

ENDOSCOPIC MUCOSAL PHENOTYPES IN THE HELICOBACTER PYLORI INFECTION

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Abstract

Introduction. *H. pylori* infection occurs secondary to the bacterial colonisation of the stomach and the first portion of the small intestine. Patients infected with *H. pylori* can develop gastritis, peptic ulcer, gastric cancer, and MALT lymphoma. *H. pylori* infection is defined as a type I carcinogen by the WHO, and its role in gastric carcinogenesis is sustained by many studies.

Objectives. The objective of this study was the description and correlation of the endoscopic aspect of the gastric mucosa in the *Helicobacter pylori* infection and the incidence in a selected patient group.

Material and method. The study was conducted in the "Dr Carol Davila" Central Military University Emergency Hospital, Section of Gastroenterology, Department of digestive endoscopy, during a period of 12 months (2012--2013) on 1690 consecutive examinations on patients with ages between 18 and 92 years, with a retrospective cohort analytic study. As diagnosis method of the individuals infected with *H. pylori*, upper digestive endoscopy was used. During the intervention, biopsies were taken and rapid urease tests were performed.

Results. Regarding the variation of these endoscopic aspects within the examined population, we determined the fact that we encounter in the highest percentage gastritis with all its forms according to the Sidney classification (described below) which represents 59.3%, followed by endoscopic determination with a normal aspect in 18.8% of cases, then follows ulcer with a percentage of 10.33%, followed by duodenitis with 8.67%, and finally the most severe conditions, gastric cancer and lymphoma, reaching only 2.70% and 0.18%, respectively, of the general population examined endoscopically.

Rezumat

Introducere. Infecția cu *H. pylori* apare secundar colonizării bacteriene a stomacului și a primei porțiuni a intestinului subțire. Pacienții infectați cu *H. pylori* pot dezvolta gastrită, ulcer peptic, cancer gastric și limfom MALT. Infecția cu *H. pylori* este definită ca și carcinogen de tip I definit de către OMS, rolul sau în carcinogeneza gastrică fiind susținut de numeroase studii.

Obiective. Obiectivul acestui studiu a fost descrierea și corelarea aspectului endoscopic al



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mucoasei gastrice în infecția cu Helicobacter Pylori și incidența într-un grup de pacienți selectați.

Material și metodă. Studiul s-a defășurat în cadrul Spitalului de Universitar de Urgență Militar Central "Dr. Carol Davila", secția de Gastroenterologie- departament endoscopie digestivă pe o perioadă de 12 luni (2012-2013) pe 1690 de examinări consecutive la pacienți cu vârstă cuprinsă între 18 și 92 de ani, sub unui studiu analitic de cohorta retrospectiv. Ca și metodă de diagnostic a persoanelor infectate cu *H. pylori* s-a folosit endoscopia digestivă superioară. În cadrul intervenției s-au prelevat biopsii și s-au efectuat teste rapide la urează.

Rezultate. În ceea ce privește variația acestor aspecte endoscopice în cadrul populației examinate, am determinat faptul că întâlnim în cel mai mare procent gastrita cu toate formele ei conform clasificării Sidney (descrise mai jos) ce reprezintă 59,3%, urmată de determinarea endoscopică de aspect normal în 18,8 % din cazuri, apoi urmează ulcerul cu un procent de 10,33% ,urmat de duodenită cu 8,67% și, în cele din urmă, cele mai severe afectări, cancerul gastric și limfomul atingând doar 2,70% respectiv 0,18% din populația examinată endoscopic.

Cuvinte cheie: *Helicobacter Pylori, gastrită, endoscopie.*

INTRODUCTION

H. pylori infection represents the most common infection encountered in humans, and additionally it is also a transmittable chronic infectious disease, in which clinical manifestations are preceded by a long asymptomatic period. Most individuals infected with *H. pylori* cohabit with the bacterium without developing symptoms due to *H. pylori*.

The infection caused by *H. pylori* occurs following the bacterial colonisation of the stomach and the initial portion of the small intestine. Patients infected with *H. pylori* can develop gastritis, ulcer, gastric cancer, or MALT lymphoma. *H. pylori* infection is defined by the WHO as being a type I carcinogen, and its role in the development of gastric cancer is sustained by famous researchers.

This naturally competent and transformable bacterium was the first species for which two entire genomes were discovered. The genome of the size of ~1.7 Mb revealed the profile of an organism well fitted for its niche in the gastric mucosa, but lacking many of the regulatory characteristics discovered in the much larger genome of *E. coli*. Indeed, much more intelligent forms of regulation allow the microorganism to present more aspects to the host regarding the expression of proteins on the external membrane and other surface structures.

Many systems of change-restriction are present in these species, but these differ between the two analysed genomes. It is interesting that the microorganism reveals a high degree of heterogeneity respecting the nucleotide sequence. These differences are due to the ability to recombine freely, specific strains. Indeed, the population can be described as almost a clonal. *H. pylori* can colonize the human host for lifetime.

Therefore it is very well adapted for life in the stomach. While any strain of *H. pylori* causes at least a few inflammation signs in the body, the microorganism should determine a balance in order not to trigger an immune response sufficiently vigorous to eliminate it. Thus the bacterium developed various strategies including molecular mimicry and a group of adhesins to avoid neutralisation by the immune system. Since it is known that usually the host does not completely clean the organism, considerable efforts were made to discover an oral vaccine to eradicate an already installed infection or at least to prevent the infection. A benefit added to these efforts was represented by the understanding of the immune response of the stomach, a domain which attracted very little attention in the past.

H. pylori is found in the gastric mucosa in less than 20% of people under the age of 30 years, but the prevalence increases to 40-60% in people reaching the age of 60 years, including asymptomatic individuals. In developing countries, the prevalence of the infection in adults can reach about 80%. *H. pylori* infection is considered a feature of defavourized social-economic environments. The transmission mode is definitively established, and it seems that *H. pylori* is transmitted by faecal-oral and oral-oral route. Transmission by direct contact is favourized in the familial environment.

Over 80% of patients with acute infection develop chronic gastritis with *H. pylori*. Once it is occurred, *H. pylori*-associated chronic gastritis represents an irreversible process. Spontaneous cure is an exceptional phenomenon (0.3% per year) and is encountered only in case of non-atrophic chronic gastritis. *H. pylori*-associated chronic gastritis can progress in severity and extension (in years or decades) or, in most



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cases, remains unchanged. Approximately 30% of the patients with *H. pylori*-positive chronic gastritis develop, in years or decades, atrophic gastritis.

Most subjects with *H. pylori*-positive chronic gastritis remain asymptomatic during lifetime. Only approximately 1 of 6 subjects develop ulcer, and 1 in 100 subjects develop gastric cancer.

The epidemiological association between chronic gastritis, *H. pylori* infection and peptic ulceration is obvious. *H. pylori* can be detected in approximately 90% of patients with peptic ulcer disease; however, less than 15% of those infected develop the disease.

From a pathophysiological point of view, in a susceptible host, *H. pylori* causes active chronic gastritis that can in turn lead to the development of a gastric or duodenal ulcer disease, gastric cancer or MALT lymphoma. *H. pylori* infection causes active chronic gastritis characterized by an infiltrate rich in neutrophils, T and B lymphocytes, macrophages, and mast cells of the gastric epithelium and the underlying lamina propria. Mast cells, usually responsible for maintaining a balance of the immune response, can be an important item in the pathogenesis of gastritis. However *H. pylori* does not appear to invade the gastric mucosa, although evidence suggests that the mucus creates a niche where the germ is protected by gastric secretions.

Generally patients infected with *H. pylori* are asymptomatic, and no specific clinical signs were described.

Patients can complain of dyspepsia or abdominal discomfort, like during a gastritis, or epigastric pain (duodenal ulcer). In some cases patients can have an accentuated sensation of hunger especially in the morning and they can have halitosis. When signs and/or symptoms are present, they can include the following: nausea, vomiting, abdominal pain, heartburn, diarrhoea, hunger in the morning, halitosis.

In this study the purpose was to determine the types of endoscopic aspects which occur in the *H. pylori* infection described until now in literature and the frequency of their occurrence within the studied population.

MATERIAL AND METHOD

The study was conducted in the "Dr Carol Davila" Central Military University Emergency Hospital, Section of Gastroenterology, Department of digestive endoscopy, during a period of 12 months (2012--2013) on 1690 consecutive examinations on patients with ages between 18 and 92 years, the median age was 55 years. As diagnosis method of the individuals infected with *H. pylori*, upper digestive endoscopy was used. During the intervention, biopsies were taken and rapid urease tests were performed.

The inclusion criteria of patients examined endoscopically were represented by:

- patients aged over 18 years
- non-specific digestive symptomatology, to which alarm signals can be associated
- indication of upper digestive endoscopy performed by the treating physician
- presence of a symptomatology suggestive of gastric or duodenal impairment
- upper abdominal or retrosternal pain
- epigastric pain
- postprandial abdominal discomfort
- postprandial bloating
- early satiety
- painful uneasiness
- heartburn
- nausea
- vomiting
- anorexia
- weight loss
- upper digestive haemorrhage (hematemesis and melena)

The exclusion criteria were represented by:

- patients aged below 18 years
- shock
- acute myocardial infarction
- peritonitis
- acute perforation
- fulminant colitis
- recent colonic surgery
- patient refusal
- low patient cooperation
- coma (except in case the patient is intubated)
- heart arrhythmias
- recent myocardial ischemia
- CHF class IV NYHA
- acute cardio-respiratory failure

- major aneurysm of the abdominal aorta or its branches
- endocarditis risk
- administration prior to the procedure of proton pump inhibitors, antibiotics, H2-receptor antagonists, and bismuth

RESULTS

1695 patients were included - 867 males and 828 females, with a distribution by genders according to Table 1.

It was noticed that the highest proportion among all patient who had an indication for upper digestive endoscopy (Table 1) was in those with ages between 60-69 years, representing 27.1% of the total of examined individuals. At a small difference, representing 22.5%, are those in the age group between 50-59 years. We can also notice by cumulating these two groups which are at the top of this graphic that patients with ages between 50-69 years represented almost half (49.6%) of those who had an indication for upper digestive endoscopy.

According to the large amount of literature data, the *H. pylori* infection causes various gastric and duodenal lesions with a degree of impairment ranging from mild to severe. Among these are gastritis, duodenitis, both gastric and duodenal ulcerative lesions, gastric cancer, and lymphoma.

Among patients with indication for upper digestive endoscopy who were examined we have visualised the specified endoscopic aspects (Table 2), with the mention that there were also patients with a normal endoscopic aspect.

Regarding the variation of these endoscopic aspects within the examined population, we determined the fact that we encounter in the highest percentage gastritis with all its forms according to the Sidney classification



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(described below) which represents 59.3%, followed by endoscopic determination with a normal aspect in 18.8% of cases, then follows the ulcer with a percentage of 10.33%, followed by duodenitis with 8.67%, and finally the most severe conditions, gastric cancer and lymphoma, reaching only 2.70% and 0.18%, respectively, of the general population examined endoscopically.

According to the Sidney classification we have determined the following gastritis types (Table 3):

- erythematous-exudative gastritis,
- macular-erosive gastritis,
- papular-erosive gastritis,
- atrophic gastritis,
- haemorrhagic gastritis,
- entero-gastric reflux gastritis,
- gastritis with hypertrophic folds.

In the general population that was examined endoscopically, from the total of 59.3% which was represented by gastritis, we have determined the fact that the most common is the erythematous-exudative gastritis which represents more than half with a percentage of 57.8%.

The next in frequency was the entero-gastric reflux gastritis with a percentage of 14%, and it was followed by papular-erosive gastritis, haemorrhagic gastritis, atrophic gastritis, macular-erosive gastritis, with small differences between them, these

representing 8%, 7.27%, 6.15%, and 5.35%, respectively.

Finally, the least encountered was the gastritis with hypertrophic folds, that barely exceeded one percent, as it was encountered in 1.45% of cases. Of the total of 1690 patients who were examined endoscopically, the rapid urease test (Table 4) was performed in 491 of these, representing a percentage of approximately 30% (more exactly 29.16%).

Regarding the distribution by age groups of the patients in whom we received a positive result after performing the rapid urease test, we can specify that there are three ample age group placed on top, and the percentage value of each is nearing 25%. In these three groups which occupy the first three places as a percentage we are mentioning the age group 50-59 years with 24%, the age group 60-69 years with 23.65%, and the age group 40-49 years with 22.5%. The next groups that follow the aforementioned ones as a percentage of certain determination of *Helicobacter pylori* infection are represented by the age group 30-39 years with 10.85%, the age group 70-79 years with 8.15%, and the age group 20-29 years with 7.75%.

It is to be mentioned that the age groups in which the lowest rate of the *H. pylori* infection was determined were for patients aged over 80 years in a percentage of 2.7%, with the mention that over the age of 90 years there was no patient with a positive

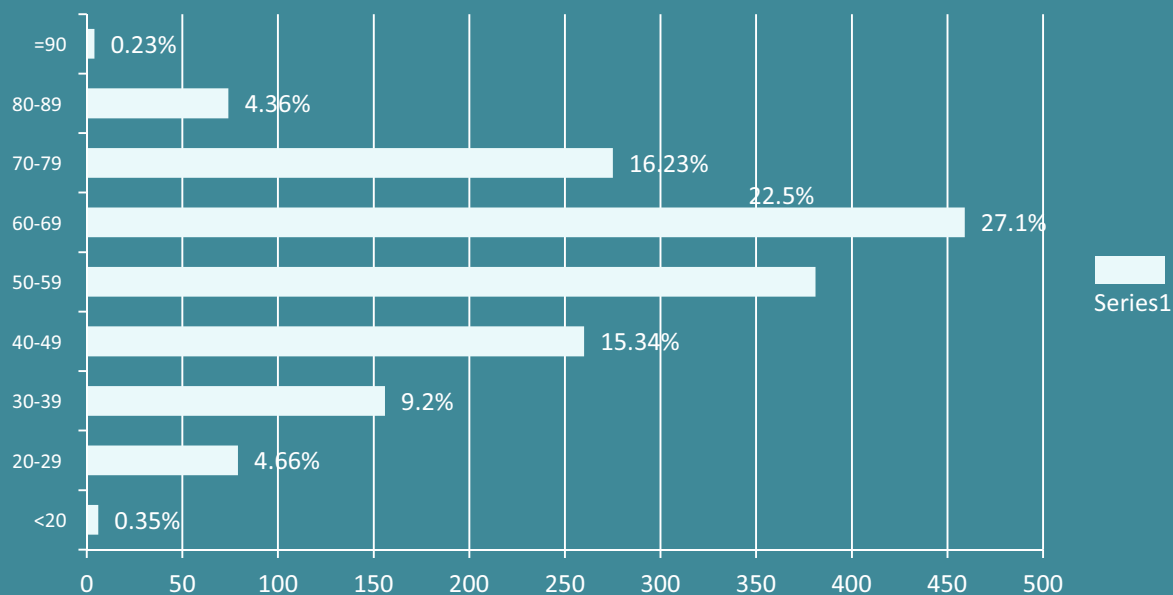


Figure 1. Patient distribution by age groups

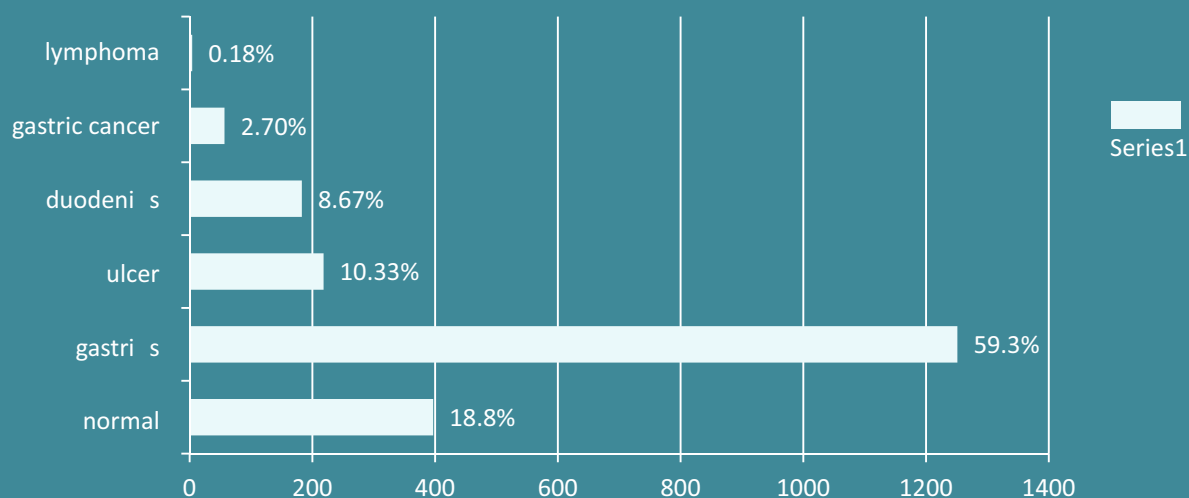


Figure 2. Distribution of endoscopic aspects encountered in the examined patients



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result. But we encountered the same very low value in patients under the age of 20 years who had an infection rate of 0.77%.

In people in which a positive rapid urease test was determined we noticed that the most frequent determination of the *Helicobacter pylori* infection is represented by gastritis, in 73.62% of cases, a much higher percentage than in the general population, where the occurrence of gastritis was determined in 59.3 % of cases. If we make a ratio between the cases of gastritis occurred following the *Helicobacter pylori* infection and those occurred in the general population which was examined endoscopically, we notice that 20.3% of the gastritis cases occurred following the *Helicobacter pylori* infection.

If we will compare this occurrence rate of these two lesion types in people infected with *Helicobacter pylori* with their occurrence rate in the general population which was examined endoscopically, we will see that there is no large percentage difference of the ulcerated lesions, as in the general population it is 10.33%, but a difference can be noticed for duodenitis, as it has a lower value in the general population, of 8.67%. Reporting again the cases in which we encountered these lesions to their occurrence rate in the general population, we can specify the fact that 17.43% of the cases of ulcerative lesions occurred in the general population were determined to be

present in the *Helicobacter pylori* infection, and regarding the duodenitis in the *Helicobacter pylori* infection, this was determined in 21.31% of the examined general population.

It is noteworthy that in patients infected with *Helicobacter pylori* a much lower rate of finding a normal endoscopic aspect was determined compared to the general population, in this case it was 2.6 % compared to 18.8%. Therefore only in 2.26% of the total of normal endoscopic determinations in the examined general population the *Helicobacter pylori* infection was also determined.

Regarding the most severe determinations of the *Helicobacter pylori* infection cited in literature, gastric cancer and lymphoma (Table 5), these had a much lower occurrence rate compared to the other endoscopic determinations of the infection, specifically 0.3% for gastric cancer and 1.16 % for lymphoma. Comparing the distribution of determination in this case with the distribution in the general population we notice that in the general population the ratios are reversed, as gastric cancer has a percentage of 2.7%, and lymphoma of 0.18%. Reporting of these determinations which were noticed in the *Helicobacter pylori* infection in the general population determines the fact that 1.72% of gastric cancer cases were with *Helicobacter pylori*

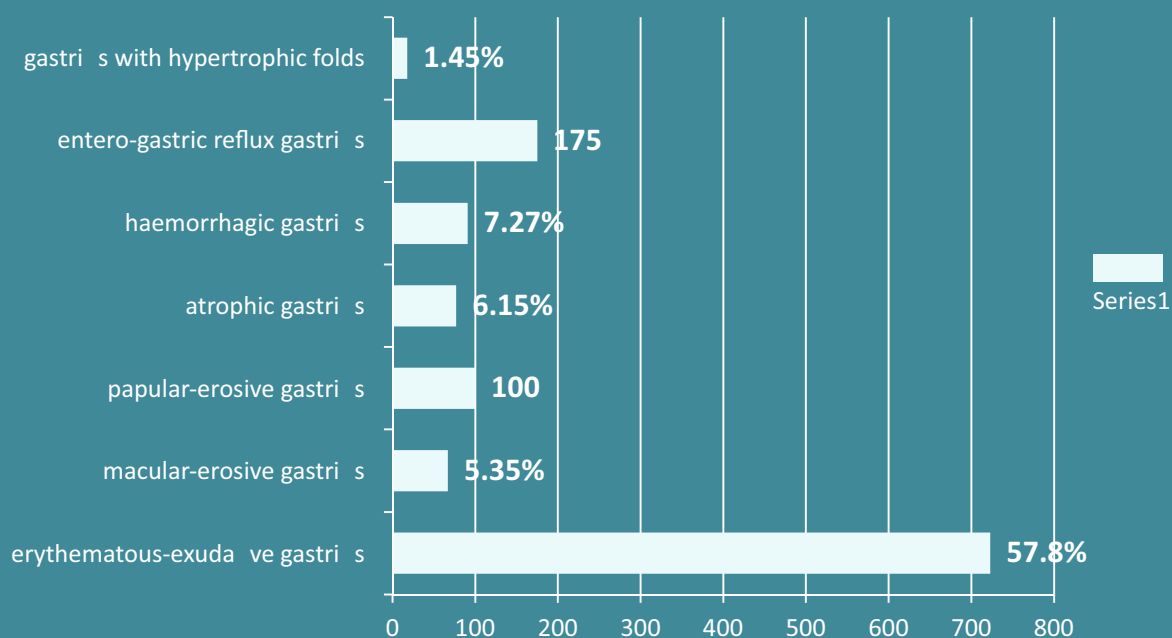


Figure 3. Distribution of the gastritis types according to the Sydney classification among patients examined endoscopically

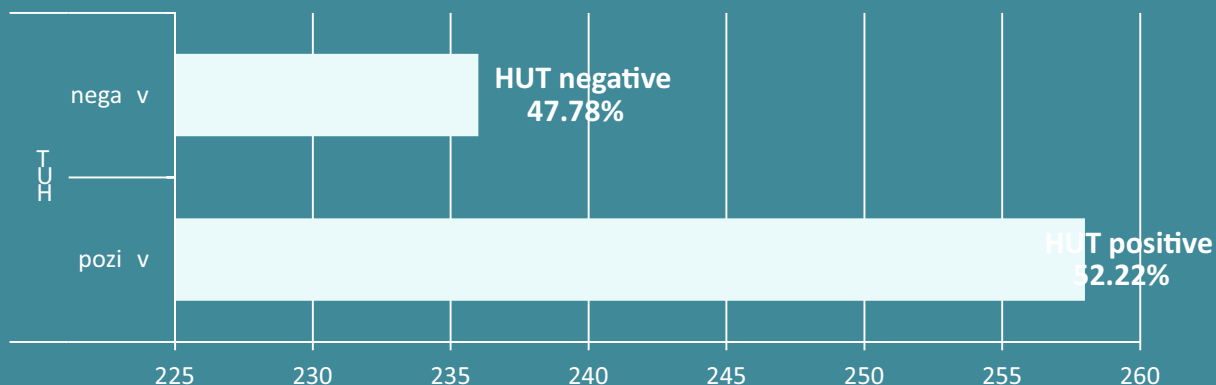


Figure 4. Results obtained after performing the rapid urease test

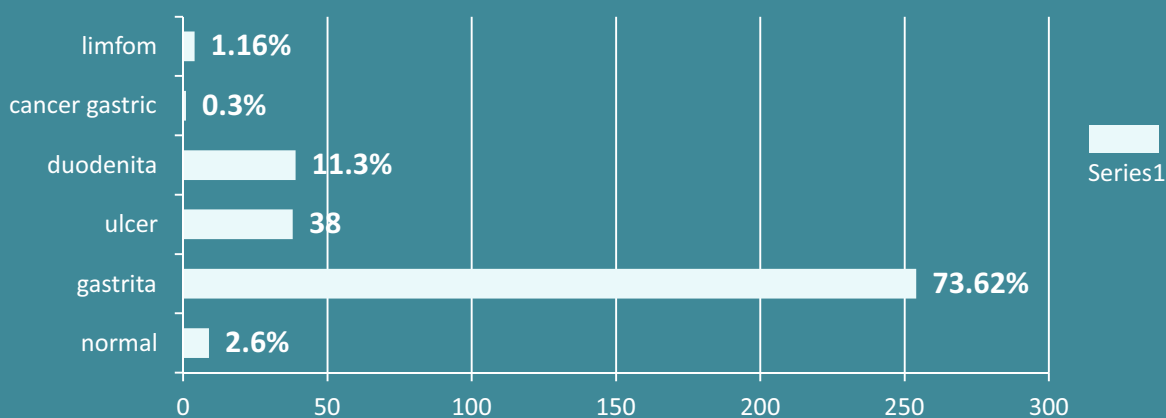


Figure 5. Endoscopic aspects encountered in the patients with positive HUT



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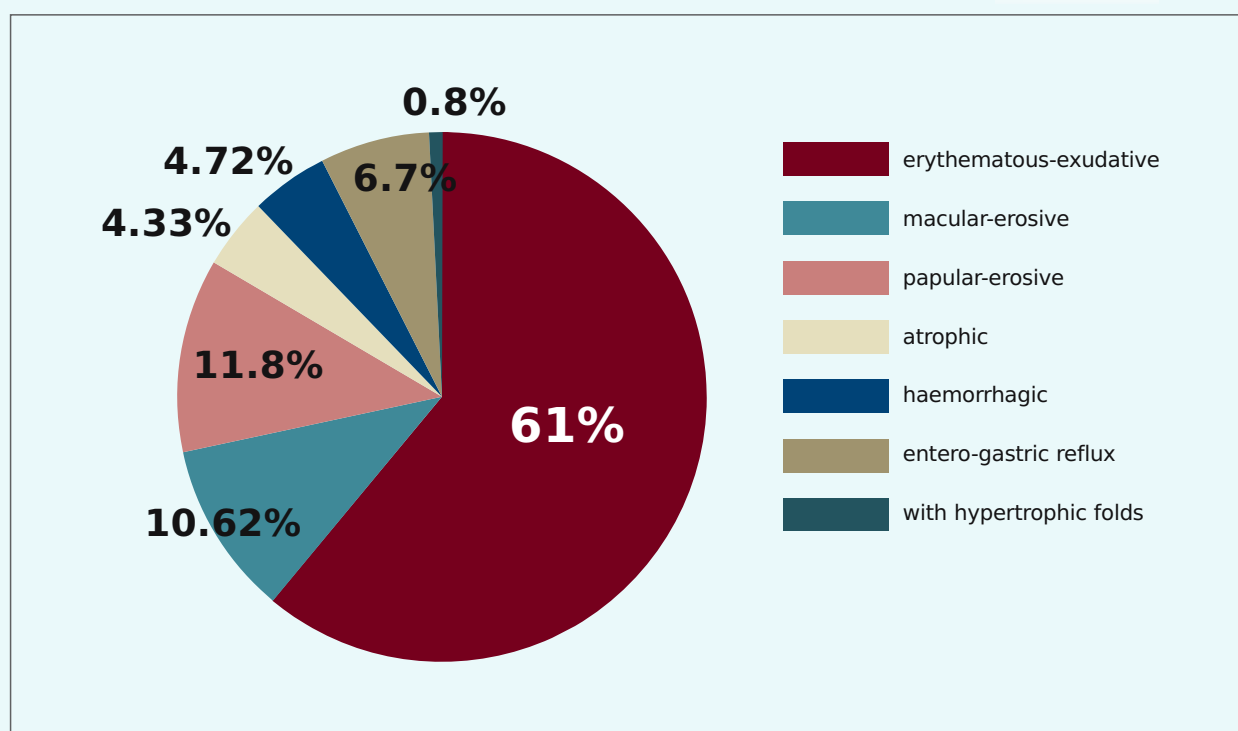


Figure 6. Distribution of the gastritis types according to the Sidney classification in patients with positive HUT

infection present, and regarding lymphoma we can specify that 100% of these cases were encountered in the *Helicobacter pylori* infection.

In this figure we have presented the distribution of the gastritis types according to the Sidney classification encountered in the population with *Helicobacter pylori* infection, and we have determined the fact that of all gastritis cases encountered in these patients, in most cases the erythematous-exudative gastritis was encountered, with a percentage of 61%. We

should specify here that 21.43% of all gastritis cases are encountered in the *Helicobacter pylori* infection.

CONCLUSIONS

1. *Helicobacter pylori* was encountered in 52.22% of the cases tested for this pathology, and in 15.23% in the general population with upper digestive symptomatology.
2. *Helicobacter pylori* infection has no gender-predominance, as it is equivalent in both genders.

3. *Helicobacter pylori* infection was most frequently determined between the ages of 40-69 years, in males it is more frequent between 40-59 years, and in females between 60-69 years.
4. In 97.4% of the cases infected with *Helicobacter pylori* a pathological aspect was determined by endoscopy, and the most frequent was gastritis with all its forms.
5. The most common gastritis type encountered in the *Helicobacter pylori* infection was the erythematous-exudative gastritis.
6. Among the ulcerative lesions encountered in the *Helicobacter pylori* infection, we have determined most frequently an ulcer in the duodenum.
7. In approximately 20% of all cases of gastritis, ulcer, and duodenitis, the *Helicobacter pylori* infection was present.
8. All cases of lymphoma were encountered in people with *Helicobacter pylori* infection.

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