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Risk factors associated with *Helicobacter pylori* infection: a retrospective analysis of patients with gastric diseases

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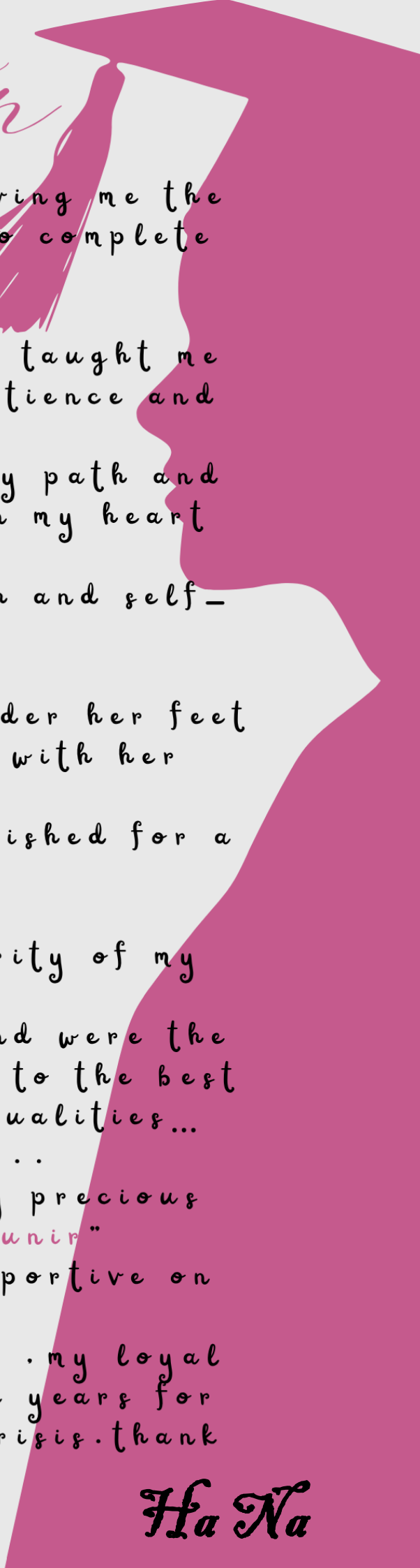
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Dedication



I thank Almighty ALLAH for giving me the strength. health and courage to complete this precious work.

I dedicate this work :

To all those who sweat and who taught me that success comes only with patience and persistence.

To the light that illuminated my path and the lamp that never goes out in my heart .....

The one who gave me my strength and self-esteem ....

" Dad "

To the one who made paradise under her feet and made my hardships easier with her prayers .....

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Abstract

Helicobacter pylori is a universally widespread bacterial pathogen affecting nearly half of the global population, with prevalence rates ranging from 85% to 95% in developing countries compared to much lower rates, often below 40%, in developed countries. The risk factors that contribute to acquiring *H. pylori* infection include low socioeconomic status, poor sanitation, crowded living conditions, consumption of contaminated water and food, and certain lifestyle habits. Although often asymptomatic, *H. pylori* is implicated in various gastrointestinal diseases, including chronic gastritis, peptic ulcers, and gastric cancer. Recognized by the World Health Organization (WHO) as a Group 1 carcinogen, *H. pylori* poses a significant public health challenge. Understanding its epidemiology and risk determinants is crucial for effective public health interventions.

This study presents a retrospective analysis of *H. pylori* infection prevalence and its associated gastrointestinal pathologies in Medea. Data were collected from medical records of patients diagnosed with *H. pylori* infection over the past five years at the cyto-hitso anatomopathology laboratory at Public Health Establishment (PHE) of Mohamed Boudiaf in the region. Demographic variables, clinical presentations, and potential risk factors such as age and gender were analyzed.

The findings reveal a high prevalence of *H. pylori* infection at 73%, with strong associations between infection and various gastrointestinal conditions, particularly chronic gastritis, which affected the majority of patients. Females were the most affected gender in this region, and adults constituted the largest infected age group.

This retrospective analysis provides valuable insights into the epidemiological patterns of *H. pylori* infection and its role in different gastric pathologies, thereby contributing to a better understanding of the burden of this bacterium in our region and highlighting the need for enhanced preventive measures.

Keywords : *Helicobacter pylori*, Prevalence, Gastrointestinal diseases, Retrospective analysis, Risk factors.

Résumé

Helicobacter pylori est un pathogène bactérien universellement répandu, affectant près de la moitié de la population mondiale, avec des taux de prévalence allant de 85 % à 95 % dans les pays en développement, comparativement à des taux beaucoup plus faibles, souvent inférieurs à 40 %, dans les pays développés. Les facteurs de risque contribuant à l'acquisition de l'infection par *H. pylori* incluent un faible statut socio-économique, de mauvaises conditions sanitaires, la promiscuité, la consommation d'eau et d'aliments contaminés, ainsi que certaines habitudes de vie. Bien que souvent asymptomatique, *H. pylori* est impliqué dans diverses maladies gastro-intestinales, notamment la gastrite chronique, les ulcères gastroduodénaux et le cancer gastrique. Reconnu par l'Organisation mondiale de la Santé (OMS) comme un agent carcinogène du groupe 1, *H. pylori* constitue un défi majeur de santé publique. La compréhension de son épidémiologie et de ses facteurs de risque est essentielle pour la mise en place d'interventions sanitaires efficaces.

Notre étude présente une analyse rétrospective de la prévalence de l'infection à *H. pylori* et des pathologies gastro-intestinales associées dans la région de Médéa. Les données ont été recueillies à partir des dossiers médicaux des patients diagnostiqués avec une infection à *H. pylori* au cours des cinq dernières années au laboratoire de cyto-histo-anatomopathologie de l'Établissement Public Hospitalier (EPS) Mohamed Boudiaf dans la région. Les variables démographiques, les présentations cliniques et les facteurs de risque potentiels tels que l'âge et le sexe ont été analysés.

Les résultats révèlent une prévalence élevée de l'infection à *H. pylori* de 73 %, avec de fortes associations entre l'infection et diverses affections gastro-intestinales, en particulier la gastrite chronique qui touche la majorité des patients. Les femmes sont le groupe le plus affecté dans cette région, et les adultes constituent la tranche d'âge la plus infectée.

Cette analyse rétrospective fournit des informations précieuses sur les profils épidémiologiques de l'infection à *H. pylori* et son rôle dans différentes pathologies gastriques, contribuant ainsi à une meilleure compréhension du fardeau que représente cette bactérie dans notre région et soulignant la nécessité de renforcer les mesures préventives.

Mots clés : *Helicobacter pylori*, Prévalence, Maladies gastro-intestinales, Facteurs de risque, Analyse rétrospective.

الملخص

البكتيريا البوابية الملتوية هي جرثومة بكتيرية منتشرة على مستوى العالم وتؤثر على ما يقرب من نصف سكان العالم، وتتراوح معدلات انتشارها بين 85% و95% في البلدان النامية مقارنة بمعدلات أقل بكثير، غالباً ما تكون أقل من 40% في البلدان المتقدمة. تشمل عوامل الخطر التي تساهم في الإصابة بعدوى البكتيريا البوابية الملتوية تدني الوضع الاجتماعي والاقتصادي وسوء الصرف الصحي والظروف المعيشية المزدحمة واستهلاك المياه والأغذية الملوثة وبعض عادات نمط الحياة. على الرغم من عدم وجود أعراض في كثير من الأحيان، إلا أن البكتيريا البوابية الملتوية متورطة في العديد من أمراض الجهاز الهضمي، بما في ذلك التهاب المعدة المزمن والقرحة الهضمية وسرطان المعدة. وقد اعترفت منظمة الصحة العالمية (WHO) بالبكتيريا البوابية الملتوية كمسرطن من المجموعة الأولى، مما يجعلها تشكل تحدياً كبيراً للصحة العامة. ويُعد فهم علم الأوبئة ومحددات الخطر أمرًا بالغ الأهمية لتدخلات الصحة العامة الفعالة.

تقدم هذه الدراسة تحليلاً بأثر رجعي لانتشار عدوى البكتيريا البوابية الملتوية وأمراض الجهاز الهضمي المرتبطة بها في المدية. وقد تم جمع البيانات من السجلات الطبية للمرضى الذين تم تشخيص إصابتهم بعدوى البوابية الملتوية على مدى السنوات الخمس الماضية في مختبر التشريح الخلوي في مؤسسة الصحة العمومية في محمد بوضياف في المنطقة. تم تحليل المتغيرات الديموغرافية والعروض السريرية وعوامل الخطر المحتملة مثل العمر والجنس.

كشفت النتائج عن ارتفاع معدل انتشار عدوى البكتيريا البوابية الملتوية بنسبة 73%، مع وجود ارتباطات قوية بين العدوى ومختلف أمراض الجهاز الهضمي، وخاصة التهاب المعدة المزمن الذي أصاب غالبية المرضى. كانت الإناث هن الجنس الأكثر إصابة في هذه المنطقة، وشكل البالغون أكبر فئة عمرية مصابة.

يوفر هذا التحليل بأثر رجعي رؤى قيمة حول الأنماط الوبائية لعدوى البوابية الملتوية ودورها في أمراض المعدة المختلفة، مما يساهم في فهم أفضل لعبء هذه البكتيريا في منطقتنا ويسلط الضوء على الحاجة إلى تعزيز التدابير الوقائية.

الكلمات المفتاحية: البكتيريا البوابية الملتوية، معدل الانتشار، أمراض الجهاز الهضمي، تحليل بأثر رجعي، عوامل الخطر.

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List of abbreviation

Ab: Antibodies.

ABO: Blood group system.

AlpA/ AlpB: Adherence associated lipoprotein A and B.

ALPK1-TIFA: Alpha Kinase 1-Traf-interacting protein.

ASPP2: Apoptosis-stimulating protein of p53 2.

ATP: Adenosine triphosphate.

ATPase: Adenosine Triphosphatase.

BHI: Brain-heart infusion.

CD4+: Cluster of differentiation 4.

CLO: Campylobacter-like organism.

DNA: Deoxyribonucleic acid.

DSBs: Double-strand breaks.

***E. coli*:** *Escherichia coli.*

ECL : Enterochromaffin-like cells.

Fla A : Flagellins A.

Fla B : Flagellins B.

GECs: Gastric epithelial cells.

GESA: Gastroesophageal.

GI: Gastrointestinal.

***H.muridarum*:** *Helicobacter muridarum*.

H&E: Hematoxylin and eosin.

***H.felis* :** *Helicobacter felis*.

***H.pylori* :** *Helicobacterpylori*.

HCL: Hydrochloric acid.

HpSA: Health Professional Shortage Area.

***H.pylori*:** *Helicobacter pylori*.

ICC: Interstitial cells of Cajal.

IgG : immunoglobulin G.

IHC : Immunohistochemical.

IL-8 : Interleukin-8.

MALDI-TOF MS: Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry.

MALT: Mucosa-Associated Lymphoid Tissue.

MSCs: Mesenchymal Stem Cells.

NF-KB: Nuclear Factor kappa-light-chain-enhancer of activated B cells.

OMPs: Outer Membrane Proteins.

ORFs: open reading Frames.

PAMPs: Pathogen-associated molecular patterns.

PCR: Polymerase Chain Reaction.

PCR-RFLP: the PCR-based restriction fragment length polymorphism.

Ph: Potentiel hydrogène.

PMF: peptide mass fingerprinting.

PMNs: Polymorphonuclear leukocytes.

PPIs: Proton pump inhibitors.

PRRs: Pattern recognition receptors.

PUD: Peptic ulcer disease.

rRNA: Ribosomal Ribonucleic Acid.

RUNX3: Run-related transcription factor 3.

RUT: Rapid urease test.

SLex: Sialyl Lewis X.

T4SS: type IV secretion system.

Th: T helper.

TNF: Tumor Necrosis Factor.

WHO: the World Health Organization.

Introduction

A common cause of peptic ulcer disease, chronic gastritis, and gastric cancer is *Helicobacter pylori,* a Gram-negative bacterium that colonizes the human stomach mucosa.**[1]** It was first discovered by Marshall and Warren in 1982, and because of its high correlation with stomach cancers, the World Health Organization currently classifies it as a Group I carcinogen.**[2]**

About 50% of people worldwide are infected, with greater prevalence rates seen in underdeveloped nations, mostly as a result of inadequate sanitation, overcrowding, and low socioeconomic standing.**[3]** Long-term infection can cause gradual stomach damage, such as atrophic gastritis and intestinal metaplasia precursor lesions for gastric cancer even though many infected people do not exhibit any symptoms.

Individual differences in *H. pylori* infection clinical outcomes are caused by a confluence of environmental variables (such as smoking, nutrition, and genetic susceptibility), bacterial virulence factors and host factors.**[4]**

Understanding these risk factors is essential for improving early diagnosis, guiding treatment strategies, and implementing effective prevention programs.

The purpose of this dissertation is to look at the risk factors for *Helicobacter pylori* infection in people who have different stomach diseases. To find trends and connections between infection status and clinical, demographic, and lifestyle-related factors, the study used a retrospective analysis of medical data from a specific patient group in Medea Public Hospital Establishment.

The specific objectives of this research are:

- ✓ To determine the prevalence of *H. pylori* infection among patients diagnosed with different gastric pathologies.
- ✓ To identify and evaluate potential demographic, clinical, and behavioral risk factors associated with *H. pylori* infection.
- ✓ To assess the relationship between *H. pylori* infection and the severity of gastric pathologies (e.g., gastritis, peptic ulcer, gastric cancer).

Bibliography section

Chapter 01:

Helicobacter pylori

I. History

The stomach's natural acidity led to the long-held belief that it was sterile. But in both humans and many animals, highly specialized microorganisms live on the surface of the digestive tract, especially the stomach. Only in the past decade has this finding been used to human medicine, yet it is not a novel one.**[5]**

After finding bacteria in the floor and margins of stomach ulcers, Bottcher and Letulle originally postulated that bacteria were the cause of ulcer illness in **1875**. The spiral organisms (*Vibrio rugula*) in stomach washings were first reported by Walery Jaworski in **1889**. He proposed that these microorganisms may be involved in the development of stomach disorders. Between then until the 20th century, a number of scientists discovered similar spiral critters in the stomachs of humans and other mammals. Bizzozero discovered spirochetes in the stomach mucosa of dogs in **1893**, for example, and called them *H. bizzozeroni*. Spirochetes were isolated in cats by Kasai and Kobayashi in **1920**, and they were then transferred to rabbits to cause ulcers. **[6]**

Year	Individual	Observations
1875	G. Bottcher/M. Letulle	demonstrated bacteria in ulcer margins
1881	C. Klebs	bacterial colonization and 'interglandular small cell infiltration'
1888	M. Letulle	experimental induction of acute gastric lesions in guinea pigs *(S. aureus)*
1889	W. Jaworski	spiral organisms *(Vibrio rugula)* in gastric washings
1893	G. Bizzozero	identified spirochetes in gastric mucosa of dogs
1896	H. Salomon	spirochetes noted in gastric mucosa and experimentally transferred to mice
1906	W. Krienitz	spirochetes in gastric contents of patient with gastric carcinoma
1908	F.B. Turck	induced gastric ulcers in dogs by *Bacillus (Escherichea) coli*
1916	E.C. Rosenow	described streptococcus induced gastric ulcers
1917	L.R. Dragstedt	identified bacteria in experimental ulcers, no significant role identified
1921	J.S. Edkins	experimental physiology of *S. regaudi (H. felis)*
1924	J.M. Luck	discovered gastric mucosal urease
1925	B. Hoffman	described *B. Hoffmani* – putative ulcerous agent
1930	B. Berg	partial vagotomy inhibits secondary infections in ulcers
1938	J.L. Doenges	spirochetes/inflammation in *Macacus* monkey and man
1940	A.S. Freedberg/L. Barron	identified spirochetes in man – no etiologic role
1940	F.D. Gorham	postulated gastric acidophilic bacteria as an etiologic agent in ulcer disease
1954	E.D. Palmer	no spirochetes detected using HE in 1,180 suction biopsies
1975	H.W. Steer	polymorphonuclear migration in ulcers – isolated *Pseudomonas aeruginosa*
1983	J.R. Warren	identified *Campylobacter (Helicobacter) pylori* in human gastritis
1983	B. Marshall	isolated and cultured *H. pylori*
1985–1987	B. Marshall/A. Morris	ingested and proved the infectivity of *H. pylori* (Koch's 3rd postulate)

Figure 1: History of *Helicobacter pylori* **[7]**

In **1983**, Warren determined that *Campylobacter pylori* was the likely cause of gastritis in humans.**[7]**. Based on its cultural, morphological (figure 2), metabolic, and ecological traits, *H pylori* was initially categorized with the *Campylobacter* species. It was then renamed Campylobacter pyloridis and *Campylobacter pylori*.



Figure 2: *Campylobacter* under an electron microscope **[5].**

Warren and Marshall's discovery of *H. pylori* came after nearly a century of dull publications about spiral bacteria, achlorhydria, gastritis, stomach urease, and antibiotic therapy for ulcers. Proper study of stomach bacteria could start in the second half of the 19th century when microscope resolution had sufficiently increased.**[6]** H. *pylori* is unusual in many aspects, specifically tailored to the human stomach, and is known to play a significant role in a variety of gastric disorders.**[8].**

Over 50% of people globally *have Helicobacter pylori* infections in their upper gastrointestinal tracts.**[3]**

II. Taxonomy:

H. pylori species taxonomy:

Kingdom	Eubacteria
Class	*Epsilonproteobacteria*
Phylum	*Proteobacteria*
Order	*Campylobacterales*
Family	*Helicobacteraceae*
Genus	*Helicobacter*
Species	*Helicobacter pylori*

Table 1: Taxonomy of *H.pylori*

There are now **30** confirmed species in the *Helicobacter* genus. *Helicobacters* are classified into two types based on the particular habitats they are linked to *enterohepatic Helicobacters*, which populate the bile ducts and gastrointestinal system, and gastric *Helicobacters*, which include *H. pylori* and *H. felis.***[9]**.

III. Bacteriological characteristics

1. Morphology:

As the name suggests, *H. pylori* is a spiral-shaped bacteria that was found in the stomach near the pylorus. *Helicobacter, Campylobacter, Arcobacter, and Wolinella* are the four genera that make up the super Family VI of Gram-negative bacilli, a novel group of bacteria that it is thought to be the leader of. In addition to the many sheathed flagella (4–6) and the presence of certain fatty acids and menaquinones of significant taxonomic importance, *H. pylori* is distinguished from the other groups mainly by the structure of its ribosomal RNA (16S).**[9]**

- Macroscopic appearance:

The findings from the culture of the four samples on blood-enriched agar reveal the formation of tiny colonies 1 to 2 mm in diameter after incubation for 2 to 5 days at 37°C in an oxygen-depleted environment under circumstances conducive to *H. pylori* growth. The colonies are circular, subtly domed, and have a consistent contour. They are either gray or translucent and glossy.

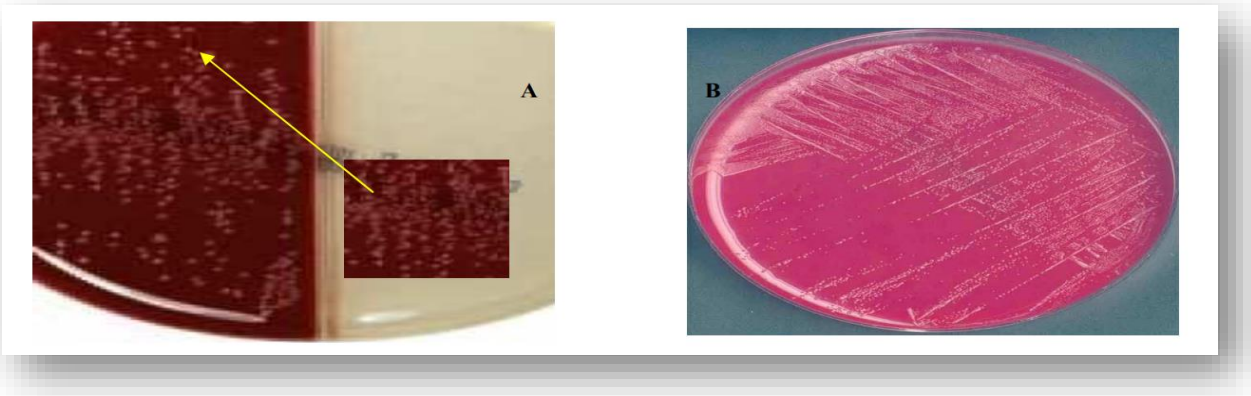


Figure 3: Macroscopic appearance of *H.pylori* colonies after 5 days incubation at 37°C in a micro-aerophilic atmosphere; A: medium (Biomérieux); B: blood agar media.

➢ Microscopic appearance:

Gram stain: microorganisms that are Gram-negative. They resemble regular-outlined bacilli that might be straight, curved, comma-shaped, C-shaped, V-shaped, or S-shaped. Over the course of outbreaks, bacteria quickly change into forms that resemble cocci (Figure 04).

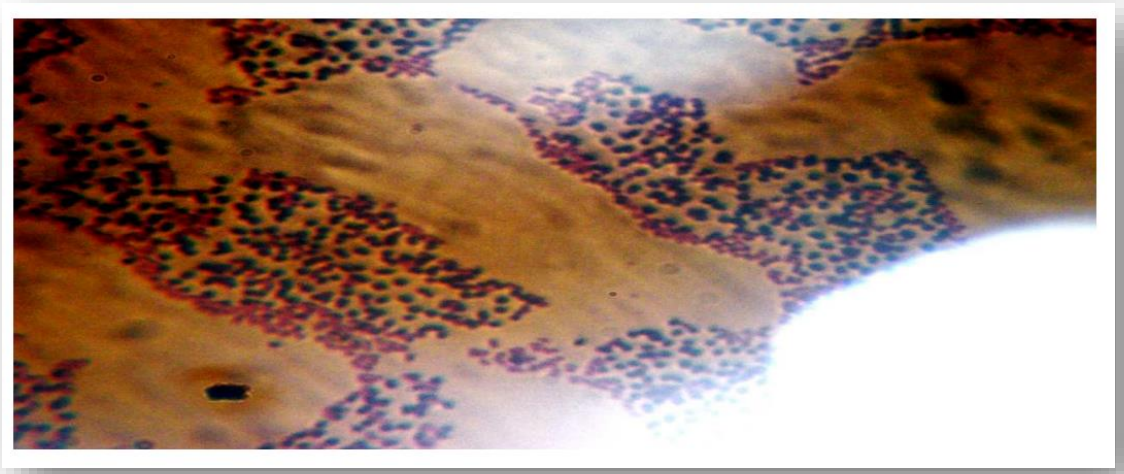


Figure 3: Microscopic appearance of *H.pylori.* **[10]**

Helicobacter pylori is a gram-negative spiral creature that grows slowly and is microaerophilic. It has many encased flagella at one end and ranges in width from 0.5 to 8.0µm.**[11]**

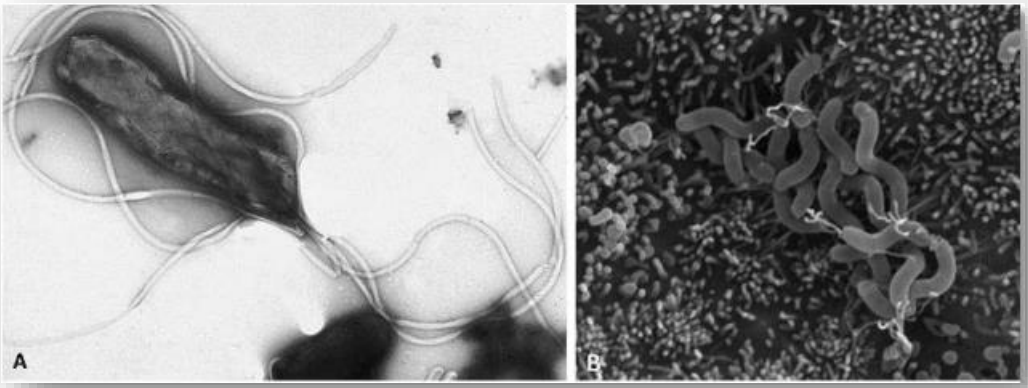


Figure 5: *Helicobacter pylori* under electron microscope; A: *H.pylori;* B: *H.pylori* clusters in gastric epithelial cells.**[12]**

There is ongoing discussion over the potential significance of the coccoid form in *H. pylori* transmission and infection recurrence following antimicrobial treatment. Morphologic change to viable but nonculturable forms has been described as a strategy enabling other microbes to withstand extreme environmental circumstances.

The morphologic transition rate of *H. pylori* ATCC 43504 changed as a result of exposure to various temperatures, fasting, and aerobiosis. The organism's viability and the pace at which helical forms of *H. pylori* changed into coccoid forms were most affected by exposure to an anaerobic environment.**[13]**

2. Biochemical characteristics:

The bacteria have a high degree of enzymatic activity since it possesses positive urease, catalase, and oxidase. The bacteria do not employ sugar substrates as carbon sources; instead, it uses citrates. The outcomes are displayed in the table.

Biochemicals	***H.pylori***
Urease	+
Catalase	+
Oxydase H	+
LDC	+
ODC	+
ADH	+
ONPG	-
Simmons citrate	+
Mannitol	-

Table 2: Biochemical characteristics of *H.pylori* : +: Positif / -: Négatif / ONPG: Ortho-nitrophenyl-β-galactoside / LDC: Lysine / ODC: Ornithine / ADH: Arginine.**[10]**

Most species of the genus *Campylobacter* have the property of not being able to ferment or oxidize carbohydrates. The primary purpose of *H. pylori*'s strong urease activity is to provide nitrogen from urea. It is still unknown how *H. pylori* meets its energy and carbon requirements. Furthermore, there are no data that provide insight into *H. pylori*'s phosphorus supply.**[14]**

3. Culture:

H. muridarum, a commensal bacterium that colonized the crypts of the mouse caecum, was really the first *Helicobacter* to be cultured. **[15]**

H. pylori is cultivated in a lab setting on culture medium that are enriched and generally nutrient-rich. Instead of addressing the true demand for growth and energy supply, the culture

techniques have "domesticated" *H. pylori* by creating ideal growth circumstances. *H. pylori* develops on enriched medium that contain complex organic elements including blood, peptones, and yeast extract. Some of these substances, such activated charcoal, soluble starch, and fetal calf serum, also promote growth. One noteworthy finding is that *H. pylori* may thrive on medium that is virtually devoid of carbs.**[14]**

In vitro, *H. pylori* develop slowly on cultivation **[16]**.

4. Genetics:

The genome of *H. pylori* strain 26695 consists of a circular chromosome with a size of 1,667,867 base pairs (bp) with 1,590 predicted coding sequences and average G+ C content of 39%.**[17]**

When the whole genome of *H. pylori* strain 26695 was sequenced in **1997**, it was proposed that 32 OMPs were encoded.**[18]** which have been divided into the hop (*helicobacter* outer membrane porins) and hor (hop-related) groups.**[19]**

As for about half of all *H. pylori* strains, it is plasmid-free and contains the two best-known polymorphic virulence determinants: a toxigenic allele of the vacuolating cytotoxin gene and the 38-kb cag pathogenicity island. Fifteen hundred and ninety open reading frames (ORFs) have been identified by TIGR in the genome sequence, two-thirds of which are homologs of known genes from other organisms and one-third of which have no significant match to genes of known function.**[20].**

About 1,100 genes make up the *H. pylori* core genome, which is shared by all strains of the bacteria. The remaining accessory portion of the genome is made up of genes that are different among strain subsets.**[21].**

Several different restriction-modification systems, which are genetic components that offer defense against foreign DNA, for instance, offer varied DNA methylation.**[22]**. Significant differences in gene sequences and genome content between strains, as well as within the bacteria that live in a single person's gut **[23]**is a notable feature of *H. pylori* that arises from the peculiar combination of extremely high rates of recombination and mutation. Due to the pro mutagenic characteristics of its DNA polymerase and the absence of a traditional mismatch repair mechanism, *H. pylori* have a high mutation frequency. Naturally capable, *H. pylori* may absorb DNA using the special ComB DNA absorption system, which resembles a type IV secretion system (T4SS) **[24].**

The micro- and macro diversity among *H. pylori* strains acts as an important driving force for adaptation to the hostile gastric environment and the variable living conditions during the inflammation process and/or during transmission between host individuals.**[25]**

IV. Habitat of bacteria

Because of its harsh environment, the human stomach has been thought to be free of major microbial colonization and variety. The human stomach acts as a gatekeeper for the entry of microbial infections into the intestinal system because of its extremely low pH and strict immunological-monitoring.

However, the understanding of microbial colonization of the stomach was altered by the discovery of *Helicobacter pylori*.**[26].**

It is the most common microbe associated with epithelial cells in the human stomach mucosa.**[9]**.

Because of its great importance to human health and propensity for carcinogenesis, it is one of the best-characterized and fully sequenced organisms genetically **[26].**

Using Polymerase Chain Reaction (PCR) techniques, *H. pylori* have been found in saliva, feces, and dental plaque outside of the stomach mucosa. These temporary extra-gastric reservoirs are believed to play a role in the bacterium's spread **[9].**

V. Major virulence factors and pathogenesis mechanisms:

1. Colonization factors:

The various obstacles posed by the harsh environment are addressed by a combination of factors that enable *H. pylori* to successfully colonize the human stomach for an extended period of time **[27].** Among these factors are the urease and flagella.**[28].**

- Acide resistance:

One of this organism's most notable characteristics is urease. Urea, a nitrogenous waste product of humans, is hydrolyzed by this high molecular weight (550 kDa) enzyme to release carbon dioxide and ammonia. Ammonia is produced by hydrolyzing urea, which neutralizes hydrochloric acid. The transient development of achlorhydria and indeed the development of natural pH may allow the organism time to tunnel through the stomach mucus to the gastric epithelium which creates a more hospitable environment **[29].**

Since the urease's ammonia enters the *H. pylori* nitrogen metabolism and is subsequently integrated into protein, its involvement in the pathophysiology of *H. pylori* associated disorders

extends beyond colonization **[30].** Urease, the enzyme produced by *H. pylori*, leads to damage in the gastric epithelium by generating ammonia in conjunction with neutrophil metabolites, which in turn form carcinogenic compounds that potentially contribute to the development of gastric malignancies. Ammonia can cause various cellular changes such as swelling of acidic intracellular compartments, alterations in vesicular membrane transport, repression of protein synthesis and ATP production, and cell-cycle arrest. Urease also helps facilitate the recruitment of neutrophils and monocytes into the mucosal tissue and the production of pro-inflammatory cytokines **[31].**

- Motility:

"Swimming motility," "spreading motility," and "swarming motility," which are characterized as movement in liquid media, movement in soft agar (0.3% agar concentration), and movement on the surface of semisolid or solid media, respectively, are among the various forms of motility produced by *Helicobacter pylori* flagella **[32]**, these bacterial flagella have an unusual feature in that they are shielded from stomach acid by a lipoprotein coating **[33]**,

The bacterium's tuft of polar flagella and spiral form make it a perfect fit for moving through the mucous layer **[29].** Every flagellum is made up of two flagellins, FlaA and FlaB; FlaB is found near the base of the flagellum, while FlaA, which is more prevalent, is found on the outside.

Following an infection, FlaA or FlaB may trigger certain antibody responses and induce humoral immunity. It has been noted that highly motile strains of *H. pylori* cause an increase in IL-8 secretion. Chemotactic substances, such as histidine, bicarbonate ions, urea, and other amino acids, guide *H. pylori*'s movement towards the stomach mucosa **[27]**.

- *H. pylori* Adhesins (OMPs):

Numerous outer membrane proteins are encoded by the *H.pylori* genome **[34],** OMP family 1 is made up of more than 30 omp genes that have been separated into two categories: hop (*Helicobacter* OMPs) and hor (hop-related groups).**[31]**

- Blood group antigen-binding adhesion (BabA):

One of the first *H. pylori* adhesins discovered, BabA, also known as HopS, is a member of the Hop family and ranges in size from 75 kDa to 80 kDa. It attaches itself to Leb antigens and ABO histo blood group antigens, which are expressed on human stomach epithelial cells.**[35]**

- Sialic acid-binding adhesion (SabA):

Approximately 40% of *H. pylori* strains include SabA. The development of stomach disorders, excessive neutrophil infiltration, and gastric atrophy during infection are all linked to the expression of this adhesin. **[36]**

- Outer inflammatory protein (OipA):

OipA is an adhesin-like outer membrane protein that is linked to elevated IL-8 production and carcinogenicity **[37]**, encoded by the hopH gene, belongs to the OMPs family and as an *H.pylori* virulence factor, it is strongly associated with the bacterial adherence, colonization, induction, and progression of gastrointestinal disorders **[36].**

- Adherence-associated lipoprotein A and B:

Adherence-associated lipoprotein A and B (AlpA/AlpB) are proteins incorporated in *H.pylori* adherence to the gastric epithelial cells and further promote bacterial colonization **[36]**

2. Virulence factors:

- Cytotoxin-Associated Gene A (CAG A):

The cag PAI is a 40 kb DNA sequence **[38],** containing approximately 30 genes **[39]**, certain genes encode proteins that combine to form a type IV secretion apparatus, whereas the cagA gene encodes an effector protein (CagA) **[40].** Approximately 70% of strains contain this 116–140 kDa protein CagA**[41]** which is categorized into two subtypes cytotoxin-associated gene A CagA-positive (type I) or CagA-negative (type II) *H. pylori* **[36]**. This type 4 secretion system (T4SS) specialize in the transfer of CagA across the bacterial membrane to the extracellular space or into gastric epithelial cells **[38]**, once inside the host cell, CagA is phosphorylated by the host tyrosine kinase Src. Phosphorylated CagA dysregulates actin cytoskeletal rearrangement in the host cell, triggering the so-called hummingbird phenotype, which is characterized by an elongated host cell shape resembling the long, thin beak of a hummingbird **[42]**. A number of illnesses are triggered by CagA. These include the development of PUD, the production of a local inflammatory response, and stomach cancer **[38].** Through a variety of pathways that impact the activity of tumor suppressor proteins such apoptosis-stimulating protein of p53 2 (ASPP2) and run-related transcription factor 3 (RUNX3) **[36]**and inducing genomic instability through the promotion of DNA double-strand breaks (DSBs) **[43].**

- Vacuolizing cytotoxin (VacA):

VacA is a pore-forming immunogenic cytotoxin which is Roughly secreted by 50 percent of *H. pylori* strains **[44]**, released by bacteria as a big 140 kDa polypeptide that is then trimmed at both ends to transfer it to host cells in an active state, to exert its activity **31].** where it assembles forming pores that facilitate the outflow of chlorine**[44],**and nutrients from the mucosa towards the gastric lumen, this results in a change in the integrity of the cells of the stomach epithelium; therefore, VacA is crucial for *H. pylori*'s survival and the development of a chronic infection.**[42]**,VacA is an essential factor in both peptic ulceration and gastric cancer etiology, which is extremely likely attributable to the release of active toxin via type 1 VacA**[44]**. VacA's activities include the development of membrane channels within endosomes and lysosomes, resulting in vacuolation in epithelia cells in-vitro. This process involves the disruption of cell receptor signaling pathways, as well as interference with cytoskeleton-related functions and cell-dependent activities. Additionally, VacA has been implicated in the induction of apoptosis and regulation of the immune response **[31]**.

- Lipopolysaccharide:

Lipopolysaccharide (LPS) is a key constituent of the outer membrane of *Helicobacter pylori*, and it is one of the most important virulence factors **[36].** *H. pylori'*s lipopolysaccharide (LPS) plays a significant role in the bacteria-host interaction and is composed of three main components: hydrophobic lipid A, O-antigenic polysaccharide region, and the polysaccharide core. This latter component serves as a bridge connecting the former two. Lipid A is the constituent responsible for LPS immunological and endotoxic properties **[45]**. One notable characteristic of *H. pylori* LPS is its significantly weaker endotoxin and immunogenic activity when compared to LPS molecules from enteric bacteria, which are considered the benchmark standard **[44]**. This reduced biological activity of *H. pylori* LPS could potentially contribute to the prolonged infection and chronic inflammation of the gastrointestinal mucosa **[31]**. *H. pylori* LPS has limited pro-inflammatory capacity, and recent studies have demonstrated its ability to bind to trefoil peptides found in the gastric lumen, which may aid in the bacterium's colonization of the gastrointestinal tract **[46]**.

There are also numerous other marker genes for disease development such as:**[46]**

The neutrophil-activating protein (HP-NAP), Induction of enzymes and cytokines by *h. Pylori* **[36]**, *H. Pylori*-induced free radicals **[33]**and Duodenal ulcer (du) promoting gene (dupa) **[31]**.

VI. Pathophysiology:

H.pylori have the ability to adapt to the stomach's acidic environment and primarily infect the mucosal layer by neutralizing the local environment through the production of urease and other mechanisms **[47]**.

Although stomach colonization with *H. pylori* causes histologic gastritis in all infected people, only a small percentage acquire any obvious clinical indications of the colonization. *H. pylori*-positive patients are predicted to have a 10 to 20% lifetime risk of contracting ulcer disease, and a 1 to 2% risk of developing distal gastric cancer and MALT lymphoma **[48]**.

H. pylori infection is an example of a "slow" infection that develops over time due to interactions between pathogenic factors of the infectious strain, the host's immune system and its environment. The most common lesion is gastritis, which is initially acute and frequently goes undiagnosed before becoming chronic. The intensity and distribution of the disease in the stomach determine how the disease manifests itself. Acid secretion is the primary alteration in stomach physiology caused by chronic gastritis. These fundamental factors account for the inconsistent and poorly understood development of gastric neoplasia or peptic ulcer disease. **[49]** Gastric adenocarcinoma is the result of a slow and sustained progression of this chronic gastritis to mucosal atrophy, followed by the development of metaplasia on this atrophy, then dysplasia, eventually leading to cancer **[50]**.

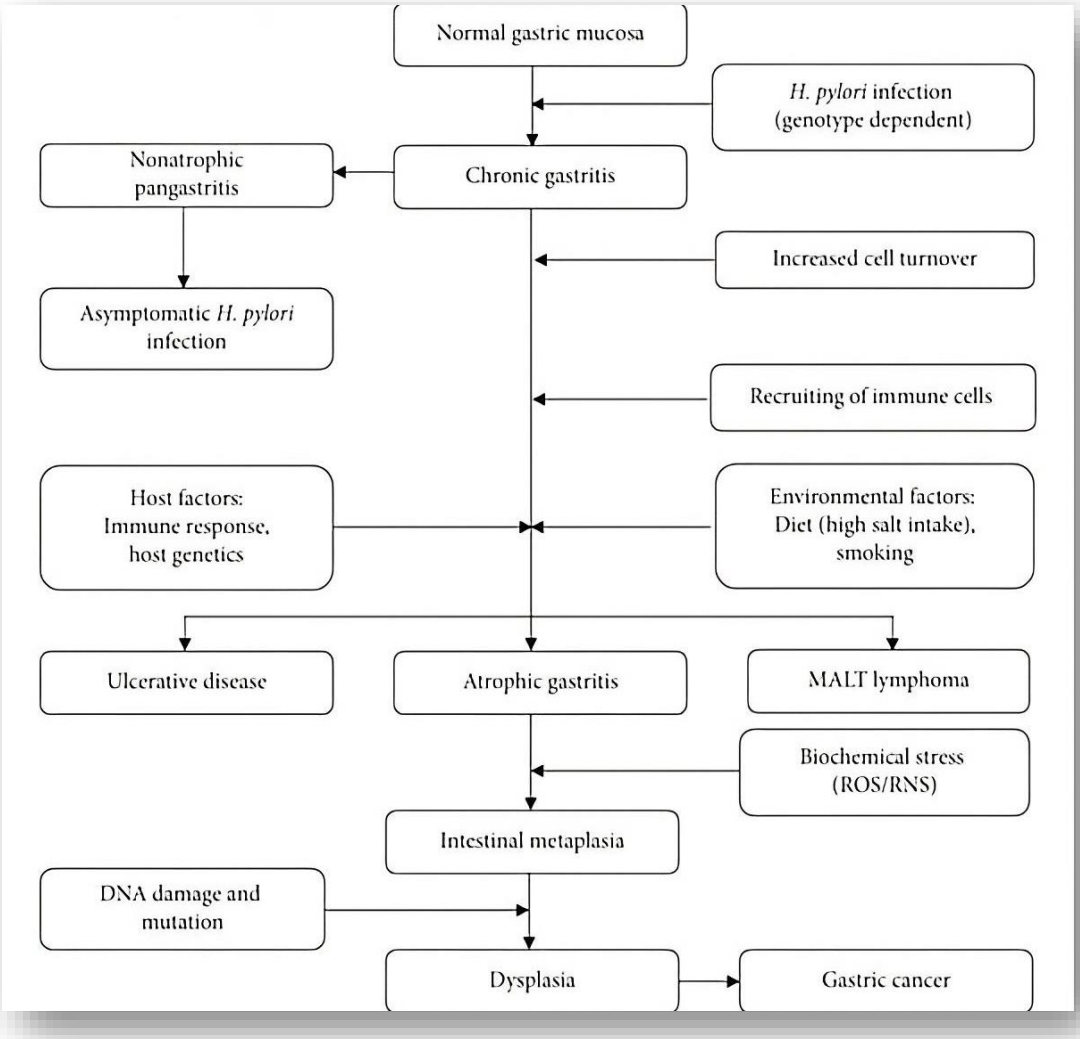


Figure 4: Schematic representation of the causative factors of diseases induced by *H.pylori* infection.[**51]**

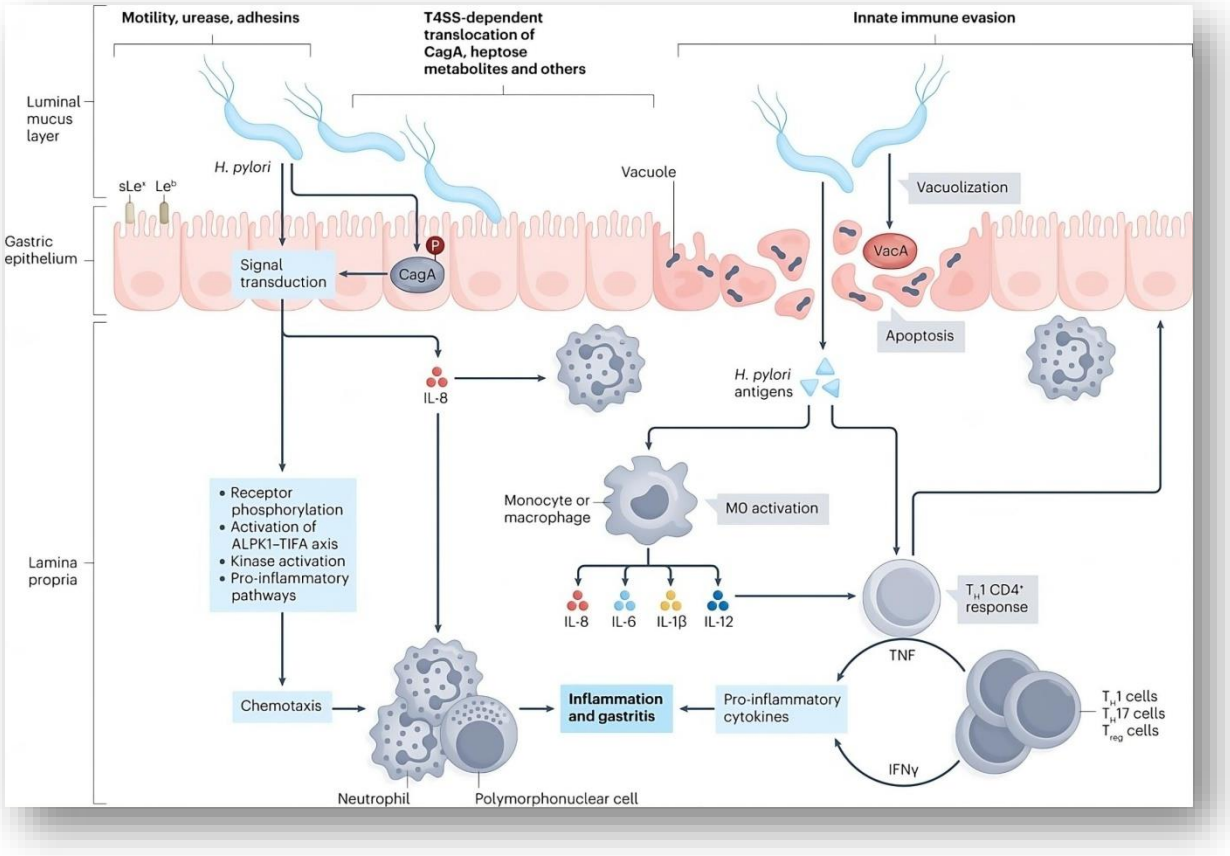


Figure 5: *H.pylori* infection and pathogenesis.**[52]**

H. pylori pathogenesis proceeds through the following key steps, as depicted in the figure (5):

- *H. pylori* use urease to neutralize gastric acid, creating a more hospitable environment at the onset of infection.
- The bacterium employs flagella for motility, allowing it to penetrate the luminal mucus layer and reach the gastric epithelium.
- Adhesion to epithelial cells is mediated by interactions with sLe^x and Le^b antigens.

- *H. pylori* utilize a type IV secretion system (T4SS) to inject CagA and other effectors into epithelial cells.
- Once inside the cell, CagA is phosphorylated and triggers several intracellular events, including receptor phosphorylation, activation of the ALPK1–TIFA axis, kinase signaling, and pro-inflammatory pathways.
- These processes stimulate the secretion of IL-8.

- IL-8 acts as a chemoattractant, recruiting neutrophils and polymorphonuclear cells to the infection site.
- This recruitment leads to local inflammation and gastritis.

- The VacA toxin is secreted by *H. pylori* and induces vacuolization and apoptosis in epithelial cells, contributing to immune evasion.

- *H. pylori* antigens are recognized by monocytes and macrophages, leading to macrophage (MO) activation.
- Activated macrophages produce pro-inflammatory cytokines, including IL-8, IL-6, IL-1β, and IL-12.

- IL-12 promotes differentiation of Th1 CD4^+ T cells.
- Th1 cells produce TNF and IFNγ, which further amplify inflammation.
- Other T-cell subsets involved include Th1, Th17, and T_reg cells.

VII. Evasion of innate immunity

1. Inhibition of innate immune recognition:

➢ Evasion of recognition by pattern recognition receptors:

Innate immune cells and epithelial cells deploy distinct immune receptors or pattern recognition receptors (PRRs) expressed at particular subcellular compartments to identify pathogen-associated molecular patterns (PAMPs) **[53]**.

These PRRs include toll-like receptors (TLRs), NOD-like receptors (NLRs), C-type lectin receptors (CLRs), and retinoic acid-inducible gene (RIG)-I-like receptors (RLRs) **[54]**

H. pylori avoids detection by PRRs in a number of ways. Making use of the bacterium's Lewis antigens and the variations found in bacterial lipid Lps structure may contribute to:

●Inhibition of CLR-Mediated Signaling expressed on Dendritic cells.

●Evasion of TLR Recognition and Manipulation of TLR-Mediated Signaling **[53]**.

➢ Disrupting macrophage function:

-The prevention of the bacterium neutralization by PMNs and monocytes through an antiphagocytic action assisted by Different virulence genes, including virB7 and virB11, as well as essential elements of the type IV secretion system (T4SS) **[55]**.

-inhibiting the transmission of phagocytic signals and the process of endocytosis via the bacterium’s lipopolysaccharide (LPS) that binds to macrophage surface glycoproteins such as CD14 and TLR4, triggering an NF-kB-mediated inflammatory response and

the release of cytokines including IL-1b, IL-6, and TNF-a **[56]**.

-LPS, CagA, and VacA binding boosts intracellular Ca^2+ concentration, which interferes with macrophage phagocytic and digesting functions **[57]**.

-Promoting macrophage polarization through the enhanced expression of heme oxygenase-1 (HO-1) and inducing Apoptosis by incorporating *H. pylori* VacA protein.

2. Evasion of adaptive immunity:

The diverse immune response that an *H. pylori* infection elicits is characterized by a mixed reaction involving T helper cells, cytotoxic T cells, and NK cells **[58].**

H. pylori subverts adaptive immune response by modulation of Th1 cells, Th17 cells and Regulating Treg cells.

H. pylori can directly impair adaptive immunological responses by reducing the nutrients necessary for T cells **[54]**.

Th1 cells are distinguished by their production of interleukin-2 (IL-2) and interferon-γ(IFN-γ). Assisting CD8+ T cells and stimulate the development of particular kinds of antibodies, which results in a strong cellular response, in order to disrupt this process,

H. pylori uses a number of strategies, such as lowering antigen presentation, antigenic variation, and production of immunosuppressive substances, which minimizes Th1 cell effectiveness **[58]**.

Gastric epithelial cells (GECs) increase the expression of B7 costimulatory molecules (B7-1, B7-2, B7-H1, and B7-H2) during *H. pylori* infection. This upregulation modulates the T cell response by increasing Treg cells and decreasing CD4+ effector T cell activity **[59]**.

CagA has a suppression effect on B7-H2 expression through phosphorylation by p70

S6 kinase, assisting *H. pylori* in eluding Th17-mediated immune responses and promoting persistent infection **[60]**.

Chapter 02: Gastric pathologies related to *Helicobacter pylori*

I. The human stomach:

1. Overview of stomach Anatomy:

The stomach plays a crucial role in the initial phases of digestion, facilitating the progression of food, mechanically breaking it down into a semi-fluid state, and secreting enzymes for chemical breakdown. Apart from digestive functions, the stomach also acts as an endocrine organ, producing hormones, and an immunological organ, contributing to immune response. **[60]**

The stomach is primarily located in the left hypochondriac region, concealed below the lower part of the rib cage. Furthermore, the lower and distal sections of the stomach are found in the epigastric and upper umbilical regions of the abdomen. As a distensible organ, the adult stomach has an average capacity of approximately 1.5 liters. **[62]**. It forms a J-shaped, enlarged sac that extends from the lower end of the esophagus near the diaphragm and extends several centimeters to the left of the midline, terminating at the gastro-duodenal junction just to the right of the midline. **[61]**

The shape of the stomach varies due to numerous factors including body position, physique, age, gender, and the filling state of the stomach. When empty, it tends to be tubular, but becomes more balloon-like when highly filled. When moderately filled, most of the stomach is situated in the left quarter rib area, with a smaller section in the upper abdominal area. The connection between the stomach and esophagus is known as the cardia, and the junction with the duodenum is called the pylorus. Sphincters regulate the flow of contents. The right portion of the stomach, between the cardia and pylorus, is known as the lesser curvature, and the left side is the greater curvature. The line connecting these curvatures partitions the stomach into three regions: the fundus, located at the top. the body following the middle, and the pyloric part at the bottom. **[63]**

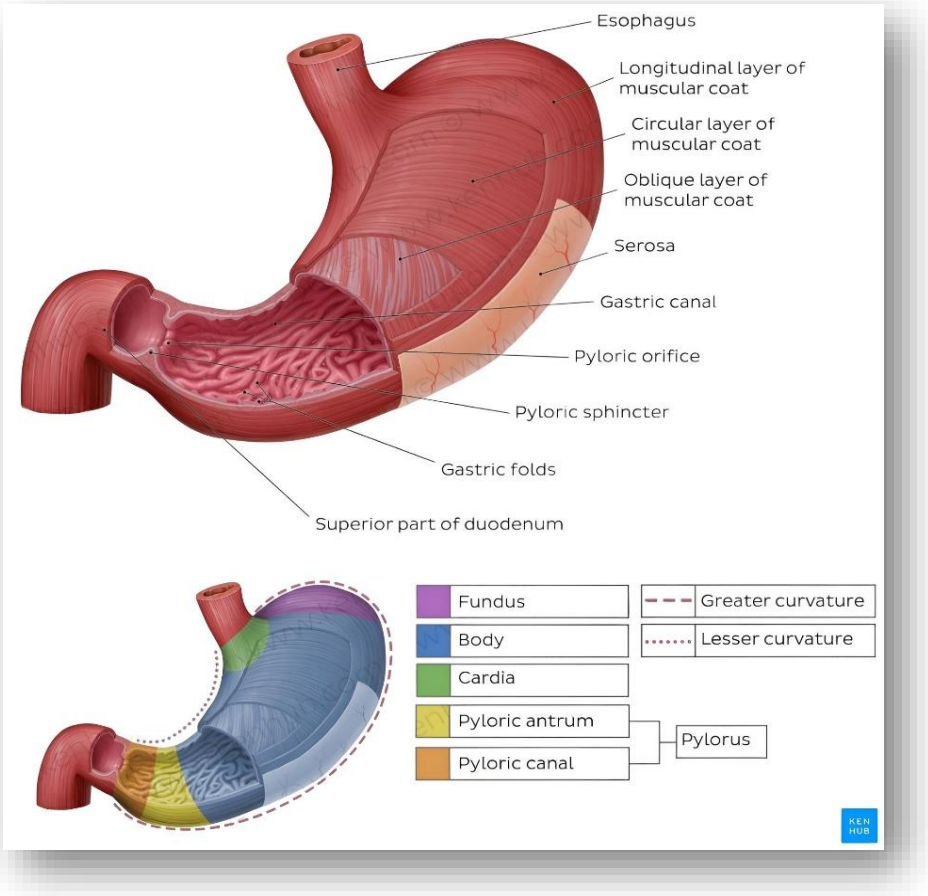


Figure 6: Anatomy of the stomach (anterior view).**[64]**

2. Histology:

The wall of the stomach has four layers: the mucosa delineated below by the muscularis mucosae, submucosa, muscularis propria and subserosa covered by the serosa. **[61]**

2.1. Gastric mucosa:

The innermost layer of the stomach wall is the mucosa, which consists of epithelium, supported by loose connective tissue, and is covered by a viscous mucus layer. This mucus layer acts as both a lubricant and physical barrier, helping to separate and protect the underlying epithelium from the luminal contents. **[65]**

The mucosa lining the fundus and body of the stomach features prominent, longitudinal folds called rugae. These structures consist of the mucosa and the muscularis mucosae, with cores of submucosal tissue. The thickness of the gastric rugae can vary depending on the degree of stomach distension. Additionally, the fundus and body mucosae are freely mobile, while the antral mucosa is flattened and more firmly anchored. **[61]**

2.1.1. Histology of the gastric epithelium:

The epithelial component of the gastric mucosa comprises two regions: the gastric pits (foveolae), which are invaginations of the epithelial surface, and the deeper glandular compartment. Within the glandular structure, three subunits can be identified in descending order from the connection with the gastric pits: the isthmus, the neck, and the base. **[66]**

The different types of glands (cardiac, fundic and pyloric) define the different zones of the stomach (cardia, fundus and body, and antrum). The antral and fundic units are very different histologically.

The fundic glands, accounting for 70-80% of the total glands in the stomach, are the most complex and consist of 5 primary cell types: mucus cells, parietal cells, chief cells, endocrine cells, and regenerative cells. In contrast, the pyloric glands, located at the pylorus, make up only 15% of the total gastric glands and are mainly composed of endocrine cells, mucus cells, and regenerative cells.**[50]**

- **Mucus cells:**

These cells are singular, or occasionally found in small clusters, and are intermingled with parietal cells in the neck region of the glands. They are also present in smaller numbers in the lower portion of the glands. Functionally, they are mucus-secreting cells, but they differ from surface epithelial cells in their shape, being lower columnar and more triangular with pale cytoplasm and basally located nuclei. **[61]**

These cells secrete mucus, primarily composed of glycoproteins, that forms a protective barrier neutralizing acidity and prevents direct contact between pepsin and the stomach wall, thereby lubricating and safeguarding the mucosa from autodigestion. Furthermore, mucins are believed to participate in the immune defense against *Helicobacter pylori*. **[50]**

- **Parietal cells:**

Parietal cells, also known as oxyntic cells, are the largest cells found in the glands of both the fundus and body of the stomach. They are responsible for the secretion of hydrochloric acid, which maintains the highly acidic environment within the stomach lumen, as well as producing intrinsic factor, which complexes with vitamin B12 in the stomach to facilitate its absorption in the distal ileum. **[67]**

- **chief cells:**

They are mainly located at the base of glands throughout the fundus and body of the stomach, play a pivotal role in the synthesis and release of pepsinogen, a proenzyme that, upon exposure to acidic conditions within the stomach, is converted into acid protease pepsin. **[68]**

- **Endocrine cells:**

Endocrine cells are dispersed diffusely but unevenly throughout the various epithelia of the stomach, and their output products have a significant impact on the regulation of gastrointestinal physiology and function. **[69]**

The types of endocrine cells found in the gastric mucosa are site dependant. In the antrum, the dominant endocrine cells are the gastrin-producing G cells, which are abundant in the neck and upper gland regions showing pale cytoplasm. In contrast, enterochromaffin-like (ECL) cells, which produce histamine, are mainly located in the body and fundus regions of the stomach and constitute the majority of endocrine cells in these areas. **[61]**

- **Stem cells:**

The gut epithelium is typically divided into two zones: the proliferative zone, situated in the isthmus of the gastric gland, and the functional zone. In the isthmus, multipotent stem cells possess the ability to generate the three distinct cell lineages found within the gastric epithelium: mucus-producing pit cells, acid-producing parietal cells, and enzyme-producing zymogenic cells. **[70]**

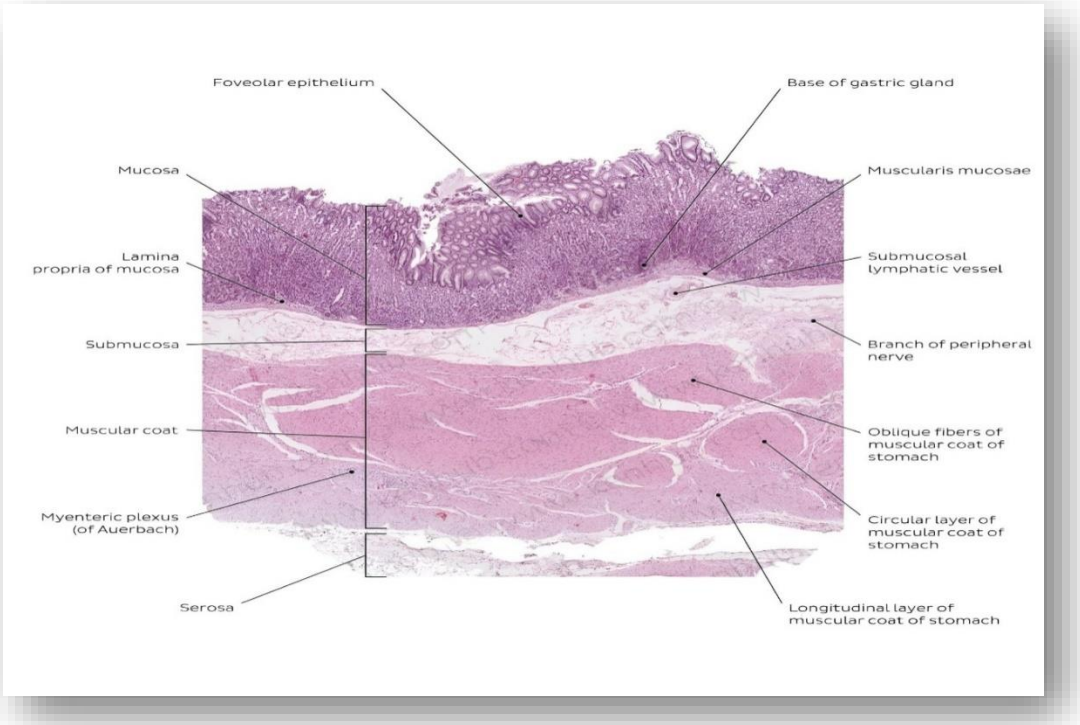


Figure 7: Microscopic Structure of the Gastric Wall (H&E, Low Magnification).**[64]**

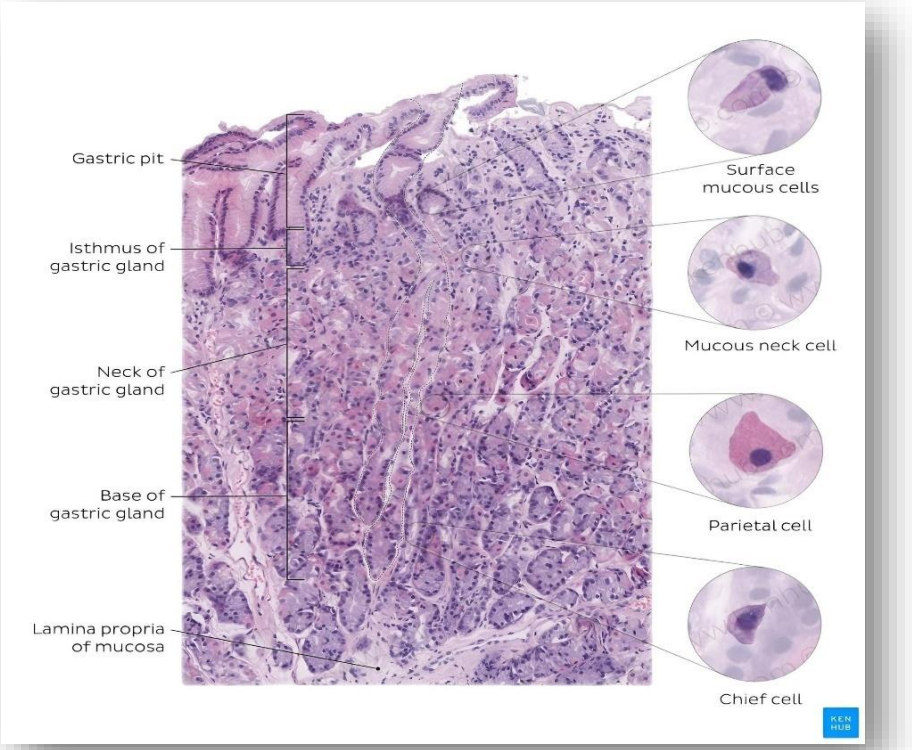


Figure 8: Histological View of Gastric Mucosa (H&E Stain, High Magnification).**[64]**

2.2. submucosa:

The submucosa is a dense layer of loose connective tissue located beneath the muscularis mucosae, distinguished by the presence of prominent arterial, venous, and lymphatic plexuses as well as nerves and the submucosal nerve plexus of Meissner.

It is richly populated with elastic fibers and contains a variety of cell types, including fibroblasts, adipocytes, smooth muscle cells, and mast cells, which contribute to its structural and functional characteristics. **[61]**

2.3. muscularis propria:

The muscularis propria of the stomach consists of three distinct layers of muscle fibers: The outermost layer of fibers is continuous with the longitudinal muscle of the esophagus, while the inner circular layer forms a distinct sphincter mass at the pylorus. This circular muscle is clearly separated from the circular fibers of the duodenum by a connective tissue septum. **[71]**

2.4. Subserosa and serosa:

The subserosa is a thin layer of loose areolar tissue, containing a network of blood vessels, lymphatics, and nerve fibers. It is enclosed by the serosa. **[61]**

Which consists of loose connective tissue covered by a single layer of cuboidal mesothelial cells. This covering serve to reduce friction during the stomach's churning movements. **[66]**

3. Histophysiology:

Once food is processed in the oral cavity, it travels as a bolus (a mass of partially digested material) down the esophagus and enters the abdominal cavity, ultimately reaching the stomach. **[72]** In the stomach, the food is broken down through mechanical and chemical processes. The partially digested contents then move to the small intestine, where digestion proceeds further, and nutrients are absorbed into the bloodstream to fuel bodily functions. **[73]**

3.1. mechanical digestion:

The stomach employs three distinct muscle layers to generate the motions required to fragment food boluses into smaller particles. A food bolus composed of partially broken-down material from the mouth and esophagus is transformed by the stomach into chyme, a substance optimized for absorption in the small intestine. This conversion is achieved through vigorous churning actions driven by the oblique muscle layer in the stomach's outer muscular wall. Meanwhile, the circular and longitudinal muscle layers assist in propelling chyme through the pyloric sphincter during gastric emptying, which only permits sufficiently liquefied and small particles to pass. Factors such as dietary fats, acids in the duodenum, stress, physical activity, and hormonal signals can delay this emptying process. Any remaining chyme undergoes continued churning until it meets the size and consistency criteria for passage through the pyloric sphincter. **[74]**

3.2. chemical digestion:

Chemical digestion in the stomach is supported by two glandular structures within the gastric mucosa: oxyntic glands and pyloric glands. **[73]**

Parietal cells secrete hydrochloric acid (HCl), the principal acidic element of stomach fluid, concentrated at about 160 mmol/L with a pH level of 0.8. The hydrogen (H^+) and chloride (Cl^-) parts of HCl are separately released by hydrogen/potassium ATPase pumps and chloride channels in the gastric lining. Pepsinogen, a proenzyme for pepsin, is secreted by chief cells. Collectively, gastric acid creates an acidic environment that denatures proteins and activates the conversion of pepsinogen to pepsin. **[75]**

Pepsin cleaves proteins into smaller peptide fragments, which undergo additional processing before absorption in the small intestine. Acid secretion is controlled by hormonal

and neural factors, such as gastric inhibitory polypeptide, secretin, gastrin, histamine, and somatostatin, released by enteroendocrine cells. Gastrin production is triggered by stomach distension, elevated gastric pH, and the presence of amino acids in the stomach, Gastrin release occurs in response to increased gastric distension, increased gastric pH, and the presence of amino acids in the stomach. **[76]**

4. Gastric microbiota:

the stomach was originally thought to be a sterile place, but the discovery of *H. pylori* directly within it led to the reconsideration of the idea that external microorganism may colonize the stomach and the whole gastrointestinal tract, However, due to its low pH, the stomach environment is especially harsh and challenging to colonize. Therefore, the microbial load is much lower in the stomach than in the colon or the small intestine 10^2–10^4CFU/mL of bacteria in the stomach compared to 10^{10}–10^{12}CFU/mL in the colon. **[77]**

The microbiota of the human stomach exhibits a completely different composition from that of upper anatomical regions such as the mouth or throat. **[78]** As a result, rather than being made up of microorganisms from the upper regions the stomach microbiota seems to be made up of Indigenous microorganisms, so based on culture analysis and under healthy conditions the predominant bacteria belong to the phylum of Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria (which include *H. pylori*). **[79]**

The role of the gut microbiota in our health is increasingly well understood and recognized. It is now known to play a part in digestive, metabolic, immune and neurological functions. As a result, qualitative and/or functional alterations of the gut microbiota caused by factors such as dietary habits, medication use, and the presence of *Helicobacter pylori* are a serious avenue for explaining certain diseases, especially those involving autoimmune or inflammatory mechanisms. This topic has become a key element to biological and medical research. **[80]**

II. Gastric pathologies caused by *H.pylori* :

1. Non-malignant *Helicobacter pylori*-Associated pathologies :

Helicobacter pylori colonization of the gastric lining can lead to various pathological states in humans, such as, such as chronic gastritis, gastric ulcers, duodenal ulcers, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma. **[81]**

A. Gastritis:

Gastritis is characterized by inflammation of the stomach's lining accompanied by mucosal damage. The duration of inflammatory activity in the mucosa serves to differentiate acute gastritis from chronic active gastritis. *H. pylori* represent the most prevalent infectious etiology linked to gastritis. **[82]**

- acute gastritis:

Acute gastritis in humans is infrequently reported, but it has been documented in situations where individuals were exposed to *Helicobacter pylori* either accidentally, **[83]** or intentionally, such as in experimental settings designed to provoke gastric disease.**[84]**

In these instances, affected individuals experienced symptoms and received endoscopic evaluation, including biopsies of the inflamed stomach lining. The initial disease phase is characterized by an influx of polymorphonuclear leukocytes into the gastric mucosa and atemporary decline in stomach acid production (hypochlorhydria). **[81]**

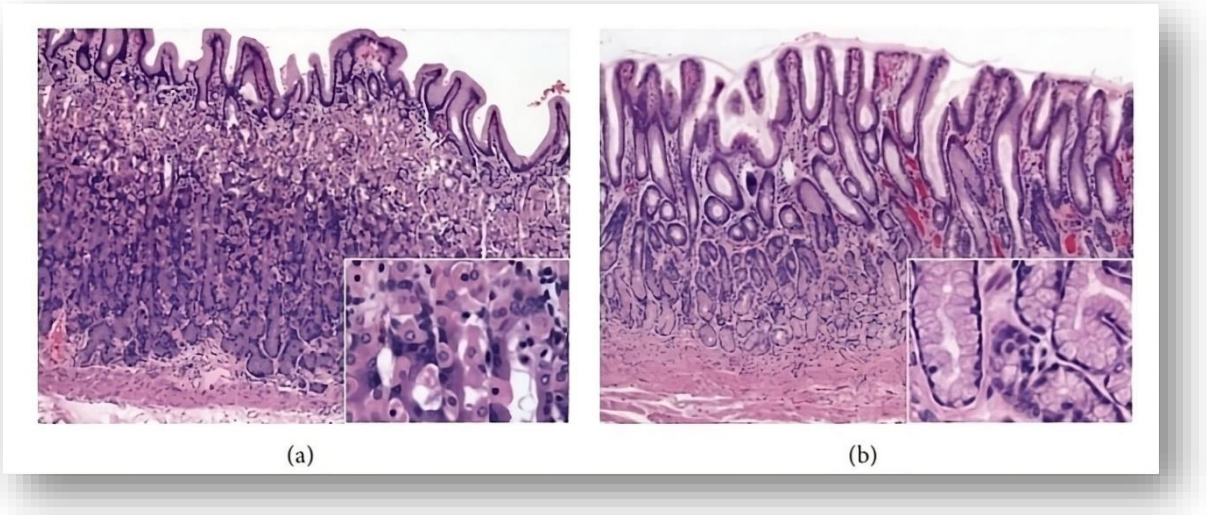


Figure 11: Normal gastric mucosa histology. ((a); H&E 10x; square 40x): Fundic glands. ((b); H&E 10x; square 40x): Antral mucosa.**[85]**

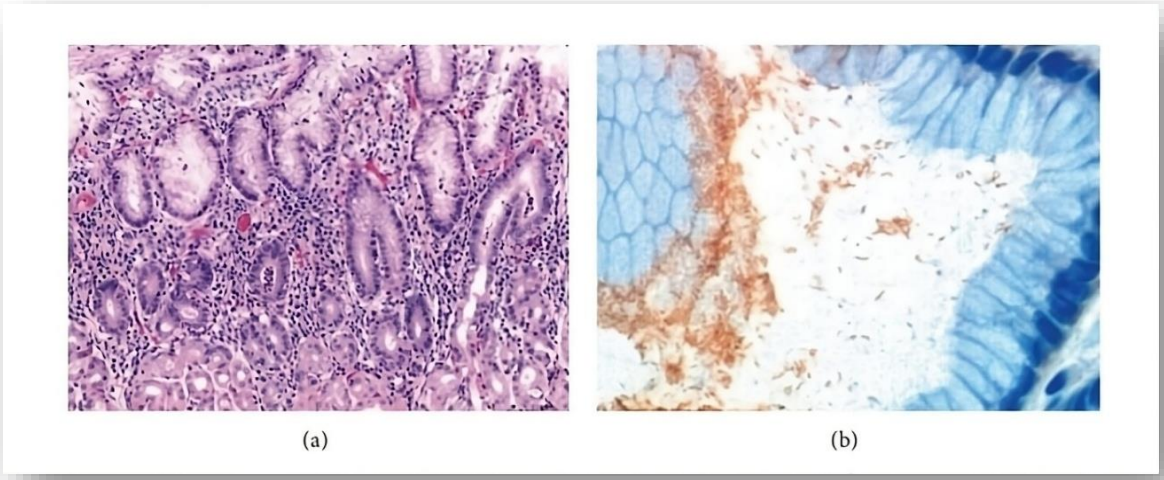


Figure 12: Early acute superficial gastritis((a); H&E 20x) Marked neutrophilic infiltrates appear in the mucous neck region and lamina with a pit micoabscess. ((b*); H. pylori* immunostaining: rabbit polyclonal; clone CH-20 429, Novocastra; 40x) Numerous H.

- Chronic gastritis:

Following an acute *H. pylori* infection, most cases of acute gastritis progress to chronic active gastritis, identified histologically by the presence of mononuclear cells primarily lymphocytes, plasma cells, and macrophages. Lymphoid follicles containing germinal centers are commonly observed and are distinctive of *H. pylori* infection. Chronic gastritis is classified into three forms: pangastritis, antrum-predominant, and corpus-predominant. Diffuse antral gastritis, linked to normal or elevated acid secretion, shows minimal gastric atrophy and is associated with duodenal ulcers (DUs). Prolonged inflammation leads to gastric atrophy accompanied by reduced acid secretion (hypochlorhydria) or absent acid production (achlorhydria). These alterations promote bacterial spread toward the corpus, resulting in corpus or multifocal gastritis, which often advances to intestinal metaplasia and eventually intestinal-type gastric cancer (GC). **[82]**

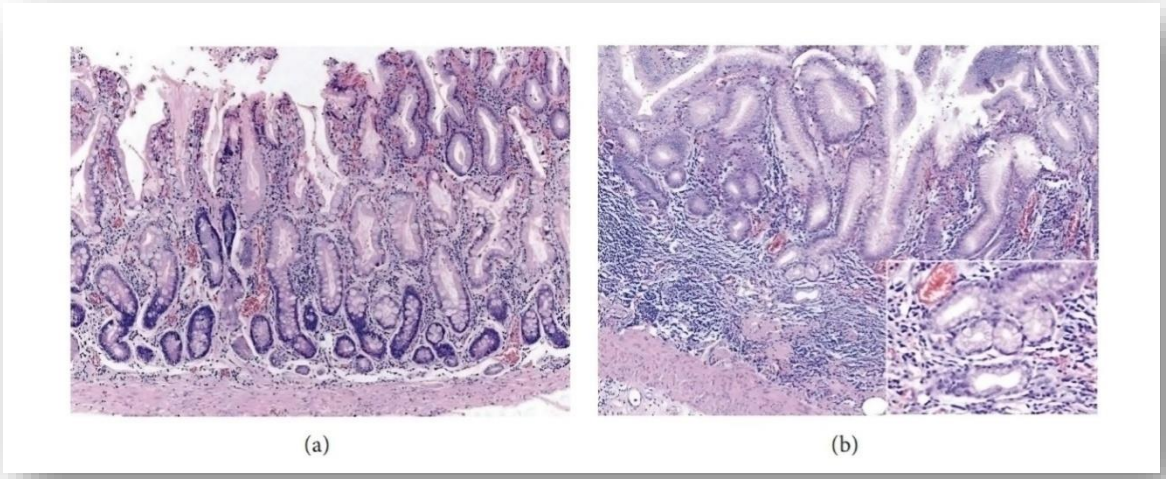


Figure 13: Atrophic gastritis ((a); H&E 10x) Antral gastric mucosa, ((b); H&E 10x; square 20x) Fundic-corporal gastric mucosa.**[85]**

- Autoimmune Gastritis:

Autoimmune metaplastic atrophic gastritis arises from T-cell–driven damage to the oxyntic mucosa and autoantibodies attacking parietal cells and intrinsic factor. In *H. pylori*-associated cases, a proposed mechanism involves cross-reactivity between bacterial antigens and host targets (e.g., parietal cells, intrinsic factor). In primary autoimmune forms, the immune response directly targets these antigens without *H. pylori* involvement. The specific molecular triggers initiating autoimmunity remain unknown. Chronic immune-mediated destruction results in mucous cell proliferation and metaplastic glandular changes (intestinal and pseudo-pyloric types) within the gastric lining. **[84]**

B. peptic ulcers:

Peptic ulcers are acid-induced lesions found in the stomach and duodenum characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria. Lesions that do not reach this depth are called erosions.

Peptic ulcer disease (PUD) has various causes; however, *Helicobacter pylori*-associated PUD accounts for the majority of the disease etiology. **[87]**

- duodenal and gastric ulcers:

Helicobacter pylori is responsible for 90% of duodenal ulcers and 70% to 90% of gastric ulcers, with both types sharing common epidemiologic and pathophysiologic traits but exhibiting key distinctions. **[88]**

The development of duodenal ulcers fundamentally depends on two key factors: gastric metaplasia in the upper duodenum and antral-predominant *H. pylori* gastritis, which elevates gastrin levels. This hypergastrinemia drives excessive acid production by stimulating parietal cells in the stomach's corpus, creating conditions necessary for ulcer formation. **[89]**

In contrast Gastric ulcers often develop in the presence of decreased acid secretion (hypochlorhydria) rather than excessive acid production, highlighting the critical role of impaired mucosal defenses in their pathophysiology. **[88]**

C. Gastrointestinal stromal tumors:

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract in adults. **[90]** GISTs are sarcomas that mostly derive from precursors of the interstitial cells of Cajal (ICC), the pacemaker cells of the gastrointestinal tract responsible for its motility. **[91]**

GISTs are considered to be rare, making up 1 % to 2 % of all gastrointestinal (GI) neoplasms. Roughly 10–30 % of GISTs progress to malignancy and 10–20 % are diagnosed with overt metastatic disease. **[92]**

Even Though GISTs are not commonly associated with *Helicobacter pylori* infection it has been linked recently to GIST as it induces an epithelial response that can home MSCs to the stomach mucosa. once there, MSCs play essential roles in the development and progression of GC. This is how *H. pylori* is linked to gastric inflammatory stromal tumors. **[93]**

D. gastric polyps related to *H.pylori* :

Gastric polyps are abnormal luminal growths projecting above the mucosal surface, they may develop in all parts of the stomach and are typically discovered incidentally during endoscopy due to their frequent asymptomatic nature, though rare presentations may include nonspecific symptoms such as abdominal pain, gastrointestinal bleeding, anemia, or gastric outlet obstruction. **[94]**

Accurate classification of gastric polyp subtypes is essential, as the likelihood of malignant progression varies based on its histopathological characteristics, with certain polyp types posing higher risks and an overall malignant potential ranging between 0.4% and 10%. **[95]**

Gastric hyperplastic polyps are the most frequently encountered polypoid lesions in the stomach developing in association with gastritis and gastric atrophy or through proliferation of the foveolar surface mucosa which are typically developing as a response to chronic inflammation, most often associated with *Helicobacter pylori* infection. **[96]**

Gastric adenomas, acting as precursors to adenocarcinoma, commonly develop against a backdrop of atrophic gastritis. Malignancy risk is linked to both size and histological subtype, with intestinal-type and fundic gland adenomas exhibiting greater malignant progression than foveolar or oxyntic gland variants. *H. pylori* likely influence the transition of intestinal-type adenomas to cancer, supported by evidence that its eradication lowers subsequent gastric cancer risk. **[95]**

2. Malignant *Helicobacter Pylori*-Associated pathologies:

2.1. Gastric Cancer:

Cancers are life-threatening diseases characterized by deregulated proliferation and invasion of cells of clonal origin, resulting from the buildup of numerous genetic and epigenetic changes within those cells. *Helicobacter pylori* is so far the only bacterium for which infection is widely accepted to play a major etiologic role in the development of human cancers. Infection with *H. pylori* is considered the leading risk factor for gastric cancer, a disease responsible for hundreds of thousands of deaths worldwide each year. **[98].** This bacterium was classified as a group I carcinogen in 1994 by the World Health Organization (WHO) **[99]**

Pathologically, gastric cancer is subclassified into **intestinal type**, which is more common in older adults, and **diffuse type**, which is more aggressive and occurs more frequently at younger ages. *H. pylori* infection has been considered to be associated with both types of gastric cancer.**[99]** The development of intestinal-type gastric cancer is believed to involve multiple factors, with *H. pylori* infection being the most significant contributor to cancer formation. This type typically progresses through a sequence of precancerous changes, including dysplasia, and is often preceded by conditions such as gastric ulcers, atrophic gastritis, or pernicious anemia.

In contrast, diffuse-type gastric cancer does not have well-defined precancerous lesions identified before its onset. **[100]**

Genetic predisposition in hosts, particularly polymorphisms within promoters or non-coding regions of genes linked to inflammatory responses during *H. pylori* infection, has been connected to gastric cancer risk. Key examples include genes encoding the pro-inflammatory cytokines interleukin (IL)-1β, IL-1 receptor antagonist, and tumor necrosis factor (TNF)-α, as well as the anti-inflammatory cytokine IL-10. Notably, individuals with such genetic susceptibility face a significantly heightened risk of gastric cancer when infected with more virulent *H. pylori* strains. This increased risk is attributed to genetic diversity in *H. pylori*, especially variations in virulence-associated genes like CagA and the VacA toxin**. [101]**

Strains of *H. pylori* that produce the VacA toxin can cause vacuole formation and cell death (apoptosis) in the stomach lining, while infection with strains carrying the CagA protein is linked to more severe inflammation of the stomach (gastritis) and an increased risk of developing gastric cancer. **[102]** The CagA protein operates as an oncoprotein that, upon host cell entry, acts as a scaffold to disrupt cellular signaling pathways. Gastric cancer progression linked to CagA involves an initial triggering mechanism: its pro-oncogenic effects are followed by accumulated genetic and epigenetic alterations, leading to the formation of cancer-susceptible cells during prolonged infection with CagA-positive *H. pylori*.**[103]**

2.2.Gastric Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma:

First described by Isaacson and Wright in 1983, MALT lymphoma is a low-grade extra nodal non-Hodgkin lymphoma. The most common site of MALT lymphoma is in the stomach, although it can also arise in the ocular adnexa, thyroid, and small intestine. **[104]**

The development of gastric mucosa-associated lymphoid tissue (MALT) lymphoma is dependent on *Helicobacter pylori* infection. Bacterial colonization of the gastric mucosa triggers lymphoid infiltration and the formation of acquired MALT.

The bacterial infection triggers and maintains a rapidly multiplying B-cell population via both direct (autoantigen-related) and indirect (tumor-infiltrating T cells targeting H. pylori) immune activation. Additionally, the infection stimulates a neutrophil-driven reaction, leading to the production of oxygen free radicals. These reactive molecules may contribute to the development of genetic mutations and the cancerous transformation of reactive B cells. **[105]**

Gastric MALT lymphoma frequently occurs in multiple sites, typically localized in the antral region or lower body of the stomach. Histologically, the neoplastic cells penetrate the marginal zone surrounding reactive lymphoid follicles and infiltrate gastric glands, creating distinctive lymphoepithelial structures. Over time, these malignant cells proliferate into a widespread invasion, extending into the deeper gastric wall layers. **[106]**

Clones of lymphoma cells that possess the t (11;18) (q21; q21) chromosomal translocation develop into MALT lymphoma that grows independently of *Helicobacter pylori* infection and thus does not respond to treatments aimed at eradicating the bacteria. In contrast, malignant clones lacking this translocation but carrying other genetic changes rely heavily on immune stimulation driven by *H. pylori* for their proliferation. In the early phases of disease, removing *H. pylori* can successfully treat the tumor, but as the lymphoma progresses and acquires additional genetic alterations, it may become independent of *H. pylori* and resistant to bacterial eradication therapy. **[105]**

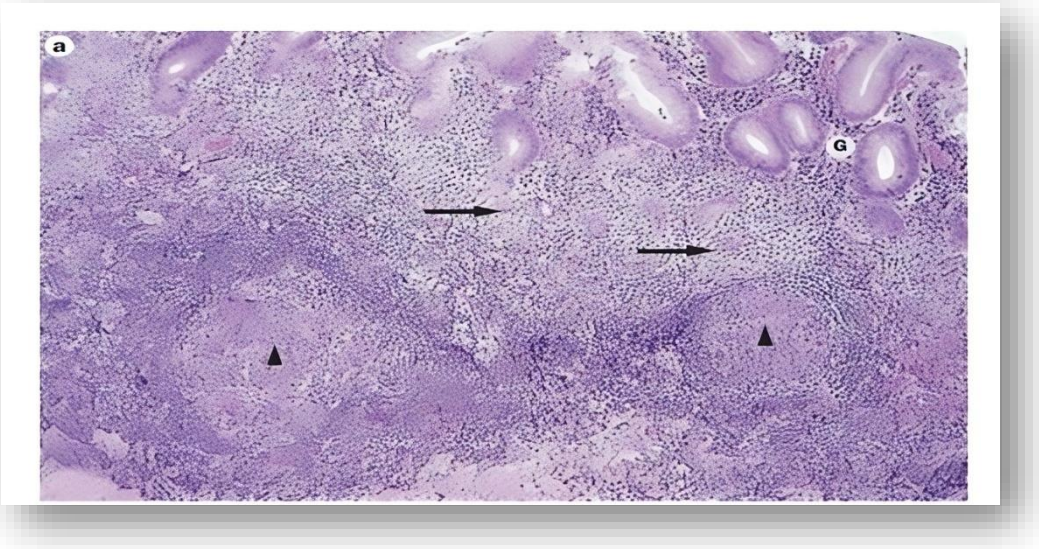


Figure 14: Morphologic and immunohistochemical features of gastric MALT lymphoma. **a** | Gastric MALT lymphoma cells surround reactive B-cell follicles (arrowheads) and invade the gastric glandular epithelium **(G)**, resulting in so-called lymphoepithelial lesions (arrows). Hematoxylin and eosin stain, original magnification ×10.**[107]**

III. Extra-Gastroduodenal Diseases:

H. pylori infection has been linked to multiple systemic conditions beyond gastroduodenal diseases, with robust evidence for its involvement in idiopathic thrombocytopenic purpura, iron deficiency and Pernicious anemia. Preliminary findings also implicate it in insulin resistance, diabetes, non-alcoholic liver disease, metabolic syndrome, coronary artery disease, and neurodegenerative diseases. **[108]**

Multiple meta-analyses have investigated the potential connection between *H. pylori* infection and cardiovascular disease, utilizing fixed and random effects models. Results indicate a possible association with myocardial infarction risk. Research in special populations, such as chronic kidney disease patients, shows they experience gastric mucosal injuries and dyspepsia more frequently than the general population. These conditions have multifactorial causes, and *H. pylori* may contribute minimally to their development. **[103]**

Chapter 03: Epidemiology and risk factors of *Helicobacter pylori*

I. Prevalence of Helicobacter pylori:

H. pylori is regarded as one of the most amazing infections that affect humans. *H. pylori* is one of the most frequent bacterial infections and one of the most widespread worldwide diseases due to its more than 10,000-year history of coexistence and current colonization estimations at about half of the human population. **[109]**. As a result, *H. pylori* prevalence ranges from less than 40% in developed nations to over 80% in underdeveloped nations. **[110]**

Africa has the highest prevalence (79.1%), followed by Asia (54.7%) and Latin America and the Caribbean (63.4%), South America (69.4%) and Western Asia (66.6%). On the other hand, the lowest prevalence of *H. pylori* is seen in Oceania (24.4%) and Northern America (37.1%). The prevalence of *H. pylori* has been falling in Western nations with high levels of industrialization around the start of the twenty-first century, whereas it has plateaued at a high level in recently industrialized nations. The increasing disparity in prevalence has significant implications for the future global prevalence of *H. pylori*-related illnesses, such as stomach cancer and peptic ulcers. These variations in *H. pylori* prevalence most likely correspond to the Geographical areas, degree of urbanization, hygienic conditions, sanitation, and socioeconomic diversity. **[111]**

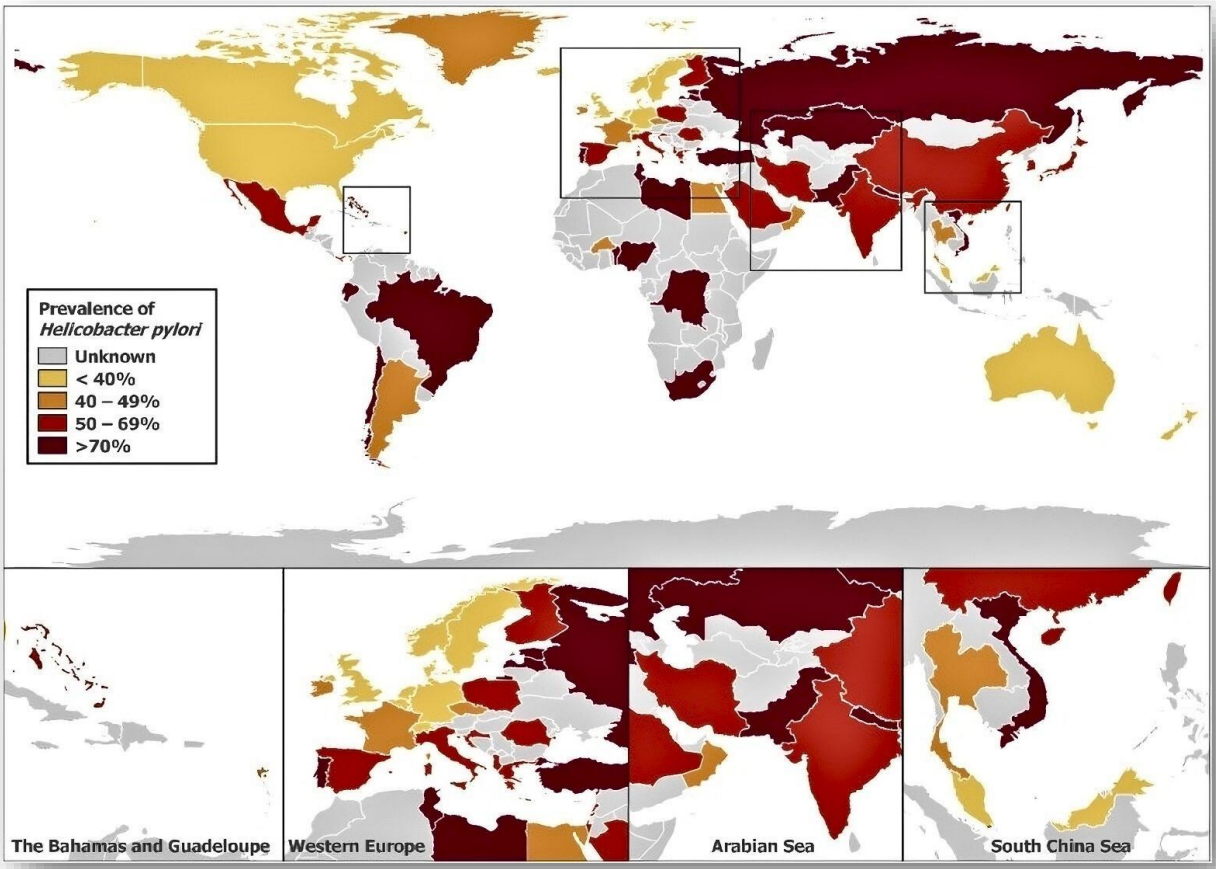


Figure 9: Global prevalence of *H.pylori* choropleth map.**[111]**

II. Risk factors of *H.pylori* infection:

1. Social demographic factors:

1.1.Age:

The majority of newly acquired *H. pylori* infections in juvenile age groups happened before the age of ten. With a range of 2.1% at ages 4–5, 1.5% at ages 7–9, and 0.3% at ages 21–23, the total crude incidence rate was 1.4% annually. **[112]**

Compared to high-income nations, the frequency of infection in children and adults was lower in Western Pacific areas but greater in low- and middle-income countries, such as those in Africa, the Eastern Mediterranean, Russia, Middle America, and South America. **[113]**

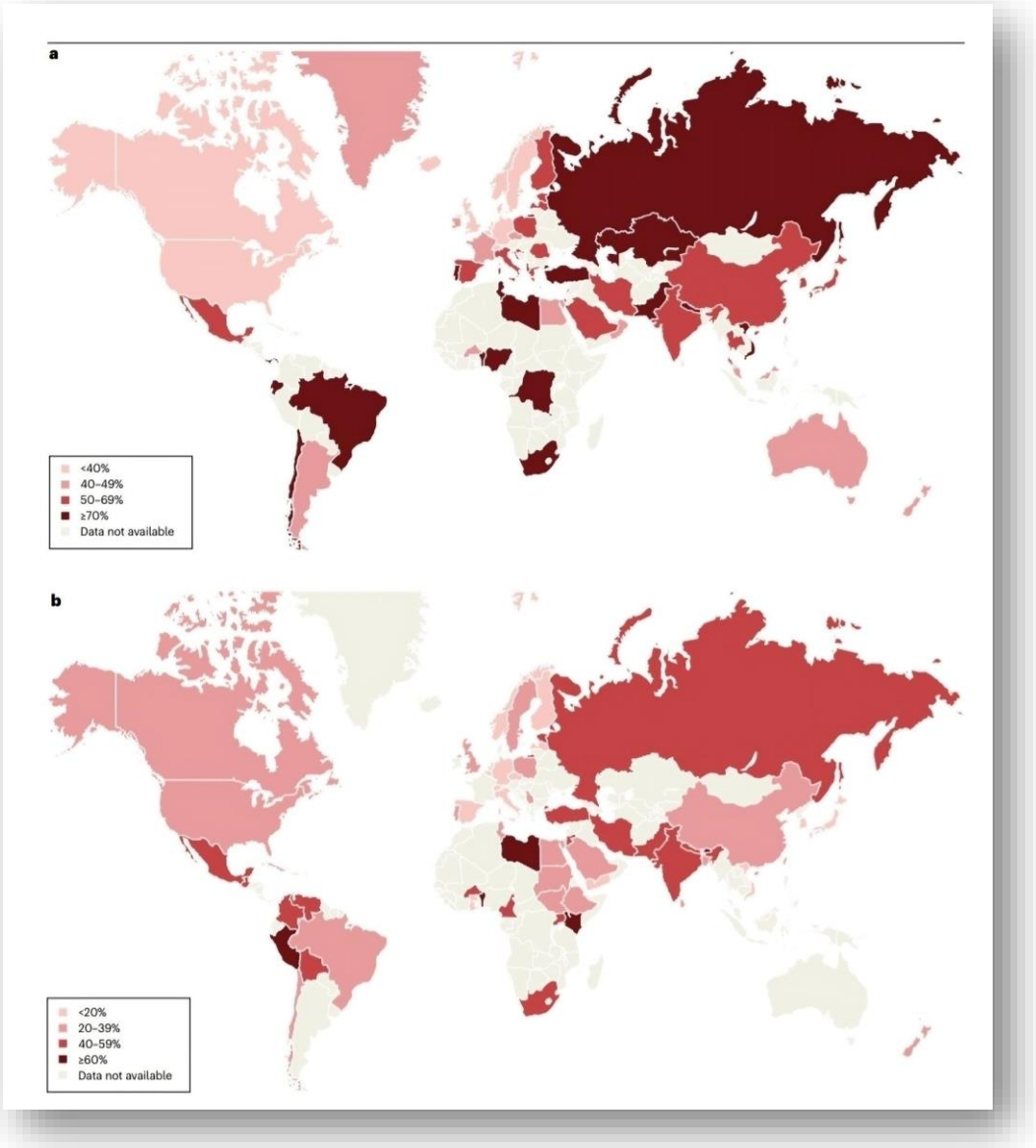


Figure 10: Prevalence of *H.pylori* in adults and children.**[52]**

Compared to children, adults have a greater frequency of infection. Additionally, compared to urban developed regions, it is higher in rural developing areas. Instead of a higher risk of infection at later ages, the majority (90%) of *H. pylori* infections are acquired in childhood and last throughout life, which explains the higher incidence in older people compared to children. **[52]**

1.2.Ethnicity:

Certain cultures may be more susceptible to *H. pylori* infection due to genetic and ethnic factors, according to some research; however, housing and food sharing practices may also play a part. **[114]**. For instance, in Indonesia's Sumatra islands, the frequency of *H. pylori* infection

is high in Batak communities but relatively low in Malay and Java groups, suggesting that genetic variables may play a role in varying host vulnerability. **[115]**

1.3.Gender:

Gender biology-including physiological and anatomical differences-plays a critical role in *H. pylori* infection and disease progression. The most apparent physiological disparity between males and females lies in sex hormones: testosterone in males and estrogen/progesterone in females, which significantly shape immune responses. Inflammatory reactions have long been observed to differ between sexes, with males typically experiencing more severe infectious disease complications and females displaying higher susceptibility to autoimmune disorders. This divergence arises from females' stronger cellular and antibody-based immune defenses, granting greater resistance to certain infections but also increasing autoimmune risks. Consequently, sex hormones likely alter *H. pylori* infection outcomes through both direct and indirect pathways. **[116]**

In gastrointestinal disorders such as reflux disease or *H. pylori* infection, women exhibit greater symptom sensitivity compared to men. Two physiological mechanisms may account for this difference:

A. Abnormalities of gastric emptying: Research has indicated that women are more prone to suffer from delayed stomach emptying, sometimes referred to as gastroparesis. A higher symptom score might result from symptoms like bloating, nausea, and early satiety caused by the stomach taking longer to empty its contents.
B. Lower threshold to esophageal pain: Research has shown that women are more sensitive to esophageal discomfort. This implies that they could experience esophageal distension or acid reflux pain or irritation more strongly than men do, which could result in their reporting symptoms more frequently or with greater severity. **[117]**

1.4.Socio-economic status:

Differences in socioeconomic position as determined by work, family income, and living conditions including crowding occupancy have been the main focus of attempts to comprehend the varying infection rates in specified groups. Regardless of current social class, there was an inverse relationship between the frequency of *H. pylori* infection and poor socioeconomic level throughout childhood. **[118]**

Poor socioeconomic status and inadequate hygiene during childhood are major risk factors for *H. pylori* infection. **[119]**

Childhood illnesses such as tonsillitis, diarrhea, and diphtheria are linked to reduced gastric acid secretion and malnutrition. Regions with high rates of childhood infections and undernutrition provide ideal conditions for *H. pylori* colonization. **[120]**

1.5.Genetic predisposition:

genetic polymorphisms in the host, particularly those increasing susceptibility to gastric cancer, may partially account for the varying clinical outcomes of *H. pylori* infection across populations. **[121]**

H. pylori trigger gastric damage beginning with chronic mucosal inflammation driven by pro- and anti-inflammatory cytokines. Polymorphisms in genes encoding cytokines like IL-1β, IL-6, and IL-8 (pro-inflammatory) and IL-1RN and IL-10 (anti-inflammatory) directly affect the intensity of cytokine responses, significantly shaping an individual's clinical outcome. Typically, patients with high-expression alleles of pro-inflammatory cytokines and low-expression alleles of anti-inflammatory cytokines exhibit amplified gastric inflammation and reduced acid secretion, elevating their risk of atrophic gastritis, gastric ulcers, or gastric cancer following *H. pylori* infection. **[120]**

2. Lifestyle habits:

2.1.Dietary habits:

Diet plays a significant role in the risk of *H. pylori* infection. Regular consumption of fresh fruits and vegetables has been linked to a lower likelihood of infection. Similarly, diets rich in whole grains, root vegetables, tubers, mushrooms, beans, vegetable oils, nuts, and seeds are associated with reduced risk. This protective effect is likely due to beneficial compounds in these foods, such as vitamin C, polyphenols, and flavonoids, which may help shield the stomach lining and prevent bacterial colonization. However, it is important to note that eating raw fruits and vegetables-especially those irrigated with water contaminated by feces-can also be a source of *H. pylori* transmission.

On the other hand, diets high in carbohydrates, processed meats, dairy products, refined grains and certain processed or preserved items are associated with an increased risk of *H. pylori* infection. High carbohydrate intake may elevate blood glucose, which in turn can cause enteric neuropathy, elevate pro-inflammatory cytokines, and lead to nerve degeneration. As a result,

this can slow gastric emptying, reduce stomach acid secretion, and promote bacterial growth, all of which make *H. pylori* infection more likely. **[122]**

2.2.Alcohol drinking and smoking habits:

Many risk factors, such as alcohol consumption and smoking, may contribute to the colonization and infection of *H. pylori* in humans. However, studies on the relationship between *H. pylori* infection and drinking or smoking have produced conflicting results **[123]**., given that some Some research **[124]** found no association between alcohol or tobacco use and *H. pylori* prevalence, other studies **[125]** reported that smoking is linked to higher rates of *H. pylori* infection, while alcohol showed no significant effect. when in contrast, others observed that both current smoking and alcohol consumption were associated with a lower prevalence of *H. pylori* infection, possibly due to increased gastric acidity from smoking. **[126]**

2.3) Profession:

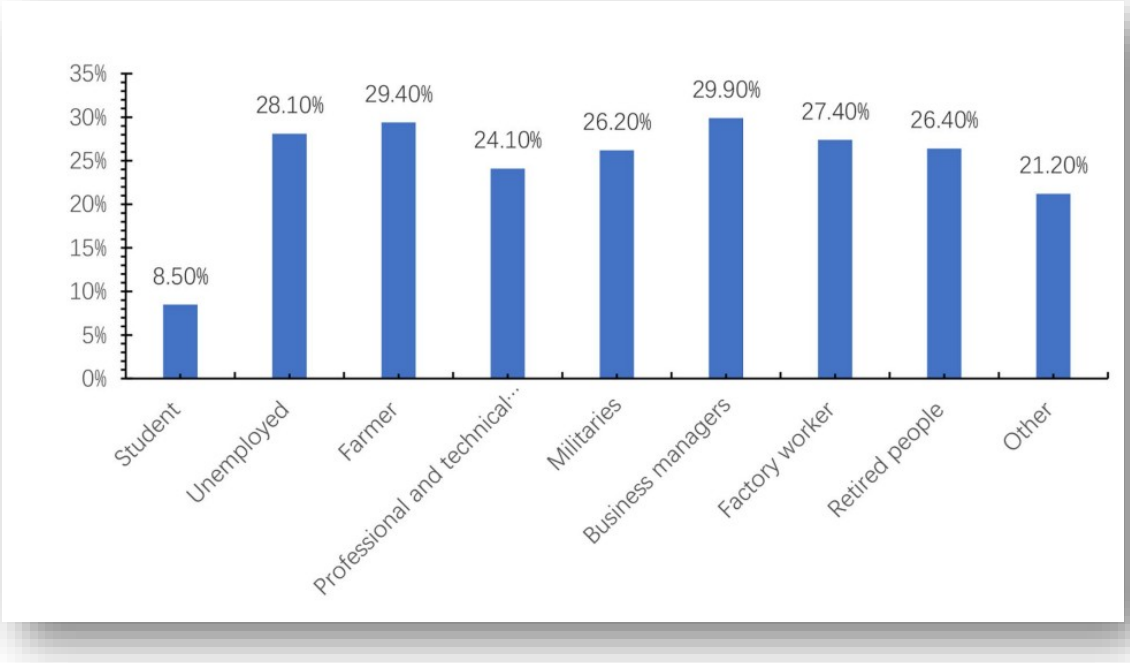


Figure 11: Percentage of *H.pylori* in different occupations **[127]**

The figure (11) illustrates the proportion of *Helicobacter pylori (H. pylori)* infections in various occupational categories. Business managers (29.9%) and farmers (29.4%) had the greatest infection rates, followed by jobless people (28.1%) and manufacturing workers (27.4%). Students, on the other hand, have the lowest infection rate (8.5%). This variance implies that the risk of *H. pylori* infection may be influenced by employment and maybe lifestyle-related variables. While the lower prevalence among students may be due to their

younger age and better hygiene habits, higher rates among manual laborers and managers may be related to stress, food choices, or access to healthcare.

3. Environmental factors:

The environment may serve as a reservoir for *H. pylori* infection, with connected external risk factors possibly holding greater significance than household socioeconomic conditions, especially in regions with developing economies. **[126]**

3.1.Water:

In impoverished nations, contaminated water might be a source of illness. the risk of *H pylori* infection was around three times higher for children living in households with external water sources than for those with internal water supplies. Thus, the children's drinking water source was linked to the prevalence of illness in the group. Children from households without internal plumbing (and perhaps unsanitary circumstances) were projected to have a greater infection rate than children from homes with normal plumbing. *H pylori* can be found in secretions like feces or saliva as well as environmental samples. **[128]**

3.2.Other factors:

People who live in places where fresh fruits and vegetables are scarce for extended periods of time and where food is preserved with salt are more likely to experience progressive stomach atrophy. These people are more likely to get gastric cancer as a result of an *H. pylori* infection at some point in their lives, and progressive stomach atrophy is linked to both gastric ulcers and gastric cancer.**[130]**

III. Routes of transmission:

1. Human-to-human transmission of *H. pylori*:

Person-to-person transmission can be classified into two main types: vertical and horizontal. Vertical transmission refers to the spread of infection from ascendant to descendent within the same family, whereas horizontal transmission occurs through contact with people outside the family or through exposure to contaminated environments. **[130]** Person-to-person transmission often happens within families, likely due to frequent close contact among members. Additionally, relatives may have a genetic susceptibility to *H. pylori* infection and are typically exposed to the same sources of infection and share similar socioeconomic backgrounds. Transmission between individuals can take place through three main routes: gastro-oral, oral-oral, and fecal-oral pathways. **[131]**

1.1. Direct human-to-human transmission: arguments gastro-Oral Transmission:

H. pylori is acquired in early life and the vomiting of achlorhydric mucus may serve as a vehicle for transmission. The transmission route could be via gastric juice, especially as a result of vomiting in childhood. **[132]** The microbe appears to survive outside the human body in unbuffered gastric juice and is often present in high quantities in vomit. **[131]**

1.2. Direct human-to-human transmission: arguments for the oral-oral route

Transmission may occur after vomiting because *H. pylori* can persist in stomach fluid for a while. The oral cavity is prone to become temporarily colonized if regurgitation takes place. **[133]**

Additionally, there are reasons to support the oral-oral approach as Mothers who premasticate their meals put their children at danger.

It is common to believe that the oral route is the primary source of contamination in industrialized nations, whereas the fecal-oral route is the primary source in underdeveloped nations. **[134]**

1.3.Transmission from the environment: arguments for the asymptomatic fecal-oral route:

H. pylori can be found in secretions like feces as well as environmental samples, it was previously believed that *H. pylori* were destroyed by bile salts and could not withstand competition from the many bacteria in the fecal flora, however this germ is really eradicated in the stool by PCR with excellent sensitivity. **[134]** Feces have lately been used to grow it. However, finding it in cultivable form is quite challenging. There are most likely survival forms (alive but non-cultivable) that are removed from the environment and change into "normal" forms when they get to the stomach. **[135]**

1.4. *H. pylori* infection can be a nosocomial infection:

In addition to potential community-based transmission routes, endoscopy rooms provide a unique risk for transmission that affects both gastroenterologists and patients. **[133]**

Because stomach fluid is contagious, touching infected equipment (such as endoscopes, pH probes, and nasogastric tubes) increases the risk of contamination. **[134]**

It has been demonstrated that gastroenterologists have a far greater infection prevalence than the overall population. Although it is uncommon, patient-to-patient transmission through infected endoscopes is feasible.

2. *H. pylori* infection: a potential zoonosis:

The bacterium *H. pylori* reside in the digestive systems of both humans and animals, and contaminated food-especially milk-is a key suspected source of human infection. Earlier

research has identified the bacteria in milk from different farming animals such as cows, camels, sheep, and pigs. Professionals handling animals and food of animal origin (e.g., veterinarians, butchers, and slaughterhouse workers) exhibit high titers of *H. pylori* antibodies (Ab). This suggests that ruminants may be the source of infection in humans. **[136]** Milk, a staple in human diets particularly for children, is widely considered a potential vector for *H. pylori* transmission from animals to humans. The bacteria have been identified in both raw and pasteurized milk, as well as in dairy products derived from cows, goats, and sheep, using conventional and molecular detection methods. **[137]** The presence of *H. pylori* in milk underscores the risk of human infection through contaminated raw milk consumption. Consequently, enforcing food safety protocols, maintaining stringent quality standards, and implementing proper dairy farming practices are essential to ensure milk safety for consumers. **[138]**

Companion animals such as Dogs and cats are important zoonotic reservoirs and public health hazards, hosting gastric *Helicobacter* species that may infect humans. *H. pylori*, a zoonotic pathogen, is theorized to spread from companion animals to humans, though the exact mechanism is undetermined. Evidence for Oro-oral or Oro-fecal transmission routes is bolstered by the detection of *Helicobacter spp*. in the mouths and fecal matter of infected pets. **[139]**

Chapter 04: Diagnosis And Treatment of *Helicobacter pylori*

I. Diagnosis of *Helicobacter pylori*:

1. Invasive methods:

Invasive approaches include endoscopy and gastric biopsy followed by either rapid urease test (RUT) or histology or culture, or molecular methods on biopsy samples.

Each invasive diagnostic tool has its own unique clinical benefit. The rapid urease test (RUT) delivers results quickly, allowing for prompt initiation of treatment. Histology offers a detailed evaluation of the gastric mucosa, aiding in both immediate and long-term patient management. Cultures are the most specific method and are especially valuable for determining antibiotic sensitivity before selecting an eradication regimen. Polymerase chain reaction (PCR) is a newer technique that can identify the bacterium directly from biopsy samples, eliminating the need for culture. **[140]**

- **Endoscopy:**

Endoscopy is the method for obtaining biopsies from the gastric mucosa that can be used in further studies on other invasive methods, such as urease testing, culture, and histologic examination to determine presence of *H. pylori* organisms. Research has shown that taking biopsies from both the antrum and fundus of the stomach provides the highest diagnostic accuracy. **[143]**

Additionally, endoscopy provides a detailed and accurate view of the gastric mucosa, although its diagnostic accuracy may not surpass that of other tests. The main drawbacks of this procedure are that it is time-consuming and demands significant skill and expertise to perform effectively. **[140]**

- **histology:**

Historically, the histological examination of the gastric mucosa was the earliest reliable method for diagnosing *H. pylori* infection. Detecting the characteristic spiral-shaped bacteria together with signs of inflammation in the tissue is regarded as a positive diagnosis. **[141]**

This approach also provides valuable information about various forms of gastritis-particularly chronic types-as well as atrophy, dysplasia, metaplasia, and malignant neoplasms. **[142]**

H. pylori can be diagnosed using this method with just a single biopsy from an appropriate site; however, collecting multiple biopsies is advised to achieve greater diagnostic accuracy and sensitivity. Due to the uneven distribution of the bacteria within the mucus layers. **[140]**

Since the identification of *H. pylori*, pathologists have employed various diagnostic methods, including immunohistochemical (IHC) techniques and specialized stains like Giemsa, Warthin-Starry and hematoxylin and eosin (H&E) which is for assessment of inflammatory cells and Giemsa for discernment of pathogen. However, it is well established that IHC staining offers high sensitivity and specificity **[143]**, and it should be reserved for cases with scarce bacterial presence, severe chronic gastritis, advanced atrophic gastritis (with extensive intestinal metaplasia), or post-eradication follow-up biopsies. **[145]**

The Sydney grading system for chronic gastritis and its updated Houston version are the most commonly used nomenclature for gastritis. This system categorized gastritis according to intensity of mononuclear inflammatory cellular infiltrates, polymorphic activity, atrophy, intestinal metaplasia, and *H. pylori* density into mild, moderate and severe categories. **[145]**

Several factors influence the diagnostic accuracy of histological examination, including the skills and experience of the pathologist and gastroenterologist, the methods used for sampling and examining biopsy specimens, and the staining techniques applied. Additionally, medications such as proton pump inhibitors (PPIs), antibiotics, and bleeding from peptic ulcers can impact the results. **[146]** Furthermore, the presence of other bacteria that structurally resemble *Helicobacter* can significantly and negatively affect the test outcomes. **[140]**

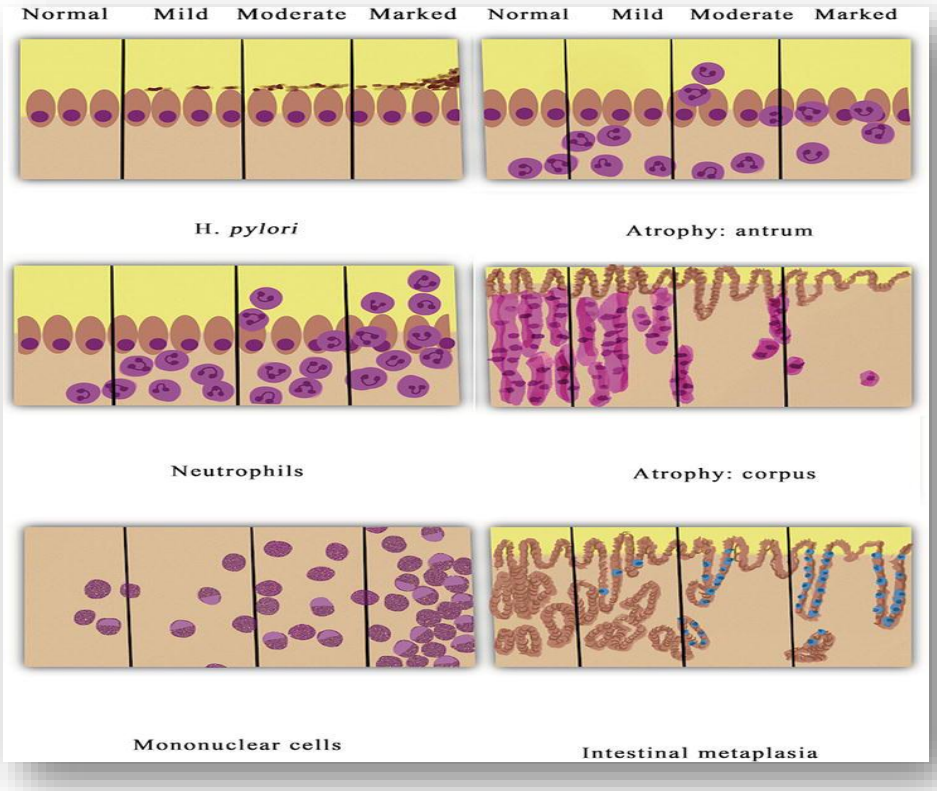


Figure 12: Grading of gastritis by Sydney system.**[141]**

- **Culture:**

The culture of *H. pylori* is performed on the gastric biopsy samples to confirm the *H. pylori* infection and While culture is very specific, its sensitivity is low because *H. pylori* is challenging to cultivate, and the process requires specialized, experienced laboratories. **[147]** Culturing gastric biopsy samples to identify *H. pylori* is not commonly used as a standard diagnostic method. This technique is primarily reserved for research purposes or cases where previous treatments have failed to identify the appropriate bacteria. It is advised that the mentioned test should be performed before initiating the next treatment phase to assess the bacteria's antibiotic susceptibility. **[140]**

H. pylori cultures should be initiated promptly after biopsy collection, since extended transport times and higher temperatures during transport reduce the success rate of cultivation. **[148]**

A biopsy sample intended for *H. pylori* culture can be preserved in transport media such as Portagerm pylori or Stuart for up to 24 hours at 4 °C, and isolates may be stored frozen at −80 °C for longer-term preservation. The GESA transport medium, a newer option that allows gastric biopsy specimens to be stored at 4 °C for up to 10 days while maintaining a quantifiable

recovery rate of *H. pylori*. Once transported, *H. pylori* requires selective media and microaerobic conditions-typically 80–90% nitrogen, 5–12% carbon dioxide, and 5–10% oxygen-for optimal growth, with incubation at 37 °C for 5–7 days. Various culture media can be used, including both selective and non-selective agars such as *H. pylori* agar, Wang media, Wilkins-Chalgren, brain-heart infusion (BHI), trypticase agar bases, Columbia agar, and blood agar, with antibiotics like vancomycin, bacitracin, and polymyxin added to suppress the growth of other bacteria. **[140]**

The identification of the bacterium is based on its characteristic colony appearance along with positive results for oxidase, urease, and catalase tests. Following initial growth, additional subculturing is required to obtain sufficient colonies for conducting antibiotic susceptibility testing. **[145]**

- **Rapid urease test (RUT):**

The rapid urease test is a widely used, invasive, and cost-effective method for detecting *H. pylori* infection. When a biopsy is performed, this test is typically the preferred initial diagnostic choice. **[140]**

This method works by exploiting the presence of urease enzyme produced by *H. pylori* in the gastric mucosa **[147]**, during the test, a gastric biopsy is placed into a medium containing urea and a colorimetric pH indicator. If *H. pylori* is present, its urease enzyme breaks down the urea into ammonia, causing an increase in pH that triggers a visible color change in the indicator, confirming the infection. **[146]**

Numerous commercial rapid urease tests (RUTs) are available in various formats, including gel-based, paper-based, and liquid-based tests.**[143]**

The CLO (Campylobacter-like organism) test typically provides results within 24 hours, whereas the Pylori Tek kit uses a reagent strip that can deliver a positive result in under an hour. Both tests demonstrate comparable sensitivity and specificity, generally exceeding 90%, but the Pylori Tek kit is often preferred in endoscopy clinics due to its faster turnaround time.**[141]**

It is important to note that several factors can affect the accuracy of these tests. A minimum bacterial density of 10^4 organisms in the biopsy is necessary for a positive result. **[149]**, while recent use of antibiotics, bismuth compounds, proton pump inhibitors (PPIs), achlorhydria, or bleeding can cause false negatives. Additionally, collecting biopsies from the corpus, or combining samples from both the antrum and corpus, has been shown to improve the sensitivity of the rapid urease test. **[147]**

2. **Molecular methods:**

- **PCR and Real-Time PCR Testing:**

H. pylori may be found in feces, saliva, dental plaque, digestive fluid, and stomach biopsies using PCR or real-time PCR testing. PCR testing is a great way to quickly and safely detect *H. pylori* because of its high specificity and sensitivity. PCR testing is on par with, if not superior than, culture methods for confirming *H. pylori* cure. **[150]**

H. pylori subtypes can be distinguished using the PCR-based restriction fragment length polymorphism (PCR-RFLP) technique. One of the main advantages of using in-house PCR tests is that they may detect spiral or coccoid strains of *H. pylori*, which other traditional diagnostic methods cannot. The ability to analyze DNA isolated from urease test samples delivered by mail without stringent transportation constraints is another benefit of PCR. Due to the low copy number of target DNA and PCR inhibitors, several studies have documented limited sensitivity identification in fecal material. **[151]**

Even while PCR testing has many therapeutic applications, its usage is limited by a number of factors, including poor yield, infection concerns, and time limits. PCR methods are heavily reliant on a number of variables in poor nations, including cost, equipment accessibility, and level of experience. Real-time PCR sample hybridization, which uses fluorescence resonance energy transfer probes to quickly and accurately determine clarithromycin tolerance in biopsy and fecal specimens, is expected to be one of the most promising molecular techniques in the years to come. **[152]**

- **Peptide Mass Fingerprinting Technology (PMF):**

Using the efficient, affordable, and precise "MALDI-TOF MS" method, peptide mass fingerprinting (PMF) technology may be utilized to identify and eliminate a wide range of microorganisms.

The time and cost reductions of this approach make it beneficial. It is also quite sensitive and accurate. It is capable to distinguishing between various *Helicobacter* species **[153]**, and is able to identify antibiotic resistance. The analysis also requires a tiny quantity of microbial biomass (around 105 CFU). Compared to earlier times, PMF has grown more precise, more inexpensive, and more quickly available in recent years. **[154]**

This technique makes it simple to identify bacteria and is now a crucial component of clinical microbiology labs.

The microbial biomass enclosed in a matrix (cyano-4-hydroxycinnamic acid) is broken up and lysed using an ultraviolet laser in accordance with the protein sequences of each bacterial

population that have been supplied. Particles are ionized, sorted by mass-to-charge ratios, and their arrival times at detectors are recorded using MALDI-TOF MS. **[156]**

3. **Non-invasive methods:**

- **Urea Breath Test UBT:**

The UBT is a noninvasive and highly reliable diagnostic test widely used for diagnosing *H. pylori* infection. The test is based on the hydrolysis of 13C or 14C isotope-labeled urea. **[156]**

The orally administered urea is hydrolyzed by bacterial urease into ammonia and isotope-labeled carbon dioxide in the stomach. The isotope-labeled carbon dioxide is diffused into the blood circulation and expelled during exhalation. The exhaled carbon dioxide is measured using an isotope ratio mass spectrometer. **[157]**

Since its introduction in clinical settings, the 13C-labeled UBT has garnered significant interest, and thus, it is recommended by several national and international guidelines and several expert consensuses reports over 14C-labeled urea because 13C is a stable, nonradioactive carbon isotope with a natural abundance of approximately 1% among all carbon isotopes. **[158]**

The measurement of 13C-labeled carbon dioxide by conventional methods is more expensive, and it requires skilled personnel. Therefore, other alternatives with less expensive methods, such as infrared spectroscope and laser-assisted ratio analyzer, have been developed to measure the 13C-labeled carbon dioxide activity. The increase in the 13C-labeled carbon dioxide activity before and 30 min after consuming the urea-based meal indicates the urease activity exploited by live *H. pylori* in the stomach. **[146]**

One of the beneficial noninvasive investigative techniques is UBT in a “test-and-treat” approach. Contrary to serological and stool antigen tests, UBTs can be successfully used in patients after gastrectomy, antibacterial use, or recent proton pump inhibitor use.

- **Stool Antigen Tests (SAT):**

If an *H. pylori* infection-induced antigen is present in saliva, blood, or stool, it can be detected using enzyme immunoassays or immunochromatography. An SAT has an overall accuracy of above 90%, making it an unquestionably valuable diagnostic tool for identifying and verifying bacterial persistence following therapy. **[160]** Regardless of the patient's

condition, doctors and patients have a propensity to choose SATs since they are less costly than alternative therapies. **[160]**

According to SAT standards, the doctor should assess the infection's eradication at least four weeks following the conclusion of the eradication treatment cycle. By using a SAT with monoclonal antibodies, diagnostic and effectiveness assessments of eradication treatment may be carried out. **[158]** After stomach surgery, these tests can be used on both adults and children. With the use of these tests, gastric neoplasia may be prevented in the future. **[160]**

The simplicity, quick return time, and affordability of the SAT are its primary benefits over other noninvasive exams, such as the UBT.

- **Serological Testing:**

Antibody levels against *H. pylori* immunoglobulin G (IgG) are now measured using enzyme-linked immunosorbent assays (ELISAs). Serological tests that are widely viable are commonly used in diagnostic contexts.

Serological tests are ineffective in regions with low infection rates, while having sensitivity ranges of 55.6% to 100% and specific ranges of 59.6% to 97.9%. These tests have a sensitivity of 95% and a specificity of 85%. During an *H. pylori* infection, IgG antibodies are generated and stay high for about a year until they drop back to normal. Serological testing is unhelpful in evaluating posttherapy eradication rates because antibodies might remain active for years after infection, making it impossible to differentiate between recent and prior infections. **[161]**

II. Treatment therapies of *Helicobacter pylori* infection:

1. Recommended treatment:

The inefficiency of the existing treatment choices makes managing an *H. pylori* infection a constant struggle for the treating physician. A combination of two or more antibiotics plus an anti-ulcer medication administered traditionally is the currently recommended therapy for *H. pylori.* **[162]**

Several regimes can be used to treat *H. pylori* infection such as PPI-based triple therapies, The three components of PPI-TT include a PPI, clarithromycin and amoxicillin or, alternatively, metronidazole as a substitute for either amoxicillin or clarithromycin. The triple clarithromycin-based therapy must be confined to patients without prior exposure to macrolides living in areas with clarithromycin resistance rates lower than 15%.

Several modifications of the combination of antibiotics may be used and they are recognized as: sequential (first 5 days of PPI and amoxicillin and then 5 more days of PPI,

clarithromycin, and metronidazole), concomitant (10 days of PPI, clarithromycin, metronidazole, and amoxicillin), and hybrid (sequential-concomitant therapy: 7 days of PPI and amoxicillin and 7 more days of concomitant quadruple therapy with a PPI, amoxicillin, clarithromycin, and metronidazole. **[163]**

The rising incidence of treatment failures with PPI-based triple therapy (PPI-TT) is largely attributed to inadequate acid suppression, poor patient adherence to the prescribed regimen and antibiotic resistance. **[52]**

As a result, in areas with high resistance to clarithromycin and/or metronidazole, alternative first-line treatments such as bismuth-containing quadruple therapy-which includes a bismuth salt, a PPI, and two antibiotics like clarithromycin, metronidazole, or tetracycline-or non-bismuth quadruple therapy for two weeks should be used. **[164]**

If the first-line therapy fails to eradicate *H. pylori* infection, a second-line regimen is required; however, selecting an effective second-line treatment can be challenging due to the potential for microbiological resistance to the antibiotics included Initially. **[165]**

As a second-line approach, eradication of *H. pylori* may involve tetracycline–levofloxacin combinations, bismuth-based quadruple therapies, or levofloxacin–amoxicillin quadruple regimens. Emerging evidence indicates that a 10-day tetracycline–levofloxacin regimen demonstrates efficacy and serves as a viable rescue therapy following the failure of all first-line treatments for *H. pylori* infection.

Following two unsuccessful treatment attempts, susceptibility-guided therapies are employed as a third-line approach. However, third-line *H. pylori* treatments demonstrate limited efficacy, even with bacterial culture guidance, primarily due to widespread antibiotic resistance. A 14-day triple therapy regimen-comprising esomeprazole (40 mg twice daily), amoxicillin (1 g three times daily), and metronidazole (500 mg three times daily)-is utilized as third-line therapy after initial clarithromycin-based and subsequent quinolone-based regimens fail. **[166]**

2. **Post-treatment monitoring:**

After treatment, eradication must be monitored. It is not systematic to use an invasive test, especially in children. It is sufficient to use a test validated for its good sensitivity and specificity to detect *HP* after treatment. Of course, it is essential to ensure that the patient has been off antibiotics or antacids for at least 4 to 6 weeks before testing.

The tests used are the 13C breath test and the stool monoclonal antigen test (HpSA) test. The disappearance of symptoms is not a good indicator of treatment success. When a follow-up endoscopy is performed, gastric biopsies should be taken as a matter of course.

The evolution of histological lesions after treatment is quite particular:

- Activity disappears within a few days.

- The mononuclear infiltrate takes a few months to disappear.

- The evolution of atrophy and metaplasia is variable and uncertain, hence the need for armed surveillance.

In the event of incomplete or inadequate treatment, *H. pylori* may migrate from the antral to the fundic region, leading to false eradication on antral biopsies with apparently inactive gastritis. In this case, there are persistent signs of activity and numerous bacteria in the fundus. It is therefore advisable to take biopsies in the antrum and fundus to verify eradication.**[167]**

3. **Eradication:**

The persistence of *H. pylori* following eradication treatment, or eradication failure, can be caused by either inadequate treatment adherence or antibiotic-resistant *H. pylori*.

A major contributing factor to treatment failure seems to be non-adherence to treatment, which may be brought on by the treating physician's lack of knowledge about the treatment plan, the difficulty of triple therapy, inadequate dosing and insufficient therapy duration or the adverse effects of the medications used. Tailoring treatment plans to individual patient needs can enhance therapeutic outcomes. **[168]**

Numerous investigations have demonstrated a link between treatment failure for *HP* gastritis and *H. pylori* antibiotic resistance. For every antibiotic that has been suggested for eradication, this has been explained. **[169]**

4. **Antibiotic resistance:**

the microbiological resistance against antibiotics is increasing worldwide and the rate of failure of *H. pylori* first and second eradication lines is increasing. **[170]** Certain cases, a patient will undergo 14 days of quadruple therapy and, subsequently, either develop the

infection again or develop complications of *H. pylori* infection **[171]**, Clarithromycin and metronidazole resistance are the primary contributors to PPI-based triple therapy (PPI-TT) failure. Global clarithromycin resistance has risen from approximately 3–11% around the turn of the century and up to 15–30% currently, while metronidazole resistance exceeds 25% in most regions worldwide. **[52]**

Medication categories	**Medication Generic name**	**Mechanism of eradication**	**Mechanism of resistance**
Macrolide	Clarithromycin	By blocking bacterial protein synthesis, this antibiotic acts as a bacteriostatic agent. Clarithromycin achieves this by binding to the peptidyl transferase loop of domain V in the 23S rRNA located in the bacterial 50S ribosomal subunit. **[172]**	Point mutations in 23S rRNA 23S rRNA, increased antibiotic efflux mediated by efflux pump systems rpl22, infB.**[172]**
PPI	Esomeprazole	Bind to H+/K + ATP pump to stop acid secretion. **[173]**	/
Antimicrobial adjuvant	Bismuth salt	Bismuth acts topically and as an antimicrobial agent against *H pylori* by disrupting the organism's cell wall. In addition, it may interfere with adhesion of *H pylori* to the gastric epithelium, as well as inhibiting the organism's urease, phospholipase, and proteolytic activity. **[174]**	To date, no resistance to bismuth has been reported.**[175]**
Fluoroquinolone	Levofloxacin	Fluoroquinolones work by blocking bacterial topoisomerase II (also known	Point mutations in quinolone resistance determination

		as DNA gyrase) and topoisomerase IV, enzymes that are essential for the synthesis of bacterial nucleic acids. This action disrupts cell division and proliferation of the bacterium. **[176]**	region of DNA gyrase gene gyrA, gyrB.**[172]**
Nitroimidazole	Metronidazole	A nitro reductase in the microorganism's cytosol reduces metronidazole's nitro group to form a toxic metabolite, The reduction of metronidazole is mainly mediated by oxygen-insensitive NAD(P)H nitro reductase (RdxA), NAD(P)H flavin oxidoreductase (FrxA), and ferredoxin-like enzymes (FdxB) in H. pylori. The resulting highly reactive compounds cause DNA strand breakage. **[177]**	Mutational inactivation of the rdxA gene. Mutations in frxA and possibly other reductase-encoding genes (such as fdxB, a ferredoxin-like protein) can contribute to or enhance resistance, these genetic changes can lead to reduced or abolished nitro reductase activity. **[172]**
Beta-lactams	Amoxicillin	Amoxicillin, in combination with acid-suppressive agents, acts by attaching to penicillin-binding proteins (PBPs). This blocks peptidoglycan synthesis, an essential part of bacterial cell walls, causing cell wall breakdown and lysis during bacterial replication. **[172]**	Mutational change of penicillin-binding protein pbp1A, pbp2, pbp3, pbp4; beta-lactamase production; outer membrane protein mutations (hefC, hopC, hofH) causing decreased membrane permeability.**[172]**

Tetracycline	acts as a topical agent on the surface of the gastric mucosa against *H. pylori*, At the bacterial cytoplasm, tetracycline binds to bacterial ribosomes and interacts with a highly conserved 16S rRNA target in the 30S ribosomal subunit, arresting translation and protein synthesis. **[178]**	Mutations in 16SrRNA.**[172]**

Table 3: Mechanisms of eradication and resistance for medication commonly used against *Helicobacter pylori* infection.

5. Effective vaccine:

Antibiotic treatment for *H pylori* does not identify these asymptomatic people who are at risk of later-life gastric adenocarcinoma, peptic ulcer disease, and gastric cancer. The creation of a therapeutic or preventative vaccination has so once again come into focus. In the past, vaccines have been used to prevent illness.

In 1990, a mouse model of *Helicobacter* infection was created to support research on *Helicobacter* vaccines, killed *Helicobacter* organisms or whole cell sonicates were employed as immunogens in early animal vaccination trials in mice and pigs. However, to ensure safety, consistency, and accurate characterization, a vaccine intended for human use would probably need to contain purified proteins. The highly conserved, surface-exposed *H. pylori* urease enzyme complex, which makes up as much as 6% of the total cell mass, has been used in several early investigations. In order to live in the stomach mucosa, it converts urea to carbon dioxide and ammonia. **[179]**

Many vaccine strategies (protein-based, DNA, viral/bacterial vectors) have been studied, mostly in animal models, although most have only had sporadic success. Important antigens that have been studied include heat shock proteins, HP-NAP, VacA, CagA, and UreB. In a Chinese phase III clinical investigation, children who received an oral immunization that included UreB and heat-labile *E. coli* toxin showed 71.8% efficacy with protection that lasted for up to three years. However, the immunization was less successful in adults or those who

had previously been infected, and some gastrointestinal side effects were noted. An effective immune response requires the right balance between the Th1, Th17, and Treg pathways, which influence inflammation and bacterial clearance.

Future vaccine development likely depends on multicomponent formulations, appropriate adjuvants, and tailoring to specific *H. pylori* strains. **[180]**

Experimental section

I. Materials and Methods:

1. Objective of the study :

Conducting a retrospective analysis of patients with gastroduodenal pathologies associated with *Helicobacter pylori* infection, based on gastric biopsies collected at the pathological anatomy laboratory of Medea Public Hospital Establishment.

The most comprehensive patient records include details such as the date of sampling, patient name, age, sex, as well as the nature and origin of the sample.

2. Study Site:

The city of Medea, which is located in the north-central region of Algeria at the crossroads between the major cities of this part of the country. Its population is estimated at around 150,000 inhabitants and it covers an area of approximately 866 km².

3. Study Population:

This retrospective study was based on the analysis of all gastric biopsies of 1058 patients aged between 03 and 90 years old referred to the endoscopy service in the period from January 2020 to December 2024.



Figure 13: The PHE Mohamed Boudiaf of Medea.

4. Data Collection :

- The initial step involved identifying cases of gastric pathologies from histopathological analyses of biopsies, including antral, fundic, antral-fundic, pyloric, and antro-pyloric samples. This was done by utilizing the hospital's centralized clinical reporting and

archiving system, as well as the pathological anatomy service's archiving and reporting system.

- The second step was to determine the cases of gastric pathologies caused by *H. pylori* or not.
- The third step was to study the distribution of gastric pathologies due to *H. pylori* by sex, age groups, sampling site, and type of gastric pathology associated with this bacterium.

Ethical review, and approval was waived for this study due to the retrospective and anonymous data collection design.



Figure 14: Archives of histopathological diagnosis reports (Personnel Photo)

5. Statistical Analysis:

Descriptive statistics, count and percentage, were calculated using Microsoft Excel 2021 (Version 2504 Build 18730.20168). A non-parametric one-sample Chi-square test ($p \leq 0.001$) was performed to assess differences among proportions of the population in terms of histopathological diagnosis results, qualitative variables (gender, age, presence of a gastric pathology, site of infection, etc.) were described by their number and percentage.

II. Results and discussion:

1. Prevalence of *Helicobacter pylori* infection in the study population:

Years	Total cases tested	Positive cases	Prevalence
2020	112	59	52.68%
2021	95	49	51.58%
2022	177	116	65.54%
2023	447	360	80.54%
2024	227	190	83.70%
Total	1058	774	73.16%

Table 4: The yearly Prevalence of *Helicobacter pylori* infection.

$\chi^2 = 20.67$, $p < 0.001$

The table presents a set of data which encompassed a total of 1058 patients with gastric pathologies that have undergone an endoscopy and histopathological diagnosis related to *Helicobacter pylori* infection.

The results summarize the total number of cases tested each year, the number of positive cases identified, and the corresponding prevalence rates.

The initial period (2020-2021) shows relatively stable prevalence (52.68% to 51.58%), which rose significantly starting in 2022, peaking at 83.70% in 2024 after rising to 65.54% in 2022 and 80.54% in 2023.

At 73%, the total prevalence across the five years is considered a high rate of infection. The results can be represented by a graph (Fig 15) to make it clearer and more readable:

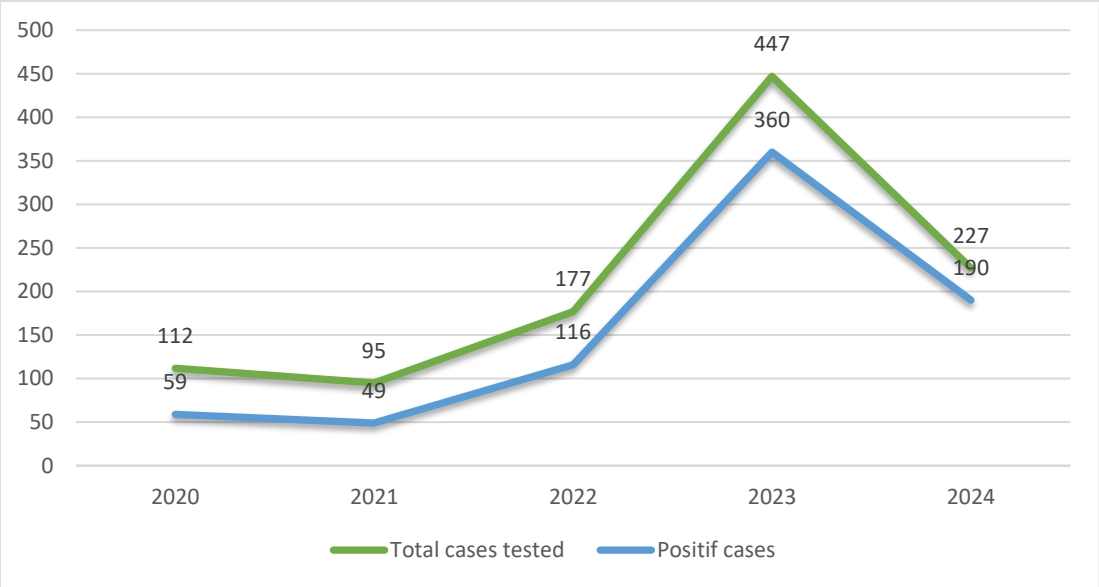


Figure 15: The annual numbers of total and positive cases tested for *Helicobacter pylori* infection.

Several epidemiological studies have established that infection with *Helicobacter pylori* represents one of the most prevalent bacterial infections globally. It was estimated that approximately 4.4 billion individuals were infected with *H. pylori* worldwide as of 2015. However, over recent decades, a decline in the prevalence of *H. pylori* infection has been observed in various countries, attributable to improvements in sanitation, healthcare, socio-cultural conditions, and the implementation of effective eradication strategies **[181]**

The infection rate of *H. pylori* varies significantly by geographical region, with prevalence rates ranging from 85% to 95% in developing countries and between 30% and 50% in developed countries **[182]**. Notably, Africa bears over 70% of the global burden of *H. pylori* infections **[181]** This observation aligns with the findings of the present study, which reported an overall *H. pylori* prevalence of 73.16% in our population, an exceptionally high rate compared to European countries, where prevalence ranges between 20% and 40% **[183].**, as well as other developed regions such as Oceania (24.4%), Switzerland (18.9%)**[184]**., and North America (37.1%) **[185]**

Our results corroborate previous research conducted within Algeria. For instance, a five-year study in Algiers revealed a *H. pylori* prevalence of 75% **[186]**., while another investigation in Tiaret reported a prevalence rate of 69% **[187]**. Comparable prevalence rates have been documented in other developing countries, including Cameroon (73.2%) **[188]**, Turkey (77.2%) **[189]**, Rwanda (75%) **[190]**, Morocco (75.5%) **[191]** and Egypt (79.8) **[192]**.

The observed variations in *H. pylori* prevalence across different studies and regions may be influenced by multiple factors, including socioeconomic status, living standards, ethnicity, geographic location, diagnostic methodologies, and prior antibiotic usage. **[193]**

2. Seasonal distribution of *Helicobacter pylori* infections:

The monthly cases presented in this study represent the cumulative number of cases recorded over a 5-year period (2020-2024).

Years/ Months	Jan	Feb	Mar	Apr	Mai	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
2020	**17**	**13**	**7**	**3**	**4**	**4**	**2**	**1**	**3**	**2**	**2**	**1**	**59**
2021	**6**	**9**	**5**	**5**	**/**	**3**	**/**	**/**	**2**	**3**	**9**	**7**	**49**
2022	**6**	**7**	**6**	**4**	**11**	**12**	**10**	**9**	**8**	**14**	**15**	**14**	**116**
2023	**21**	**18**	**26**	**10**	**42**	**32**	**45**	**30**	**20**	**45**	**42**	**29**	**360**
2024	**24**	**17**	**13**	**21**	**21**	**9**	**14**	**4**	**9**	**19**	**21**	**18**	**190**
Total	**74**	**64**	**57**	**43**	**78**	**60**	**71**	**44**	**42**	**83**	**89**	**69**	**774**

Table 5: Monthly distribution of cases of *H.pylori* infection from January 2020 to January 2024.

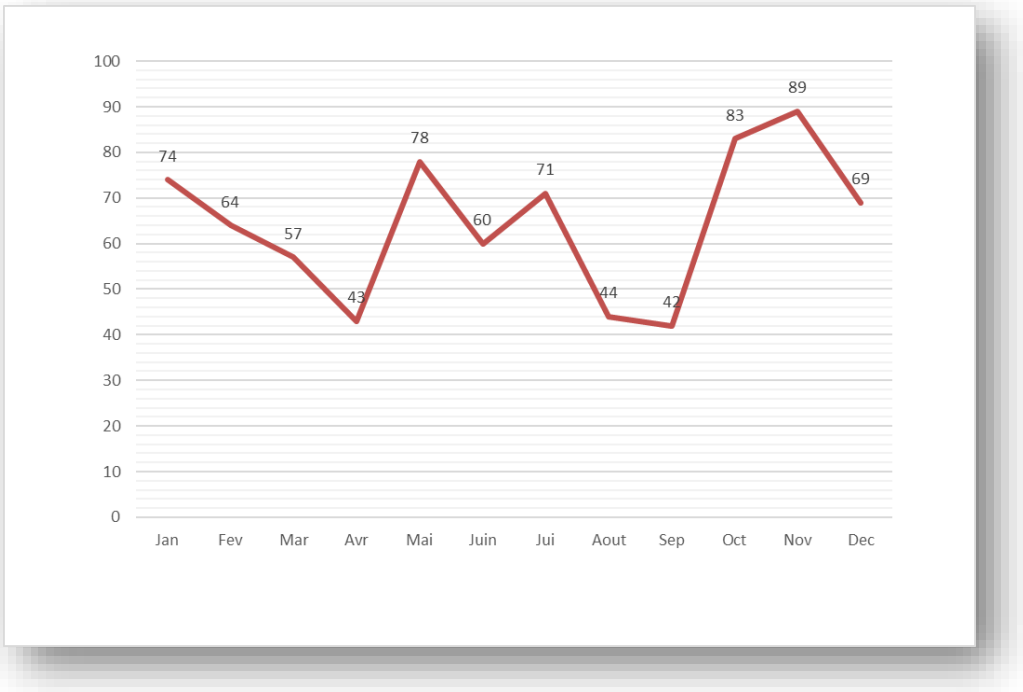


Figure 16: The monthly distribution of *Helicobacter pylori* infection cases from 2020 to 2024.

The monthly distribution of Helicobacter pylori infection cases from 2020 to 2024 is shown in this graph (figure 16). The number of instances varies noticeably from month to month, with many distinct peaks and troughs but no discernible pattern. The biggest occurrences occur in May (78 cases), October (83 cases), and November (89 cases), suggesting times of the year when illness is most common.

On the other hand, the lowest numbers of instances occur in April (43 cases), August (44 cases), and September (42 cases). From January to March, there is a steady decline in the number of cases, which goes from 74 in January to 43 in April.

The numbers fluctuate after a notable increase in May, with a further decline in August and September, and then a notable increase in October and November. December (69 instances) was little below the yearly average, remaining at a moderate level.

The seasonality of *H. pylori* is not well understood. **[194]**.

Our seasonality results showed that the highest level of *H. pylori* infection during 2020-2024 was in autumn, the second level of *hp* infection was late spring exactly in May.

According to another study conducted in Iran by Ranjbar et al **[195],** the highest frequency of *H. pylori* (4.54%) was seen during the summer. The primary cause of Iran's

greatest *H. pylori* strain prevalence during the summer months is that the weather heat, rain, and thunderstorms as well as changes in barometric pressure may have an impact on the bacterial prevalence during this period.

The results of a different study conducted in Venezuela revealed that the incidence of *H. pylori* infections was considerably greater during the rainy season (96%) compared to the dry season. **[196]**

The prevalence rate of *H. pylori* strains in each season is correlated with its average temperature, according to an analysis of the average temperatures of these four seasons in Isfahan province (17 °C for spring, 32 °C for summer, 16 °C for autumn, and 5 °C for winter. **[197]**

Similar seasonal distributions of *H. pylori* were described by Yahaghi et al **[198],** who also demonstrated statistically significant changes in *H. pylori* incidence between the year's hot and cold seasons.

3. Distribution of *Helicobacter pylori* infection by age:

The bar charts bellow shows an overview of the distribution of *H. pylori* positive cases across different age groups over a five-year period (2020-2024).

The data demonstrate a unimodal, right-skewed distribution, with prevalence rising from youth to a peak in middle age, then slightly declining but remaining elevated in older adults.

The difference of values between ages gave a maximum rate of 33.98% in patients aged between 41 and 60 years which presents the most affected category. The over 60 years group also shows a significant number of cases with 27.13% followed by the least affected age group was (1-20) years at 5.67% while the (20-40) years group shows a moderate prevalence of 25.58%.

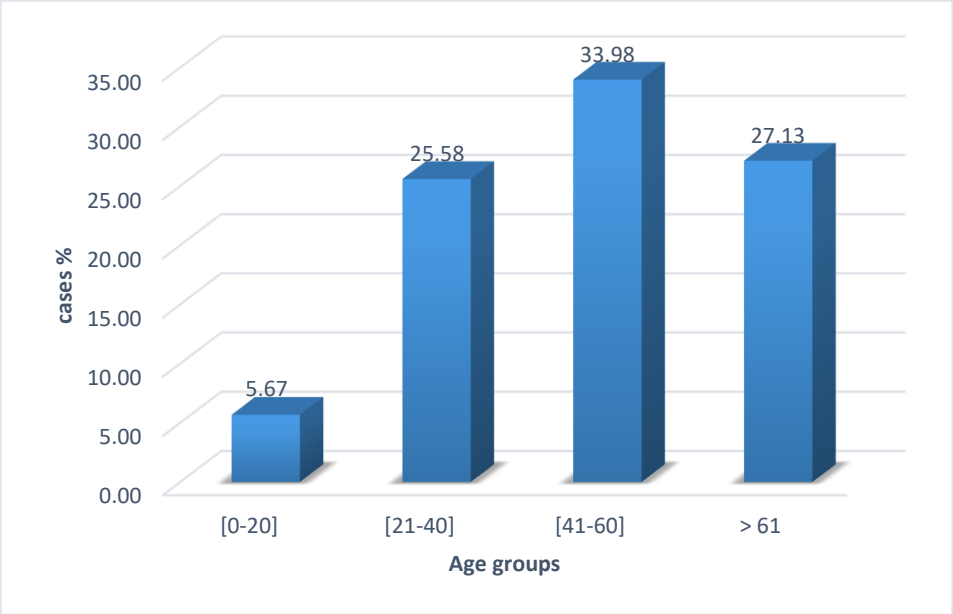


Figure 17: Distribution of *H. pylori* infection according to patient age groups.

Age is a critical determinant in the acquisition and prevalence of *Helicobacter pylori* infection. Numerous studies have demonstrated a significant association between this factor and the incidence of *H. pylori* infection **[199]**. It is widely asserted that childhood represents the primary period during which initial infection occurs **[200]**. It is often claimed that childhood is the main period during which individuals are infected with *H pylori*; however, there is conflicting evidence suggesting that prevalence continues to rise throughout adulthood.**[201]** Our findings support this latter view, as we observed an age-related increase in infection rates, with the highest prevalence among adult subjects in our study population. This pattern is characteristic of chronic infections that are typically acquired early in life but may only be detected or become symptomatic later.

Several authors **[202, 49]**. have reported that, generally, infection rates in developed countries remain substantially lower in children compared to their developing country counterparts. Interestingly, our study diverges from this trend, revealing comparatively lower infection rates in children within our Algerian cohort. This discrepancy may be attributable to improvements in hygiene-related practices and living conditions in Algeria. Supporting this observation, multiple Algerian studies **[203, 204, 205]** have documented that *H. pylori* infection predominantly affects adults, with adolescents and children exhibiting markedly lower prevalence rates. Similar age-related prevalence patterns have been reported in other developing countries. For instance, a study in Pakistan **[206]** found that the highest infection rate (55.6%) occurred in individuals over 30 years, whereas children under 18 years had a significantly lower

prevalence (9.5%). Likewise, Melese et al. **[207]** in a systematic review and meta-analysis, noted an increasing prevalence of *H. pylori* infection with age in Ethiopia.

This trend of increasing prevalence with age has also been observed in various developed and developing regions worldwide. In France, few children under 10 years were infected, with prevalence gradually rising to 36.7% by the sixth decade of life. Similar age-related increases have been documented in Vietnam and the Ivory Coast, albeit at higher overall rates **[208]** The elevated prevalence observed in older age groups can be partially explained by the cohort effect, where individuals born in earlier decades such as the 1920s in Northern Africa experienced higher rates of childhood **[209]** Moreover, recent hypotheses suggest that aging is associated with a diminished epithelial cell turnover rate and a reduced capacity to repair the gastric mucosa **[210]**and this has been attributed to decreasing prostaglandin levels in the gastric mucosa making age a major risk factor for *H. pylori* colonization.**[211]**

4. Distribution of *Helicobacter pylori* infection by gender:

The pie chart shows the distribution of *Helicobacter pylori* cases by gender:
At 62% of infections, the percentage of female cases is far greater than the 38% of male cases. This noteworthy disparity implies that within the study population, women are more likely to have *Helicobacter pylori* infections.

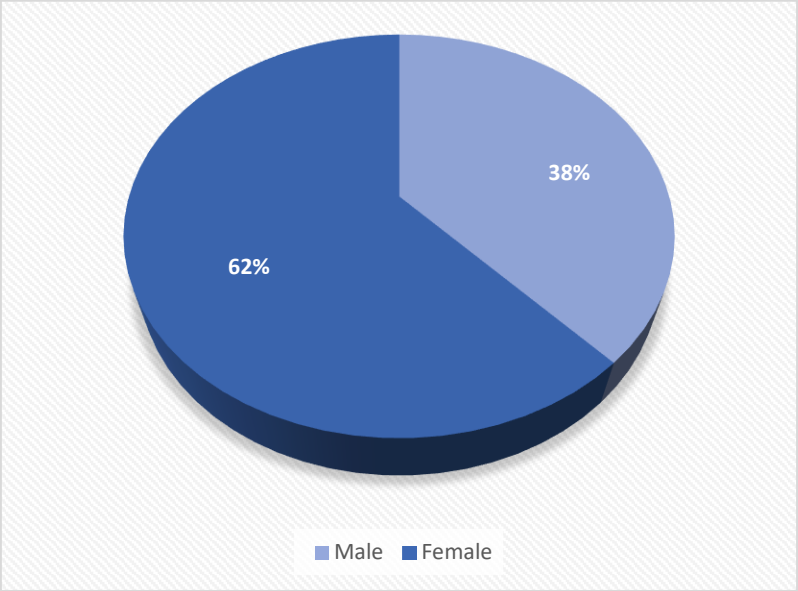


Figure 18: The distribution of *Helicobacter pylori* cases by gender.

Numerous Seroepidemiologic surveys have investigated the relationship between gender and *Helicobacter pylori* prevalence, revealing a complex and sometimes contradictory

pattern. While several studies report a higher prevalence of infection among males, others find no significant gender difference or even a predominance in females. **[212]**

For instance, research conducted in Algeria demonstrated that women exhibited a significantly higher prevalence of H. pylori infection (66.1%) compared to men (33.9%) **[205, 187]**. Similarly, a study in the Xinjiang Uyghur Autonomous Region found infection rates to be greater among Uyghur women (55.1%) than men (44.9%) **[213]** In contrast, Diomande et al. reported a predominance of infection among males in their cohort from Ivory Coast. **[214]** Nonetheless, Malaty emphasizes that both men and women are generally equally susceptible to *H. pylori* infection across all age groups.**[215]** Moreover, several studies have indicated that ethnic origin does not directly influence the onset of gastric pathology solely linked to *H. pylori*; rather, socio-economic conditions and hygiene levels are the primary determinants, with gender not consistently identified as a significant risk factor **[216]**

5. Rate of *Helicobacter pylori* infection by site of infection:

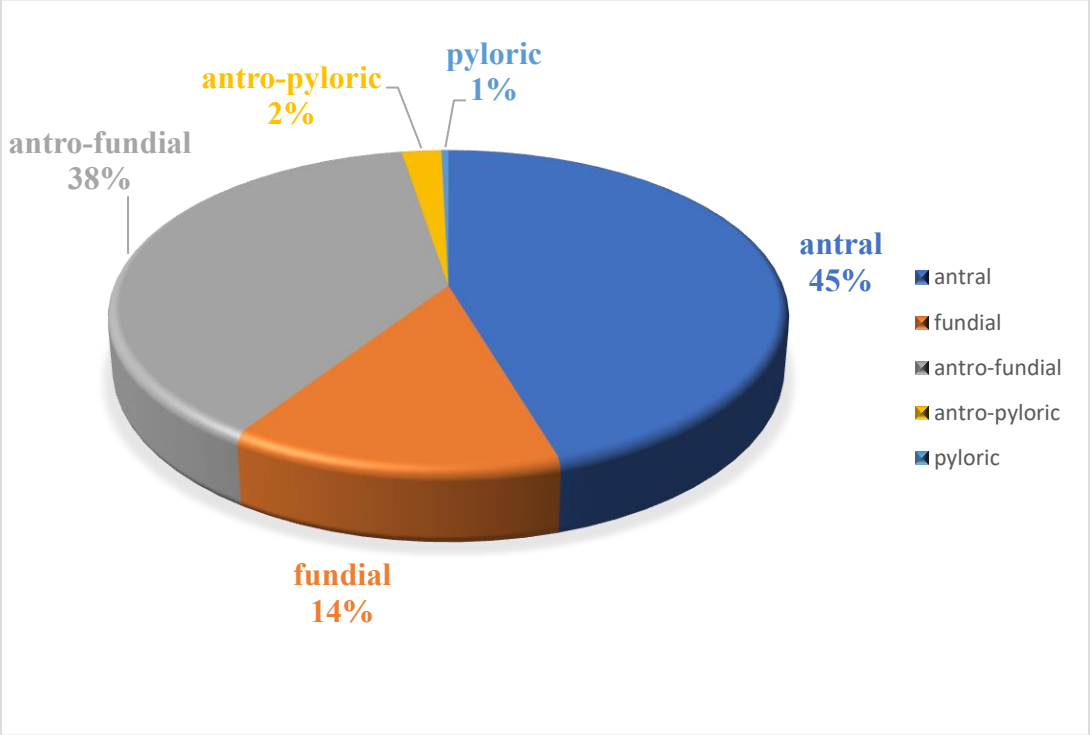


Figure 19: Rate of *Helicobacter pylori* infection according to Site of infection.

The frequency of *Helicobacter pylori* infection by stomach infection location is shown in this pie chart. With 45% of instances, the antral site is by far the most common. With 38%

of instances, antro-fundal localization comes in second, suggesting that the gastric fundus is also implicated, albeit less so.

The significantly lower frequency of fundal (14%), antro-pyloric (2%) and pyloric (1%) localizations suggests that these areas are rarely involved.

In another study, Marshall BJ and Warren JR **[217]** emphasized that *H. pylori* was first found in the antrum. They observed that these bacteria existed in the antral region of the stomach, where they were able to withstand the acidic environment. The antrum is more conducive to bacterial life because its pH is comparatively less acidic than that of other stomach regions.

Thus, there is a link between our findings and the literature, since the antral mucosa is colonized more often than other places. **[218]**

These numbers, however, are still more than those published by Binan et al. and Seoane et al., who said that the antral location was responsible for 40.0% and 48.1% of *H. pylori* lesions, respectively. **[219]**

The fundus is more acidic, which makes it less conducive to bacterial colonization, according to Kusters JG et al **[48]** They demonstrate the fundal site's (14%) and the outside regions' Explain how *H. pylori* can cause mixed infections by spreading to the area where the antrum and fundus meet. This explains why the fundus has a lower infection rate because of its higher acidity, but the antrum and antro-fundal area have the greatest rates.

6. Rate of different gastroduodenal pathologies among positive *H.pylori* patients:

Gastroduodenal pathologies	No.	%
Atrophic gastritis	537	69,37
Non-atrophic gastritis	197	25,45
Adenocarcinoma	2	0,25
MALT lymphoma	2	0,25
Hyperplastic Polyps	18	2,32
Duodenitis	41	5,29
Pangastritis	15	1,93
Autoimmune atrophic gastritis	19	2,45

Table 6: Rate of various gastric pathologies in our studies population.

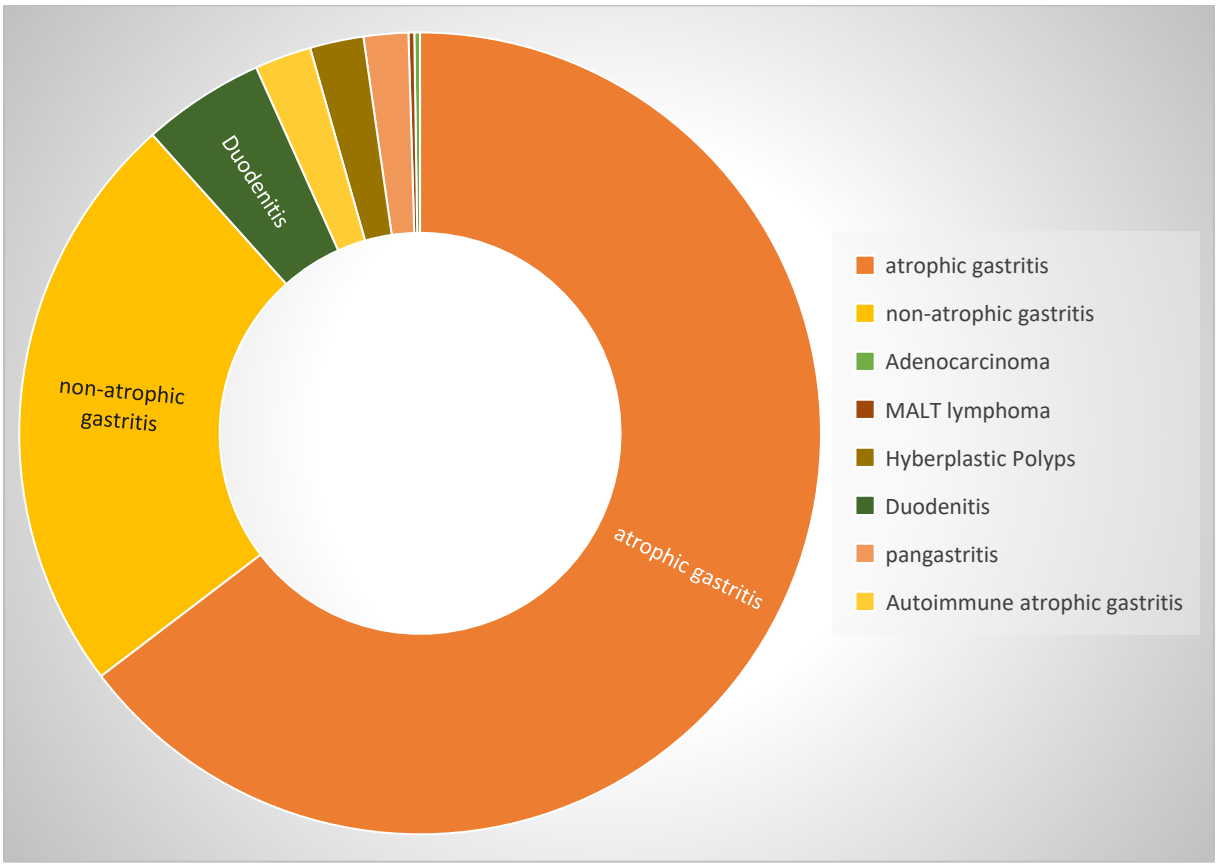


Figure 20: The distribution of various clinical outcomes due to *H.pylori*

The pie chart represents the distribution of various gastric pathologies among a group of 774 infected patients with more than one clinical outcome could be found in the same infected patient.

Results showed an overwhelming majority of cases are chronic gastritis, accounting for 94.82%of the total, Chronic gastritis is further subdivided into:

- Atrophic gastritis: 69.37%
- Non-atrophic gastritis: 25.45%

Other pathologies, such as duodenitis (5.29%), autoimmune atrophic gastritis (2.45%), hyperplastic polyps (2.32%), pangastritis (1.93%), MALT lymphoma and adenocarcinoma (0.25%), are much less common.This highlights that chronic gastritis is by far the most prevalent outcome in this patient population, while malignant and premalignant conditions are relatively rare.

Helicobacter pylori infection is widely recognized as the principal causal factor for various histological changes that predispose individuals to severe gastric conditions, including duodenal ulcers, gastric ulcers, chronic gastritis, and atrophic gastritis.**[220]**

Among these, chronic atrophic gastritis is most commonly linked to *H. pylori* infection, primarily due to the persistent inflammatory and immunological responses elicited by the bacterium. **[221]** Both atrophic gastritis and gastric ulcers are acknowledged as early pathological events in the cascade leading to gastric carcinogenesis. **[222]**

Despite the fact that approximately 50% of the global population harbors *H. pylori*, only a minority develop clinically significant disease. Less than 2% of infected individuals progress to gastric cancer, while about 20% develop peptic ulcer disease during their lifetime. Nonetheless, chronic gastritis appears to be nearly universal among those infected. **[223]**

In the context of Morocco, several epidemiological studies have underscored the high prevalence of *H. pylori* infection and its strong association with chronic gastritis. Bounder Ghizlane et al. **[224]**and Jouteiet al. **[221]** reported chronic gastritis as the predominant gastric pathology linked to *H. pylori* infection. Specifically, Joutei et al.'s analysis revealed that 92% of the studied population with digestive symptoms were infected and exhibited chronic gastritis. Similarly, Essadik et al.study which spread over 13 years (1998–2011) found that among 837 patients with gastric pathologies, 718 patients (85.8%) suffer from gastritis.**[225]**

Our study corroborates these findings, demonstrating a significant association between *H. pylori* presence and chronic gastritis across the entire studied population, with a predominance of atrophic gastritis and a comparatively lower rate of non-atrophic gastritis. This pattern aligns closely with results from Kasmi et al. **[205]** In Sidi Bel Abbes, Algeria, where atrophic gastritis accounted for 73.6% (358/486) of cases, while non-atrophic gastritis represented 17.4% (85/486). Another Algerian investigation conducted at Chadli Bendjedid Hospital in El Tarf **[226]** similarly reported a higher prevalence of chronic atrophic gastritis compared to superficial chronic gastritis among *H. pylori*-positive patients.

Our findings also resonate with those of Boussouab et al. **[227]**, who confirmed chronic gastritis in all cases studied, with active gastritis present in 93%. However, there is a notable discrepancy regarding the distribution of atrophic versus non-atrophic gastritis; Boussouab et al. reported 24.2% atrophic gastritis and 75.8% non-atrophic gastritis, contrasting with our observed predominance of atrophic gastritis.

The prevalence of atrophic gastritis varies globally and tends to be higher in countries with elevated H. pylori infection rate **[228]**. Collectively, these studies reinforce the clear and consistent association between H. pylori infection and the development of atrophic gastritis.
The prevalence of duodenitis among *H. pylori*-positive patients varies significantly across different geographical regions, as demonstrated by multiple studies. Our findings with a prevalence of (5.29%) in the *H.pylori* positive patients contrast with those reported in other populations, highlighting the influence of regional and methodological factors

In Nigeria, Abiodun Christopher Jemilohun et al. **[229]** found that 14.5% (8/55) of *H. pylori*-positive patients had duodenitis, while Cheli et al. (Italy) **[230]** reported a prevalence of 17.3% (21/121). Similarly, an Egyptian study **[231]** observed microscopic duodenitis (independent of gastritis) in 10.27% of the population. In contrast, a Lebanese study documented a higher rate of 31.9% (47/147).

Notably, our study showed a higher prevalence compared to Tanih et al. study which documented the lowest prevalence (0.59%, 1/168) in their cohort, further emphasizing the wide variability in disease manifestation. To explain the relatively low prevalence of duodenitis among *H. pylori*-positive patients in our Algerian study compared to higher rates reported elsewhere, several scientific factors should be considered. These include variations in diagnostic criteria, differences in study design, as well as geographical and population-specific factors. According to numerous studies **[232, 233, 234]** , one plausible explanation is the predominance of atrophic gastritis over non-atrophic gastritis in our population, coupled with the high prevalence of H. pylori infection and the low incidence peptic ulcer disease (PUD) in Africa **[235]**,likely contributes to the reduced incidence of duodenal inflammation and ulceration, as atrophic gastritis is associated with decreased gastric acid secretion, which in turn lowers the risk of duodenal mucosal injury and subsequent inflammation.
The incidence of gastric polyps (GPs) reported in the literature varies widely, ranging from 0.30% to 6.8% depending on the population studied. **[236]**. The most common types of gastric polyps include hyperplastic polyps (HPs), fundic gland polyps (FGPs), and adenomatous polyps (APs). Detection rates differ geographically, with reported prevalences of 6.35% in the United States **[237]**, 1% to 4.3% in China **[236]**, and 4.2% in Egypt **[238]**

Hyperplastic polyps are notably the predominant subtype in populations infected with *Helicobacter pylori* **[239]** This observation is consistent with our study, where HPs represented the most frequent polyp type, with a prevalence of 2.32%. Our prevalence exceeds that reported

by Bassene et al. in Senegal, who documented a gastric polyp prevalence of 0.8% **[240]**, but aligns closely with findings from Egypt, where Sharaf et al. reported an HP prevalence of 2.41% among *H. pylori*-positive patients

Concerning the rates of adenocarcinoma and MALT lymphoma observed in our study, which were 0.25%, we note a significant difference compared to the findings of Koula, Doukani et al. in Algeria (Tiaret), who reported a gastric cancer prevalence of 29.7% (253/849) in their population **[187]** However, the prevalence of MALT lymphoma in both studies was similarly low, around 0.2%. This low prevalence aligns with the understanding that gastric lymphoma is a rare complication of *H. pylori* infection, occurring in less than 1% of infected individuals. **[241]**

Another study conducted in the same region reported a gastric cancer prevalence of 7.89% (12/152) **[205],** which closely parallels findings from a Moroccan study that documented a 9% gastric cancer rate in their population **[226]**. Additionally, two other Moroccan studies by Essadik et al. and Joutei et al. reported gastric cancer prevalence rates of 7.6% and 3%, respectively.

In contrast, Asian countries exhibit significantly higher gastric cancer rates among *H. pylori*-positive individuals. For instance, Malaysia, Myanmar, and the Philippines report gastric cancer prevalences of 37%, over 20%, and 36%, respectively **[242]**. This significant difference in gastric cancer rates in our study compared to Asian populations is likely due to the substantially higher overall gastric cancer burden in Asia than in Africa **[243].**

Helicobacter pylori infection, particularly when accompanied by atrophic gastritis, is widely recognized as a primary risk factor for the development of gastric cancer **[244]**, the findings from our study present a notable contradiction.

Despite the high prevalence of atrophic gastritis among our *H. pylori*-infected population, the incidence of malignant gastric pathologies, including gastric cancer, remains notably low. This paradox, often referred to as the "African enigma," describes the discrepancy between the widespread *H. pylori* infection in Africa and the relatively low rates of severe gastric diseases such as gastric cancer**[245]**.Authors suggested that while the progression from *H. pylori* infection to atrophic gastritis in African populations resembles that observed in Western countries, some factors may inhibit further evolution to gastric cancer, such as the genetic makeup of both the bacterium and the host, as well as environmental factors**. [246]**

III. Limitation of the study:

It is important to recognize several limitations inherent to our study. Firstly, our research was confined to a single region and was based solely on histopathological diagnosis which may limit the generalizability of the findings to broader populations and might have influenced the observed distribution of gender and the spectrum of pathologies related to *H. pylori*. This methodological constraint could have introduced bias in interpreting the disease burden and its associated factors.

Secondly, the study design was retrospective with a relatively short duration and the lack of a systematic patient record registration system within our medical facilities posed challenges in data completeness and accuracy particularly in the assessment of *Helicobacter pylori* infection risk factors, which were the primary focus of our study.

Despite these limitations, the study provides valuable insights into the prevalence of *H.pylori* and the distribution of various gastroduodenal pathologies within the studied region.

Conclusion

Helicobacter pylori is recognized as a key factor in the development of a variety of gastric diseases, notably due to its ability to disrupt the delicate balance between protective and harmful influences within the gastric mucosa. Its persistent colonization of the stomach has reshaped our understanding of gastric pathology, highlighting the complex interactions among microbial, host, and environmental factors. In this context, the present study investigates the epidemiological characteristics and clinical significance of *H. pylori* infection in the population of Medea, Algeria, through a five-year retrospective analysis of gastric biopsy data conducted at the EPH Mohamed Boudiaf.

Helicobacter pylori was detected in 73% of the studied population, aligning with rates observed in other developing countries and confirming that Algeria remains a high-burden region for this pathogen.

The most affected age group over this five-year period was 41 to 60 years, accounting for 33.98% of cases followed by those over 60 years (27.13%), while children and adolescents were the least affected (5.67%).

A notable gender disparity was observed, with women representing 62% of cases compared to 38% for men. While this difference was significant in our cohort, the literature remains inconclusive about a true gender predisposition, suggesting that socio-economic and hygiene factors are more of risk factors than sex itself.

Our study demonstrated that *H. pylori* was involved in the majority of gastritis cases, duodenitis accounted for 5%, autoimmune atrophic gastritis (AAG) and hyperplastic polyps each represented 2%, while gastric cancer (GC) and MALT lymphoma together accounted for 0.25%. Regarding the site of infection, the antrum was the preferred site, followed by the antrofundic region and the fundus, with the antro-pyloric and pyloric sites being less frequently affected

Seasonal analysis revealed peaks in infection during autumn and late spring (notably May), with troughs in April, August, and September. However, no regular or fully understood seasonal pattern was established, echoing the complexity noted in international studies.

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Appendices

I. Appendix A:

Medical reports of year 2020

No.	Age	Gender	Service	Medical report	Hp status
33.20	58	F	Ext	-Muqueuse antro fundique bien différenciés sièges de lésions de gastrite légère peu active non atrophiante -Absence de dysplasie.	Hp (+)
99.20	62	M	Ext	- une muqueuse gastrique antrale, siège de lésions de gastrite chronique non atrophique, d'intensité et d'activité légères. -Absence d'amas lymphoïdes. -Absence de métaplasie intestinale. -Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements.	Hp (+)
161.20	32	M	Ext	-Gastrite chronique antro fundique active, d'intensité modérée	Hp (++)
163.20	41	M	Ext	-Deux fragments biopsiques l'un est antral et l'autre fundique, siège de légère lésion de gastrite chronique peut intense.	Hp (+)
272.20	/	M	MH	-muqueuse gastrique antro-fundique siège de légère lésion de gastrite.	Hp (+)
386.20	16	M	MH	-Gastrite chronique d'activité modérée	Hp (++)
445.20	51	F	Ext	- une muqueuse gastrique (03 fragments fundiques et 02 fragments antraux), siège de lésions de pan gastrite chronique, d'atrophie légère, d'intensité et d'activité modérées. -Présence de lésions de dysplasie de bas grade au niveau de la muqueuse antrale. -Présence de 04 amas lymphoïdes. - Absence de métaplasie intestinale. - Patient à surveiller.	Hp (++)
583.20	54	F	Ext	-Gastrite chronique fundique modérée avec petit polype hyperplasique.	Hp(+)
668.20	54	F	Ext	-une muqueuse antro-fundique siège de légères de gastrite.	Hp(+)
670.20	55	F	MF	- une muqueuse prépylorique et antrale hyperplasique simple sur le relief siège de légère lésions et discrète de gastrite.	Hp(+)
752.20	31	M	Ext	-une muqueuse antrale siège de lésions de gastrite chronique non atrophique, d'intensité et d'activité légères. -Présence d'un petit amas lymphoïde. -Absence de métaplasie intestinale. -Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements.	Hp(+)

839.20	58	F	Ext	- une muqueuse antro-bulbaire, siège d'une gastrite chronique d'atrophie et d'intensité modérées d'activité marquée. - une dysplasie de bas grade focale. -Absence d'évidence de métaplasie intestinale ni de follicules lymphoïdes dans la limite de ces prélèvements. - D'autres biopsies sont souhaitables après traitement.	Hp (+++)
1047.20	41	F	Ext	- une muqueuse antro fundique siège d'une gastrite chronique d'atrophie et d'intensité légères d'activité modérée. - Présence 02 follicules lymphoïdes. -Absence d'évidence de dysplasie ni de métaplasie intestinale dans la limite de ces prélèvements.	Hp (++)
1093.20	65	F	Ext	-Muqueuse gastrique antrale, siège de lésions de gastrite chronique d'atrophie modérée, d'intensité et d'activité légères. - Présence de métaplasie de type intestinal. - Absence d'amas lymphoïdes. -Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements	Hp (+)
1902.20	/	F	Ext	- une muqueuse gastrique de type antral, siège de lésion de gastrite chronique d'intensité, d'atrophie et d'activités modérées. - Notons un amas lymphoïde. - Absence de métaplasie intestinale. - Absence de dysplasie et/ou néoplasie dans les limites de ces prélèvements.	Hp (++)
2095.20	/	M	Ext	-une muqueuse gastrique de type antral, siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie modérées. -Présence de 04 amas lymphoïdes. -Absence de métaplasie intestinale. - absence de dysplasie et fou néoplasie dans les limites de ces prélèvements.	Hp (++)
1501.20	62	F	Ext	-une muqueuse gastrique de type antro-fundique, siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie modérées. -Présence de deux amas lymphoïdes. -Absence de métaplasie intestinale. -Absence de dysplasie et/ou néoplasique, dans les limites do ces prélèvements.	Hp (++)
1528.20	56	M	Ext	-Une paroi gastrique antrale, siège adénocarcinome gastrique moyennement différencié de stade PT3N1Mx (TNM 2017)	Hp (+)

				- La muqueuse adjacente présente des lésions de gastrite légère	
1717.20	23	F	Ext	-microscopique une muqueuse gastrique de type antro-fundique siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie modérée. -Absence d'amas lymphoïde. -Absence de métaplasie intestinale. -Absence de dysplasie et/ou néoplasie dans les limites de ces prélèvements.	Hp (++)
1913.20	76	F	Ext	-une muqueuse gastrique de type antral, siège de lésion de gastrite chronique, d'atrophie modérée et d'activité, d'intensité légères. - Absence d'amas lymphoïde. - Absence de métaplasie intestinale. -Absence de dysplasie et/ou néoplasie dans les limites de ces prélèvements.	Hp (++)

Medical reports of year 2021

No.	**Age**	**Gender**	**Service**	**Medical report**	**Hp status**
79.21	51	F	Ext	Une muqueuse antrofundique siège d'une gastrite chronique d'atrophie modérée, d'intensité et d'activités légères. Présence d'une métaplasie intestinale modérée et focale avec 5 amas lymphoïdes. Absence d'évidence de dysplasie dans la limite de ces prélèvements.	Hp (+)
94.21	/	F	Ext	Muqueuse gastrique de type antral, siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie modérée. Notons trois amas lymphoïdes Absence de métaplasie intestinale Absence de dysplasie et /ou néoplasie dans les limites de ces prélèvements.	Hp (++)
162.21	47	F	Ext	Une muqueuse antrale siège d'une gastrite chronique d'atrophie et d'activité légères, d'intensité modérée. Absence d'évidence de métaplasie intestinale, de dysplasie ni de signes de prolifération néoplasique dans la limite de ces prélèvements.	Hp (+)
236.21	41	F	Ext	Muqueuse antrale siège d'une gastrite chronique d'atrophie, d'intensité et d'activité légères. -Présence d'un amas lymphoïde et d'une dysplasie de bas grade focale	Hp (+)

				sans évidence de métaplasie intestinale dans la limite de ces prélèvements.	
258.21	53	F	M	Une muqueuse gastrique de type antral siège de lésion de gastrite chronique d'intensité, d'atrophie et d'activité modérée. Présence de deux amas lymphoïdes. Notons une métaplasie intestinale complète focale. Absence de dysplasie et /ou néoplasie.	Hp (++)
310.21	22	M	Ext	Une muqueuse antrale siège d'une gastrite chronique d'atrophie et d'intensité légères, d'activité modérée. -Présence une dysplasie de bas grade focale. -Absence d'évidence de follicules lymphoïdes ni de métaplasie intestinale dans la limite de ces prélèvements.	Hp (++)
353.21	24	M	Ext	Muqueuse gastrique antro-fundique siège de lésions de gastrite chronique d'atrophie légère d'intensité et d'activités modérées avec présence de 10 Follicules lymphoïdes. Absence d'évidence de métaplasie intestinale. Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements	Hp (+)(+)
386.21	39	M	Ext	Une muqueuse antrale siège d'une gastrite chronique non atrophique d'intensité et d'activité légères. Présence de deux amas lymphoïdes sans évidence de métaplasie intestinale ni de dysplasie dans la limite de ces prélèvements.	Hp (+)
398.21	61	M	Ext	Muqueuse gastrique de type antral siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie légère. Un amas lymphoïde est observé. Absence de métaplasie intestinale Absence de dysplasie et /ou néoplasie dans les limites de ces prélèvements.	Hp (+)
489.21	29	F	Ext	Gastrite chronique légère à minime antro-fundique	Hp (+)
565.21	33	F	Ext	Gastrite chronique antro-fundique légère.	Hp (+)
580.21	47	M	Ext	Une muqueuse gastrique antrofundique siège de lésions de pan gastrite chronique d'atrophie et d'intensité légères, d'activité modérée. Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements. Présence de métaplasie intestinale focale. Présence de 02 amas lymphoïdes.	Hp (+)

				Une muqueuse duodénale dont le relief villositaire est de hauteur conservée. Elle est le siège de lésions d'une légère duodénite chronique non spécifique. Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements.	
628.21	/	M	MH	Muqueuse de type antral siège d'une gastrite chronique d'atrophie, d'intensité et d'activité légères. Présence de 3 follicules lymphoïde avec une dysplasie de bas grade sans évidence de métaplasie intestinale dans la limite de ces prélèvements.	Hp (+)
866.21	35	M	MH	Une muqueuse gastrique de type fundique siège de lésions de gastrite chronique atrophique d'intensité légère, d'activité modérée. Présence de 2 amas lymphoïdes. Pas d'évidence de dysplasie épithéliale ou de métaplasie intestinale dans les limites des prélèvements adressés.	Hp (++)
903.21	53	F	Ext	Gastrite chronique antrale d'activitée modérée.	Hp (++)
959.21	52	M	Ext	Une muqueuse gastrique dont 4 de type fundique,1 antral et 1 jonctionnel siège de lésions de gastrite chronique non atrophique d'intensité et d'activité légères. Pas d'évidence de métaplasie antrale ou intestinale ni de prolifération tumorale dans les limites des prélèvements adressés.	Hp (++)
1031.21	27	F	MF	Une muqueuse gastrique siège de lésions de pan gastrite chronique d'atrophie légère d'intensité et d'activité modérées. Présence de 05 amas lymphoïdes. Absence de métaplasie intestinale. Absence d'évidence de dysplasie épithéliale dans la limite des prélèvements.	Hp (+)
1053.21	46	F	MF	Une muqueuse antrofundique siège d'une légère gastrite chronique non atrophique pue active. Présence de 6 amas lymphoïdes. Présence d'une dysplasie de bas grade focale sans évidence de métaplasie intestinale dans la limite de ces prélèvements.	Hp (+)
1094.21	73	M	Ext	Gastrite chronique fundique d'activité, d'atrophicitée modérée entre dans la maladie de Biermer.	Hp (++)
1102.21	34	M	Ext	Une muqueuse gastrique de type antral siège de lésions de gastrite chronique d'atrophie	Hp (+++)

				légère, d'intensité modérée et d'activité marquée. -Pas de dysplasie épithéliale ou métaplasie intestinale. -Presence de 03 amas lymphoides.	

Medical reports of year 2022

No.	Age	Gender	Service	Medical report	Hp status
16.22	42	F	Ext	Aspect morphologique d'une gastrite fundique chronique d'intensité légère à modérée peu active. Absence de métaplasie intestinale. Absence de caractère de dysplasie ou de malignité.	Hp (+)
114.22	/	M	Ext	Aspect morphologique d'une gastrite antro-fundique chronique d'intensité et d'activité modérée. Absence de caractère de dysplasie ou de malignité. Absence de métaplasie intestinal.	Hp (++)
241.22	51	M	Ext	Muqueuse gastrique (02 antrales,01 fundique) siège de lésions de pan gastrite chronique d'atrophie légère, d'intensité et d'activité modérées. Présence de 03 amas lymphoïdes. Absence de métaplasie intestinale. Absence d'évidence de dysplasie et/ou de néoplasie dans la limite des Prélèvements adressés.	Hp (++)
312.22	54	F	MF	Une muqueuse antro-pylorique, siège de lésion de gastrite chronique. D'intensité, d'activité modérée et d'atrophie sévère. -Notons deux amas lymphoïdes. -Absence de dysplasie et/ou néoplasie. -Absence de métaplasie intestine ale.	HP (++).
528.22	/	M	Ext	Une muqueuse gastrique antro-pylorique siège de lésions de gastrite chronique non atrophique, d'intensité et d'activité légères. Absence d'amas lymphoïdes. Absence de métaplasie intestinale. Absence d'évidence de dysplasie et/ou de néoplasie dans la limite des prélèvements.	Hp (+)
641.22	70	F	Ext	Gastrite chronique fundique d'activité modérée pouvant entrer dans le cadre de Maladie de Biermer.	Hp (+)

757.22	65	F	Ext	Une muqueuse gastrique de type antral siège de lésion de gastrite chronique d'intensité d'activité et d'atrophie légère. Absence d'amas lymphoïde. -Absence de métaplasie intestinale. -Absence de dysplasie et/ou néoplasie. -Aspect histopathologique d'une duodénite aiguë non spécifique.	Hp (+)
760.22	17	F	MF	Une muqueuse gastrique (3 de type fundique 2 de type antral) siège de lésions de gastrite chronique d'intensité et d'activité modérées d'atrophie légère. -Présence de 3 amas lymphoïdes. -Pas d'évidence de métaplasie intestinale ou de signes de malignité dans les limites des prélèvements adressés. -Aspect histopathologique d'une duodénite chronique légère non spécifique sans évidence de signes de malignité dans les limites des prélèvements adressés.	Hp (++)
830.22	30	M	PHTH	Une muqueuse gastrique de type fundique siège de lésions de gastrite chronique, d'intensité légère à modérée, d'activité modérée, non atrophique. Présence d'un amas lymphoïde. Absence de métaplasie de type antral, de type intestinal ni de dysplasie épithéliale dans la limite des prélèvements.	Hp (+)
901.22	38	F	Ext	Une muqueuse gastrique siège de lésions de gastrite chronique d'atrophie d'intensité et d'activité modérées. -Présence d'un amas lymphoïde. -Pas d'évidence de dysplasie épithéliale ou de signes de malignité dans les limites des Prélèvements adresses.	Hp (+++)
1720.22	43	F	Ext	Une gastrite chronique fundique d'atrophie et d'intensité légère peu active, associée à un polype des glandes fundiques. Absence de métaplasie intestinale. Absence de caractère de dysplasie ou de malignité.	Hp (+)
1879.22	58	F	Ext	Une muqueuse gastrique de type fundique siège de lésions de gastrites chroniques d'intensité et d'activité légères non atrophique. Absence d'évidence d'amas lymphoïde Absence de métaplasie intestinale ou de dysplasie épithéliale. Aspect histopathologique compatible avec une duodénite chronique non Spécifique.	Hp (+)

2147.22	36	M	Ext	Aspect histopathologique d'une gastrite chronique fundique atrophique en métaplasie intestinale marquée d'intensité modérée et d'activité légère. Ces aspects morphologiques peuvent entrer dans le cadre de la maladie de Biermer. Aspect histopathologique d'une duodénite légère non spécifique.	Hp (+)
2153.22	17	M	Ext	Une muqueuse gastrique de type antral siège de lésion de gastrite chronique d'atrophie légère, d'activité modérée et d'intensité marquée. Pas de dysplasie épithéliale ou de métaplasie intestinale. Présence de 05 amas lymphoïdes Aspect histologique d'une duodénite légère non spécifique.	HP (+)(+)
2359.22	50	F	Ext	Gastrite chronique fundique atrophiante d'intensité modérée, entre dans le cadre de la maladie de Biermer.	Hp (+)
2360.22	40	F	Ext	Gastrite chronique antrale active avec foyers de dysplasie de bas grade d'allure lié à l'inflammation nécessite un control biopsique après traitement.	Hp (++)
2395.22	54	M	Ext	Une muqueuse gastrique de type antral siège de lésion de gastrite chronique d'atrophie et d'activité modérée. Notons deux amas lymphoïdes. Absence de métaplasie intestinale. Absence de dysplasie et/ou néoplasie dans les limites de ces prélèvements.	Hp (++)
2518.22	67	F	CHH	Paroi gastrique siège d'un adénocarcinome bien différencié (grade 1) classe pT3N0 (0N/08N) (OMS 2019, AJCC,8éme édition 2017). La muqueuse gastrique avoisinante est le siège d'une gastrite chronique modérée non atrophique.	Hp (++)
2641.22	52	M	Ext	Muqueuse antro-fundique, comporte un infiltrat chronique d'intensité modérée réalisé des amas par endroits. -Les glandes sont le siège d'images d'exocytoses intra PNN. -Absence de dysplasie. Pan Gastrite chronique d'activité modérée	Hp (+)
2750.22	65	F	Ext	Muqueuse gastrique exiguë de type antral, siège de lésions de gastrite chronique d'atrophie, d'intensité et d'activité légères Pas d'évidence de métaplasie intestinale ou de	Hp (+)

				dysplasie épithéliale dans la limite des prélèvements adressés. Une muqueuse gastrique de type fundique comportant des glandes dilatées, sans anomalies cytologiques évoquant un polype des glandes fundiques.	

Medical reports of year 2023

No.	Age	Gender	Service	Medical report	Hp status
25.23	/	F	Ext	Une muqueuse gastrique de type antro-fundique siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie légère. Notons deux amas lymphoïdes. Absence de métaplasie intestinale. Des suffusions hémorragiques minimes et des vaisseaux sanguins congestifs sont observés. Absence de néoplasie/dysplasie dans les limites de ces prélèvements.	Hp (+)
28.23	76	F	Ext	Une muqueuse antro-fundique siège de lésion de gastrite chronique d'intensité d'activité et d'atrophie modérée. -Absence d'amas lymphoïde. -Absence de dysplasie et/ou néoplasie. -Notons une métaplasie intestinale focale minime incomplète. Une muqueuse fundique d'allure polypoïde réalisant l'aspect histopathologique d'un polype fundique hyperplasique non spécifique sans évidence de malignité dans les limites de ces prélèvements.	HP (++)

120.23	44	F	Ext	Une muqueuse gastrique fundique siège de lésion de gastrite chronique d'atrophie d'intensité et d'activité légères. Absence de métaplasie ou de dysplasie Absence de signes de malignité	Hp (++)
126.23	44	M	Ext	Une muqueuse gastrique antrale siège de lésion de gastrite chronique d'atrophie légère d'intensité modérée et peu active. Présence de 02 amas lymphoïdes. Absence de métaplasie ou de dysplasie. Absence de signes de malignité.	Hp (+)
131.23	63	M	Ext	Une muqueuse gastrique fundique siège de lésion de gastrite chronique d'atrophie, d'intensité et d'activité légères. Absence d'amas lymphoïdes. Absence de métaplasie ou de dysplasie.	Hp (+)
134.23	60	F	Ext	Muqueuse gastrique antrale siège de lésion de gastrite chronique d'atrophie, d'intensité et d'activité légères. Absence d'amas lymphoïde. Absence de métaplasie et de dysplasie. Absence de signes en faveur de la malignité.	Hp (+)
136.23	73	F	Ext	Une muqueuse gastrique fundique siège de lésion de gastrite chronique d'atrophie, d'intensité et d'activité légères. Absence d'amas lymphoïdes. La lamina propria oedémaciée, absence de métaplasie ou de dysplasie.	Hp (+)
355.23	43	F	Ext	Muqueuse gastrique de type antral siège de lésions de gastrite chronique non atrophique, d'activité marquée d'intensité modérée -Présence d'un amas Lymphoïde.	Hp (+++)

				-Pas d'évidence de métaplasie intestinale ou de signes de malignité dans la limite des prélèvements adressés.	
408.23	50	M	Ext	Une muqueuse gastrique antral siège de lésions de gastrite chronique à HP d'atrophie légère à modérée, d'intensité, activité modérée. -Pas de dysplasie épithéliale ou métaplasie intestinale. -Présence de 02 amas lymphoïdes. -Aspect histopathologique d'une duodénite chronique légère non spécifique.	Hp (++)
551.23	60	F	Ext	Une muqueuse gastrique fundique non atrophique siège d'un infiltrat inflammatoire lymphocytaire et plasmocytaire d'intensité et d'activité légères. Présence de 02 amas lymphoïdes. Absence de dysplasie ou de métaplasie. Absence de signes de malignité.	HP (+)
1054.23	41	M	Ext	Une gastrite chronique antro-fundique d'atrophie modérée, d'intensité et d'activité légères, avec métaplasie intestinale et antro-pylorique. Absence de caractère de dysplasie ou de malignité.	Hp (+)
1327.23	62	F	Ext	Gastrite chronique antrofundique d'atrophicitée modérée d'intensitée et d'activitée minime, pouvant entrer dans le cadre de maladie de Biermer.	Hp (+)
1395.23	62	F	MF	Muqueuse gastrique antrofundique siége de lésion de gastrite chouque non atrophique d'intensité et d'activité légère. Absence d'amas lymphoïdes.	Hp (+)

				Absence de signes de malignité.	
1511.23	56	M	Ext	Aspect morphologique d'une gastrite chronique antro-fundique, d'intensité et d'activité modérées. Absence de métaplasie intestinale. Absence de caractère de dysplasie ou de malignité.	Hp (+)
1700.23	46	F	Ext	Une muqueuse gastrique antro-fundiques siège de lésion d gastrite chronique d'atrophie légère à modérée, d'intensité modérée et d'activité sévère Présence de 07 amas lymphoïde. Absence de dysplasie et de métaplasie. Aspect d'une pan gastrite atrophique chronique, Malade à recontrôler après traitement	Hp (+)
1773.23	38	F	Ext	Une muqueuse gastrique siège de lésions de gastrite chronique d'atrophie marquée d'intensité et d'activité modérées. Présence d'une métaplasie intestinale focale. Présence d'une hyperplasie des cellules entérochromaffine likes nécessitant une étude immunohistochimique. Absence d'évidence de signes de dysplasie.	Hp (+)
1813.23	27	M	Ext	Une muqueuse gastrique de type antral siège de lésions de gastrite chronique à HP d'atrophie légère, d'activité, intensité marquée. - Pas de dysplasie épithéliale ou métaplasie épithéliale. -Présence de 09 follicules lymphoïdes. -Présence de 05 amas lymphoïdes. -Patient à contrôler après traitement.	HP (++)

1954.23	60	M	Ext	Une gastrite chronique granulomateuse tuberculoïde d'atrophie d'intensité et d'activité modérées sans évidence de nécrose caséeuse. -Absence d'évidence de métaplasie intestinale ni de dysplasie -Acorréler aux données cliniques, endoscopiques et biologiques.	Hp (+)
2005.23	43	F	Ext	Une muqueuse antro fundique siège de lésions de gastrite chronique à HP d'atrophie activité modérées et d'intensité marquée. Présence de foyers locaux de métaplasie intestinale. Présence de 06 amas lymphoïdes.	Hp (++)
2083.23	52	F	Ext	Une muqueuse antro fundique siège d'une pan gastrite chronique d'atrophie légère d'intensité modérée et d'activité marquée Présence de 8 follicules lymphoïdes avec une dysplasie de bas grade antrale sans évidence de métaplasie intestinale dans la limite de ces prélèvements.	Hp (++)

Medical reports of year 2024

No.	**Age**	**Gender**	**Service**	**Medical report**	**Hp status**
02.24	52	M	Ext	-Une muqueuse gastrique antro fundique siège d'une gastrite chronique d'activité légère, d'atrophie et d'intensité modérées, -présence de trois amas lymphoïdes, de foyers métaplasie intestinale intéressant 20% des cellules et des images de dysplasie de bas grade focale	Hp (+)
53.24	62	M	Ext	-Aspect histopathologique d'une gastrite antro fundique d'intensité, d'activité et d'atrophie légères. -Absence d'amas lymphoïdes, de métaplasie intestinale ou de dysplasie épithéliale.	Hp (+)
55.24	29	F	Ext	-une muqueuse gastrique de type antro fundique (01 fragment antral et 02 fragments fundiques)	Hp(+)

				siège de lésions de gastrite chronique d'intensité modérée, d'atrophie et d'activité légères. -Présence de 02 amas lymphoïdes. -Absence de métaplasie intestinale ou de dysplasie épithéliale dans la limite de ces prélèvements	
66..24	40	F	Ext	-Gastrite chronique d'activité minime d'atrophcitée légère pouvant entrer dans le cadre de maladie de Biermer. -Muqueuse duodénale normale.	Hp (+)
96.24	71	M	Ext	-une muqueuse gastrique antrale siège de lésion chronique d'atrophie légère, d'intensité modérée et d'activité marquée. - Présence d'un amas lymphoïde. - Absence de dysplasie ou de métaplasie.	Hp (++)
99.24	69	M	Ext	-Biopsie gastrique siège de lésion de pan gastrite chronique légèrement atrophique et active. - Absence de malignité dans la limite des prélèvements adressés.	Hp (++)
116.20	46	F	Ext	-Aspect morphologique d'une gastrite chronique antrale, d'intensité modérée, d'activité légère. -Absence de métaplasie intestinale. -Absence de caractère de dysplasie ou de malignité dans la limite des prélèvements adressés.	Hp (+)
121.24	45	M	Ext	-Aspect morphologique d'une gastrite chronique antrale, d'intensité modérée, d'activité légère. -Absence de métaplasie intestinale. -Absence de caractère de dysplasie ou de malignité dans la limite des prélèvements adressés.	
149.24	56	M	Ext	-une muqueuse gastrique superficielle de type antro fundique siège de lésions de gastrite chronique d'atrophie, d'intensité et d'activité légères. -Présence d'un amas de lymphoïdes. -Absence d'évidence de métaplasie intestinale ni de dysplasie épithéliale.	Hp (+)
156.24	36	F	Ext	-une muqueuse gastrique de type antro fundique siège de lésion de gastrite chronique d'atrophie légère, d'intensité et d'activités modérées. -Présence de 04 amas lymphoïdes. -Absence d'évidence de signe de métaplasie ni de dysplasie.	Hp (++)
319.24	38	F	Ext	-une muqueuse gastrique de type antral siège de lésions de gastrite chronique à HP d'atrophie, intensité légère et d'activité modérée. - Pas de dysplasie épithéliale ou métaplasie intestinale. - Présence de 02 amas lymphoïdes.	Hp (+)

331.24	/	M	Ext	-une muqueuse fundique siège de lésions de gastrite chronique d'atrophie modérée à marquée, d'intensité et d'activité minimes. -Présence d'une métaplasie intestinale et antrale, diffuse modérée. -Présence d'un amas lymphoïde. Absence de signes de dysplasie dans les limites des prélèvements adressés. -Ces aspects morphologiques peuvent rentrer dans le cadre de la maladie de Biermer.	Hp (+)
334.24	50	F	Ext	-une muqueuse gastrique de type fundique siège de lésions de gastrite chronique d'atrophie et d'activité marquée -Présence de quatre amas lymphoïdes. -Absence d'évidence de métaplasie intestinale ni de dysplasie dans les limites du prélèvement adresse	Hp (+++)
362.24	74	F	Ext	-une muqueuse gastrique de type antral siège de lésion de gastrite chronique d'intensité, d'activité et d'atrophie légère. -Absence d'amas lymphoïde. -Absence de dysplasie et/ou malignité dans les limites de ces prélèvements. -Absence de métaplasie intestinale	Hp (+)
365.24	33	F	Ext	-Aspect histopathologique plaide en faveur d'une duodénite chronique modérée non spécifique sans évidence de dysplasie et/ou malignité.	Hp (+)
431.24	/	M	Ext	-Aspect histopathologique compatible avec une gastrite chronique antro-fundique d'atrophicité modéré d'intensité minime avec métaplasie intestinale pouvant entrer dans le cadre de la maladie de biemer	Hp (+)
441.24	17	F	Ext	- une muqueuse fundique présentant une légère congestion vasculaire dans le chorion superficiel - La muqueuse antrale siège d'un minime infiltrat chronique éparse.	Hp (+)
444.24	66	F	Ext	-une muqueuse gastrique antro-bulbaire,et fundique tapissée d'un relief à pol muqueux fermé siège de multiples foyers de métaplasie intestinale s'étendant jusqu'aux glandes. -Le chorion comporte des glandes dystrophiques à ramifiés, espacées par un important infiltrat chronique agencé en amas.	Hp (+)
474.24	34	F	Ext	-une muqueuse gastrique de type antral siège de lésions de gastrite chronique à HP d'atrophie légère d'activité modérée et d'intensité légère à modérée.	Hp (+)

				-Pas d'évidence de dysplasie épithéliale ou métaplasie intestinale. -Présence de 02 agrégats lymphoïdes.	
511.24	73	M	Ext	-une muqueuse antrale siège de lésions de gastrite chronique d'atrophie et d'intensité minimes et d'activité modérée. -Absence d'évidence de métaplasie intestinale ni de dysplasie.	Hp (+)

II. Appendix B:

a. Medical report of a certain patient

Nom et Prénom :
Service demandeur : Externe.
Médecin demandeur : Dr ZERGA. A
Date de réception : 03/12/2023
Nature du prélèvement : Biopsies gasto-duodénales.

Médéa le 17/12/2023
Age :78 ans

Compte rendu d'anatomie pathologique
H 4917 . 23

Il nous a été adressé 03 flacons :

Flacon 1 : « Biopsies duodénales : L'examen microscopique a intéressé 02 fragments biopsiques d'une muqueuse duodénale au relief villositaire de hauteur conservée bordée par une muqueuse cubocylindrique bien différenciée, sans majoration de l'indice lymphoépithélial.
- La lamina propria est dissociée par un infiltrat inflammatoire polymorphe avec présence de polynucléaires éosinophiles .
- Il s'y associe une discrète hyperplasie des cryptes .
- Présence de quelques structures basophiles au niveau du film muqueux pouvant correspondre à des germes parasitaires.
- Pas d'évidence de néoplasie dans la limite des prélèvements examinés .

Flacon 2 : « biopsie antrale » : Trois fragments biopsiques perendoscopiques, allant de 02 mm à 03 mm de grand axe, ayant intéressé à l'examen histologique une muqueuse gastrique de type antro fundique siège de lésions de gastrite chronique d'intensité, d'activité et d'atrophie légères.
Une infestation à HP est notée.
Pas d'évidence d'amas lymphoïdes.
Pas d'évidence de métaplasie intestinale ni de dysplasie épithéliale dans la limite de ces prélèvements.
Pas d'évidence de signes de malignité ni d'infiltration tumorale dans la limite de ces prélèvements.

Flacon 3 : « polype » : Trois fragments biopsiques perendoscopiques allant de 03 mm à 05mm de grand axe, ayant intéressé à l'examen histologique une formation polypoide dont l'axe n'est pas bien évident. Elle est tapissée par un épithélium cylindrique fovéolaire pseudostratifié par endroits.
Le chorion renferme des glandes d'aspect festonné, kystique et adossées par endroits siège d'une parte minime de la mucosécrétion.
Il s'y mêle un léger infiltrat inflammatoire polymorphe.
Des plages d'hémorragie sont notées.

Conclusion :
Flacon1 : Aspect histopathologique **d'une duodénite chronique en poussée aigue.**
A compléter par un examen coproparasitologique.

Flacon 2 : Aspect histopathologique d'une gastrite d'intensité, d'activité et d''atrophie légères, à HP(+).

Flacon 3 : Aspect histopathologique **d'un adénome avec dysplasie de bas grade.**
Absence de signes de malignité dans la limite de ces prélèvements.

DR HENNICHE.A
PATHOLOGISTE

b. Questionnaire for risk factors of *Helicobacter pylori*

REPUBLIQUE ALGERIENNE DEMOCRATIQUE ET POPULAIRE

MINISTERE DE L'ENSEGNIEMENT SUPERIEURE

UNIVERSITE YAHIA FARES-MEDEA

DEPARTEMENT DE SCIENCES-OUZERA

Un questionnaire permet de collecter de manière systématique et structurée les informations nécessaires pour analyser les prélèvements réalisés dans le cadre de l'identification de *Helicobacter pylori*.

1. **Type de prélèvement**
   Veuillez cocher le type de prélèvement effectué :
   - ☐ Biopsie gastrique
   - ☐ Biopsie antrale
   - ☐ Biopsie fundique
   - ☐ Autre (précisez) : _____
2. **Date du prélèvement**
   Veuillez indiquer la date du prélèvement :
   _____ (JJ/MM/AAAA)
3. **Origine du prélèvement**
   Veuillez préciser l'origine du prélèvement :
   - Nom du service hospitalier ou médecin prescripteur : _____
   - Région précise (si le service n'est pas connu) : _____
4. **Contexte clinique du patient**
   Cochez les antécédents médicaux pertinents :
   - ☐ Ulcères gastriques
   - ☐ Gastrites chroniques
   - ☐ Cancer gastrique
   - ☐ Autres (précisez) : _____
5. **Symptômes rapportés**
   Cochez les symptômes rapportés par le patient :
   - ☐ Dyspepsie
   - ☐ Douleurs abdominales
   - ☐ Nausées
   - ☐ Vomissements
   - ☐ Perte de poids
   - ☐ Autres symptômes (précisez) : _____
6. **Traitements antérieurs**
   Cochez les traitements que le patient a reçus avant le prélèvement :

- ☐ Antibiotiques
- ☐ Inhibiteurs de la pompe à protons (IPP)
- ☐ Antihistaminiques
- ☐ Autres (précisez) : _____

7. **Méthode d'identification de H. pylori**
   Cochez la méthode utilisée pour l'identification de H. pylori :
   - ☐ Coloration histologique spécifique (ex. : Giemsa, coloration argentique Warthin-Starry)
   - ☐ Immunohistochimie (IHC)
   - ☐ Tests moléculaires (PCR)
   - ☐ Autre (précisez) : _____
8. **Âge et sexe du patient**
   - Âge : _____ (en années)
   - Sexe :
     - ☐ Masculin
     - ☐ Féminin
     - ☐ Autre
9. **Facteurs de risque associés**
   Cochez les facteurs de risque présents :
   - ☐ Tabagisme
   - ☐ Consommation d'alcool
   - ☐ Antécédents familiaux de pathologies gastriques
   - ☐ Régime alimentaire (ex. : riche en graisses, en épices)
   - ☐ Possession d'un animal de compagnie (chien, chat, etc.)
   - ☐ Autres facteurs (précisez) : _____
10. **Résultat du test de détection de H. pylori**
    Le résultat du test est-il :
    - ☐ Positif
    - ☐ Négatif
11. **La profession de malade**
    Est ce que c'est un artiste ?
    - ☐ _____

    Quel genre d'art (musique, peinture,....) ?
    - ☐ _____
