and enriches global knowledge on this topic (Ko et al., 2020; Gaur et al., 2025).

4. Conclusion

This study systematically and comprehensively analyzed the pathophysiological mechanisms that explain the development of iron deficiency anemia in patients with chronic gastritis caused by *Helicobacter pylori*, answering the research question posed and providing a solid theoretical basis that supports the need for a more comprehensive diagnostic and therapeutic approach to this association in clinical practice.

Based on the evidence analyzed, it is concluded that chronic gastritis caused by *H. pylori* generates iron deficiency anemia through three main pathophysiological pathways that act synergistically and mutually potentiate each other. First, the inflammatory pathway mediated by hepcidin, in which the chronic inflammatory response stimulates the production of IL-6, activating hepatic hepcidin synthesis via the JAK2/STAT3 pathway, blocking ferroportin in enterocytes, macrophages, and hepatocytes, and generating a functional hypoferremia that compromises erythropoiesis independently of the status of body iron stores. Second, the structural pathway mediated by hypochlorhydria, in which progressive parietal cell atrophy raises the intragastric pH above the values required for the reduction of ferric to ferrous iron, severely compromising the duodenal absorption of dietary non-heme iron. Third, the direct bacterial competition pathway, in which *H. pylori* uses specialized molecular systems, including LbpB, hemoglobin-binding proteins, siderophores, and the FeoB system, to capture iron from the gastric microenvironment at the expense of the host, actively contributing to the depletion of body iron stores.

Regarding the hypothesis posed, the research results allow for its acceptance, given that the reviewed scientific evidence confirms that *H. pylori* chronic gastritis effectively generates a multi-mechanistic pathophysiological alteration comprising sustained hepcidin elevation mediated by chronic inflammation, hypochlorhydria secondary to parietal cell atrophy, and direct bacterial competition for host iron, collectively conditioning a significant reduction in iron absorption and systemic availability that explains the development and perpetuation of iron deficiency anemia in affected patients.

From an epidemiological perspective, the coexistence of an *H. pylori* infection prevalence exceeding 60% in the adult Mexican population with a high burden of iron deficiency anemia in vulnerable groups establishes a scenario of particular relevance for national public health, where timely identification and eradication of the bacterium could have a significantly favorable impact on the prevalence and recurrence of iron deficiency anemia in our population.

From a clinical viewpoint, it is concluded that systematic investigation of *H. pylori* must be integrated into the diagnostic algorithm of any patient with unexplained, recurrent, or conventional oral iron treatment-refractory iron deficiency anemia, and that successful eradication of the bacterium must be considered an indispensable component of etiological

treatment in all cases where active infection is documented, as it simultaneously interrupts the three pathophysiological pathways that perpetuate iron deficiency. The oral iron absorption test, with a sensitivity of 89.2% and a negative predictive value of 97.6% for identifying malabsorption secondary to *H. pylori*, represents an accessible and effective diagnostic tool that can guide etiological treatment in these patients early and precisely.

Finally, this study identifies the need to develop primary clinical studies within the Latin American and Mexican context to more accurately characterize the magnitude and specific features of the association between *H. pylori* chronic gastritis and iron deficiency anemia in our population, as well as to evaluate prospectively and under controlled conditions the impact of bacterial eradication on the recovery of hematological parameters, generating local evidence that complements available global knowledge and guides the design of more effective and contextualized public health policies for the comprehensive management of iron deficiency anemia in Mexico.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this manuscript.

Statement of ethical approval

This article is a systematic review of available literature and secondary data. It does not contain any studies with human participants or animals performed by any of the authors; therefore, formal ethical approval was not required for this study.

Statement of informed consent

For this type of study (systematic literature review), formal informed consent from patients was not required as no clinical trials or direct interventions were performed.

References

[1] Abramowitz, B. R., Saba, H., Aytaman, A., DiLeo, D. A., & Roland, B. C. (2024). Diagnostic yield of bidirectional endoscopy for iron deficiency anemia in young patients. BMC Gastroenterology, 24(1), 269. https://doi.org/10.1186/s12876-024-03372-y
PDF

[2] Auerbach, M., DeLoughery, T. G., & Tirnauer, J. S. (2025). Iron deficiency in adults: A review. JAMA, 333(20), 1813-1823. https://doi.org/10.1001/jama.2025.3001
PDF

[3] Ayala, G., Escobedo-Hinojosa, W., de la Cruz-Herrera, C. F., & Romero, I. (2014). Exploring alternative treatments for Helicobacter pylori infection. World Journal of Gastroenterology, 20(6), 1450-1469. https://doi.org/10.3748/wjg.v20.i6.1450
PDF

[4] Becquart, P., Labrousse, V. F., Peyroux, J., Dhieux, B., Hidalgo, S., Joffre, C., Layé, S., & Ruel, J. (2017). Helicobacter pylori infection and low dietary iron alter behavior, induce iron deficiency anemia, and modulate hippocampal gene expression in female C57BL/6 mice. PLoS One, 12(3), e0173108. https://doi.org/10.1371/journal.pone.0173108
PDF

[5] Camaschella, C. (2019). Iron deficiency. Blood, 133(1), 30-39. https://doi.org/10.1182/blood-2018-05-815944
PDF

[6] Cappellini, M. D., Comin-Colet, J., de Francisco, A., Dignass, A., Doehner, W., Lam, C. S., Macdougall, I. C., Rogler, G., Camaschella, C., Kadir, R. A., Kassebaum, N. J., Spahn, D. R., Taher, A. T., & Muckenthaler, M. U. (2017). Iron deficiency across chronic inflammatory conditions: International expert opinion on definition, diagnosis, and

management. American Journal of Hematology, 92(10), 1068-1078. https://doi.org/10.1002/ajh.24820
PDF

[7] Crowe, S. E. (2019). Helicobacter pylori infection. New England Journal of Medicine, 380(12), 1158-1165. https://doi.org/10.1056/NEJMcp1710945
PDF

[8] DeLoughery, T. G., Jackson, C. S., Ko, C. W., & Rockey, D. C. (2024). AGA clinical practice update on management of iron deficiency anemia: Expert review. Clinical Gastroenterology and Hepatology, 22(8), 1575-1583. https://doi.org/10.1016/j.cgh.2024.03.046
PDF

[9] Ganz, T. (2019). Anemia of inflammation. New England Journal of Medicine, 381(12), 1148-1157. https://doi.org/10.1056/NEJMra1903213
PDF

[10] Ganz, T., & Nemeth, E. (2012). Hepcidin and iron homeostasis. Biochimica et Biophysica Acta, 1823(9), 1434-1443. https://doi.org/10.1016/j.bbamcr.2012.01.014
PDF

[11] Gaur, S., Sharma, V., Gaur, V., & Bagrodia, V. (2025). Oral iron absorption test as a predictor of response to oral iron therapy and gastrointestinal malabsorption syndromes in iron deficiency anemia. Journal of the Association of Physicians of India, 73(11), 20-23. https://doi.org/10.59556/japi.73.1222
PDF

[12] Iolascon, A., Andolfo, I., Russo, R., Sanchez, M., Busti, F., Swinkels, D., Aguilar-Martinez, P., Bou-Fakhredin, R., Muckenthaler, M. U., Unal, S., Porto, G., Ganz, T., Kattamis, A., De Franceschi, L., Cappellini, M. D., Munro, M. G., & Taher, A. (2024). Recommendations for diagnosis, treatment, and prevention of iron deficiency and iron deficiency anemia. HemaSphere, 8(7), e108. https://doi.org/10.1002/hem3.108
PDF

[13] Kawabata, H. (2024). Diagnosis and treatment of iron deficiency anemia. Rinsho Ketsueki, 65(6), 503-513. https://doi.org/10.11406/rinketsu.65.503
PDF

[14] Ko, C. W., Siddique, S. M., Patel, A., Harris, A., Sultan, S., Altayar, O., & Falck-Ytter, Y. (2020). AGA clinical practice guidelines on the gastrointestinal evaluation of iron deficiency anemia. Gastroenterology, 159(3), 1085-1094. https://doi.org/10.1053/j.gastro.2020.06.046
PDF

[15] Lanas, A., & Chan, F. K. L. (2017). Peptic ulcer disease. The Lancet, 390(10094), 613-624. https://doi.org/10.1016/S0140-6736(16)32404-7
PDF

[16] Leung, A. K. C., Lam, J. M., Wong, A. H. C., Hon, K. L., & Li, X. (2024). Iron deficiency anemia: An updated review. Current Pediatric Reviews, 20(3), 339-356. https://doi.org/10.2174/1573396320666230727102042
PDF

[17] Malfertheiner, P., Megraud, F., Rokkas, T., Gisbert, J. P., Liou, J. M., Schulz, C., Gasbarrini, A., Hunt, R. H., Leja, M., O'Morain, C., Rugge, M., Suerbaum, S., Tilg, H., Sugano, K., & El-Omar, E. M. (2022). Management of Helicobacter pylori infection: The Maastricht VI/Florence consensus report. Gut, 71(9), 1724-1762. https://doi.org/10.1136/gutjnl-2022-327745
PDF

[18] Muckenthaler, M. U., Rivella, S., Hentze, M. W., & Galy, B. (2017). A red carpet for iron metabolism. Cell, 168(3), 344-361. https://doi.org/10.1016/j.cell.2016.12.034
PDF

[19] Nemeth, E., & Ganz, T. (2021). Hepcidin-ferroportin interaction controls systemic iron homeostasis. International Journal of Molecular Sciences, 22(12), 6493. https://doi.org/10.3390/ijms22126493
PDF

[20] Palacios Martínez, D., Muñoz Pérez, M., Pérez Ros, P., & Martínez-Arnau, F. M. (2021). Iron deficiency anemia: Etiology, diagnosis and treatment. Medicina General y de Familia, 10(2), 53-58. https://doi.org/10.24038/mgyf.2021.021
PDF

[21] Tolkien, Z., Stecher, L., Mander, A. P., Pereira, D. I. A., & Powell, J. S. (2015). Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: A systematic review and meta-analysis. PLoS One, 10(2), e0117383. https://doi.org/10.1371/journal.pone.0117383 PDF

APPENDIX (Acronyms & Abbreviations)

Acronym	Meaning
AGA	American Gastroenterological Association
DcytB	Duodenal cytochrome b reductase
DMT-1	Divalent metal transporter 1
EGD	Esophagogastroduodenoscopy
Fe^{2+}	Ferrous iron (absorbible form)
Fe^{3+}	Ferric iron (dietary non-heme form)
H. pylori	*Helicobacter pylori*
HCP-1	Heme carrier protein-1
IDA	Iron deficiency anemia
IL-6	Interleukin-6
JAK2/STAT3	Janus kinase 2 / Signal transducer and activator of transcription 3
LbpB	Lactoferrin-binding protein B
LILACS	Latin American and Caribbean Health Sciences Literature
MCV	Mean corpuscular volume
NPV	Negative Predictive Value
OIAT	Oral Iron Absorption Test (corrected from 'PAHO')
PPV	Positive Predictive Value
TIBC	Total iron-binding capacity
WHO	World Health Organization