Evaluation of *Helicobacter pylori* infection in patients with eso-gastro-duodenal pathology

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Abstract

*Helicobacter pylori* (HP) infection is one of the most frequent bacterial infections in humans. The studies performed in the last 30 years showed that this bacterium is the main cause of chronic gastritis and the main etiological agent of peptic ulcer and gastric cancer. We investigated the prevalence of HP infection in a group of 1525 patients who addressed a gastroenterology medical center between 2010–2014, in Craiova, Romania, for dyspeptic symptoms. The patients underwent a clinical, endoscopic and serologic investigation for highlighting a possible HP infection. The age of the patients with gastric duodenal pathology varied between 16 and 87 years old. Of the 1525 patients, a number of 971 (63.67%) were diagnosed with HP infection, while the rest of 554 (36.33%) were not infected. The study on the distribution of gastric duodenal pathology and HP infection showed that the lesions of the upper digestive tract and HP infection emerged quite early, a number of 29 patients being aged less than 20 years old; among these, 21 (72.41%) patients were HP positive and only eight (27.59%) were HP negative. In the age group of 20–29 years old there were recorded 184 patients, of which 120 (65.22%) were HP positive and only 64 (34.78%) were HP negative. There may be observed that in the age group of 20–29 years old, both the patients with gastric duodenal pathology and the ones with HP infection increased six times in comparison to the first decade. Most cases were recorded in the patients aged between 50 and 69 years old. The two decades comprised a total number of 607 (39.8%) patients, of which 375 (61.78%) were HP positive and 232 (38.22%) were HP negative. By evaluating the distribution of HP infection according to the social environment, there was observed that there were no significant differences between the patients coming from the urban area and the ones from the rural area, as far as the HP infection was concerned.

Keywords: *Helicobacter pylori*, esophagitis, gastritis, erosive gastroduodenitis, duodenal ulcers.

Introduction

The discovery of *Helicobacter pylori* (HP) bacterium in 1984 in the gastric mucosa epithelium and the studies that followed changed many data regarding the physiopathology of gastric duodenal pathology. There was observed that this microaerophilic, Gram-negative bacterium is the main cause for chronic gastritis and the main etiological agent of peptic and gastric cancer [1–3]. The pathological lesions induced by HP infection are mediated by the complex interactions between the causing factors of the bacterial virulence, the host constituting factors and the environment factors. Approximately 89% of all gastric cancer cases may be attributed to HP infection [4].

The studies performed in the last 30 years showed that the HP infection represents a major public healthcare problem worldwide; there was estimated that in 2015, all over the world, about 4.4 billion persons infected with HP (almost half of the globe population) [4, 5].

The presence of HP in the gastric mucosa triggers a chronic inflammatory response that, correlated with the cellular lesions and other etiopathogenic factors (alcohol intake, strong tart substances or medicines), starts a cascade of histopathological changes that may progress from acute gastritis, chronic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia up to gastric cancer [6]. The permanent production of free oxygen radicals, as a result of chronic inflammation, may lead to the DNA cell deterioration from the gastric epithelium, causing multiple mutations, considered to be enough for triggering carcinogenesis lesions [6, 7].

In the present study, we proposed to evaluate the incidence and prevalence of HP infection in a group of patients with gastric duodenal pathology and to correlate these data with the age and gender of the patients, their social environment and main lesions of the upper digestive tract.

Patients, Materials and Methods

The study included 1525 patients who addressed the “Renaștere” Medical Center of Craiova, Romania, between
2010–2014, for various symptoms of the upper digestive tract (most often of the dyspeptic type), both from their own initiative or because they were sent by their general practitioners (GPs). The main subjective complaints were epigastralgia, postprandial bloating, burps and psoriasis. In this medical center, the patients underwent a clinical and endoscopic examination. The determination of \textit{H. pylori} infection was performed directly by the urease test and indirectly by testing the anti-\textit{H. pylori} antibodies from the patients’ serum.

The gastric biopsies harvested endoscopically were fixed in 10% neutral formalin and included in paraffin for performing the histopathological and immunohistochemical studies. For the histopathological study, there was used the Hematoxylin–Eosin (HE) staining, while for the immunohistochemical study, the anti-\textit{H. pylori} antibody (code ab7788, 1/100 dilution, Abcam) was used in order to highlight the presence of the bacterium in the gastric mucosa.

For highlighting the correlations between the \textit{H. pylori} presence and various pathologies, there were performed the $\chi^2$ (chi)-square statistics in SPSS (Statistical Package for Social Sciences) software. All the differences were considered significant for $p<0.05$.

\section*{Results}

Our study investigated the distribution of HP infection on age groups, social environment, gender and correlation of infection with the main gastric duodenal pathology in a group of patients with various symptoms of the upper digestive tract, who required specialized consult in a Clinic of Gastroenterology. Of the total number of 1525 patients included in the study, 1089 (71.41%) came from urban area, while 436 (28.59%) from the rural area. The presence of a higher number from the urban area may be due to the patients’ easier access to medical services, the social, professional and financial status, as well as to a better medical education, in comparison to the rural area.

The endoscopic evaluation of the patients showed that most of them presented associated lesions, present in two of the three organs or even in all examined organs, of the esogastric, gastric duodenal or esogastric duodenal type. Less than 10% of the examined patients presented lesions exclusively in the esophagus or in the stomach or duodenum.

Of the 1525 patients, a number of 971 (63.67%) were diagnosed with HP infection, and the rest of 554 (36.33%) were not infected.

The age of patients with esogastric duodenal pathology varied from 16 to 87 years old. The distribution of esogastric duodenal pathology, according to age and presence or absence of HP infection, showed that the esogastric duodenal lesions and the HP infection emerged quite early, 29 (1.9%) patients aged less than 20 years old; among these, 21 (72.41%) patients were HP positive and only eight (27.59%) were HP negative. In the age group of 20–29 years old, there were recorded 184 patients, of which 120 (65.22%) were HP positive and only 64 (34.78%) were HP negative. There may be observed that in the age group of 20–29 years old, both the number of patients with esogastric duodenal conditions and the ones infected with HP increased six times in comparison to the first age decade (Figure 1).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Distribution of HP infection according to age. There may be observed a relatively high increase of HP infection in the age group of 20–29 years old. HP: Helicobacter pylori.}
\end{figure}

Also, in Figure 1, there may be observed an increase with age in the patients with esogastric duodenal pathology and in the HP infected patients. After 30 years old, the esogastric duodenal pathology and the number of HP-infected patients increased progressively, the most affected by this pathology being the ones included in the age group of 50–59 years old, where there was recorded a number of 322 patients, representing 31.11% of the studied group, of which 201 (62.42%) patients were HP positive and 121 (37.58%) were HP negative. The study of the distribution of esogastric duodenal pathology and HP infection showed that most cases were recorded in the patients aged between 50 and 69 years old. The two age decades totalized a number of 607 (39.8%) patients, of which 375 (61.78%) were HP positive and 232 (38.22%) were HP negative. In the age group of 70–79 years old,
there was observed a decrease of the number of patients requiring a medical gastroenterology consult, but the percentage of HP-infected patients presented quite high values. Thus, of the 175 examined patients, 113 (64.57%) were HP positive, the rest of 62 (35.43%) being HP negative. These data show that the percentage of the HP infected patients in all age groups was higher than 61%, varying from 61.78% up to 72.41%. The highest percentage values of the HP-infected patients were recorded in young people, aged less than 30 years old.

By evaluating the distribution of HP infection in the patients with esogastric pathology according to social environment, there was observed that there were no significant differences between the percentages of HP-infected patients from the urban area and the ones from the rural area. Therefore, in the urban area, there were recorded 62.63% of the HP-positive patients, while in the rural area there were recorded 63.65% of the HP-positive patients. This insignificant difference shows that, overall, the HP infection is quite relatively spread, both in the rural and in the urban area.

The endoscopic examination highlighted the presence of esophagitis lesions in 1241 patients, representing 81.38% of the total of the patients included in the study, of which 852 (68.65%) were HP positive, while 389 (31.35%) were HP negative (Figure 2). Of these, a number of 905 patients were diagnosed with esophagitis A [of which 578 (63.87%) were HP positive, while 327 (36.13%) were HP negative], 315 patients had esophagitis B [of which 213 (67.62%) were HP positive, while 102 (32.38%) were HP negative] and 21 patients with esophagitis C [of which 15 (67.43%) were HP positive and six (28.57%) were HP negative].

Gastritis lesions were diagnosed in 1122 patients, representing 73.5% of the total number of patients, of which 791 (70.5%) were HP positive and 331 (29.5%) were HP negative (Figure 3). The gastric lesions presented extremely varied forms (erythematous, erythematous erosive, papulo-erosive, atrophic gastritis). Of the gastritis, the most frequent types were the erythematous exudative ones, present in 280 patients.

Gastroduodenitis was diagnosed in 238 patients, representing 15.61% of all patients. Of these, 178 (73.11%) patients were HP positive, while 64 (26.89%) were HP negative (Figure 4).

Duodenitis was diagnosed in 307 patients, representing 20.13% of the total number of patients, of which 218 (71%) were HP positive, while 89 (29%) were HP negative (Figure 5).

Ulcerous disease was diagnosed in 141 (9.24%) patients, of which duodenal ulcer was found in 136 (8.92%) patients, while gastric ulcer only in five patients. Of the patients with duodenal ulcer, 113 (83%) were HP positive and 23 (17%) were HP negative (Figure 5).

The dysfunctions of the pyloric sphincter, manifested most often by prolonged pyloric spam, were present in 1271 (83.34%) patients; of these, 827 (65.07%) were HP positive and 444 (34.93%) were HP negative.
The endoscopic examination allowed the diagnosis of 19 gastric malignant lesions (16 adenocarcinomas and three gastric lymphomas), of which 15 (78.95%) were HP positive.

The histopathological examination and gastric biopsies highlighted a multitude of lesional aspects of the gastric mucosa: atrophic gastritis, intestinal metaplasia, hemorrhagic gastritis or gastric adenocarcinoma (Figures 7–9) and the immunohistochemical reactions for HP were positive in most harvested biopsies, both for inflammatory lesions and for tumoral lesions (Figures 10 and 11).

Figure 5 – Overall duodenitis frequency was inferior to non-gastroduodenitis patients, but its frequency was increased especially in patients that associated HP positivity, \( \chi^2 (2, N=1525) = 49.82, p<0.0001 \).

Figure 6 – Overall duodenal ulcers frequency was inferior to non-gastroduodenitis patients, but its frequency was increased especially in patients that associated HP positivity, \( \chi^2 (2, N=1525) = 66.41, p<0.0001 \).

Figure 7 – Image of chronic antral atrophic gastritis (HE staining, ×100).

Figure 8 – Chronic gastritis with superficial erosions and complete intestinal metaplasia (HE staining, ×100).

Figure 9 – Microscopic image of moderately differentiated gastric carcinoma (HE staining, ×100).

Figure 10 – Chronic antral gastritis with positive reaction to anti-HP antibody (Anti-HP antibody immunostaining, ×200).
that a part of the HP infected patients do not present clear clinical symptoms that should require medical consult, the chronic infection with this microorganism may cause chronic gastritis, gastric and duodenal ulcers, gastric adenocarcinomas and lymphomas of the gastric mucosa [3, 10]. Recent epidemiological studies showed that, in adult patients, HP is associated with 40–75% of the ulcerous diseases [11, 12] and with 63–80% of gastric cancers [13]. Based on some studies performed in the USA and Europe, there was estimated that peptic ulcer appears in approximately 10% of the infected patients, with an annual incidence between 0.12–1.5%, while gastric cancer develops in 1–3% of the patients infected with HP [7, 14, 15]. In 1994, the experts of the National Agency for Cancer Research declared that HP bacteria is a type I carcinogen, responsible for about 5.5% of cancer cases, worldwide [16, 17].

Although, at present, the diagnosis of HP infection is quite easy to establish, and the medical costs are low, in many countries of the world, including Romania, there are no national programs that allow the evaluation of HP infection epidemiology, nor any programs for preventing this disease. Our study showed that over 63% of the patients with eso-gastro-duodenal pathology were infected with HP, while the ratio of the patients infected is relatively similar both in urban and rural areas. Taking into consideration that a part of the HP infected patients do not present clear clinical symptoms that should require medical consult, we think that the prevalence of HP infection within the Romanian population is much higher.

The epidemiological studies showed that the HP infection can be found in all world countries, but its prevalence varies considerably, being quite high in developing countries, in compared to developed ones [18]. Thus, the HP infection prevalence in industrialized countries varies from 20% up to 50%, while in developing countries from 50% up to over 80% [19–21]. The highest prevalence (75–83%) is recorded in Latin American countries and the lowest (17–40%) in Western Europe, Japan and the USA [22, 23].

In our study, we observed that the HP infection, associated with dyspeptic disorders, had its onset during childhood, 29 of the patients being aged less than 20 years old. The infection prevalence increased with age, the most spectacular increase being in the patients aged between 20 and 29 years old. Also, our study showed that most patients with dyspeptic disorders, infected with HP, were identified in the age group 50–59 years old.

The data we obtained are similar to other studies that show the HP infection onset is from childhood in most patients, the bacteria transmission ways being oral–oral or fecal–oral [24–27]. Also, contaminated water and food were mentioned as possible ways of HP bacteria transmission [28, 29]. As well as other authors, we consider that the number of HP infected people is quite high, but only few of them will develop severe clinical diseases, such as gastritis, peptic ulcer or gastric carcinoma [17].

The infection of gastric mucosa by HP is possible because the bacteria has the ability to secrete urease, an enzyme that decomposes urea into ammonia, and thus it succeeds in reducing the high acid pH of gastric juice and in creating favorable conditions for colonization of gastric mucosa [12, 30–32]. In the gastric mucosa, HP adheres to the epithelium surface and produces more soluble factors that ensure its survival, adherence factors (adhesines, lipoproteins), inflammatory proteins or cytotoxic proteins, that alterate the activity and survival of the gastric epithelium cells and cause a local inflammatory reaction [33–36]. The inflammatory reaction appeared in the gastric mucosa, according to its intensity, may have, or not, clinical signs, most often of the dyspeptic type. Most studies showed that only part of the HP-infected ones will develop a clear pathology, but even in the absence of an obvious disease, the HP-positive patients will develop chronic gastritis [37, 38].

We consider that the inflammatory reaction of gastric mucosa induced by HP has negative consequences not only on the stomach function, but also on the esophagus and duodenum. In our study, gastritis was frequently associated with esophagitis or duodenitis, with gastro-esophageal reflux or with changes of the pyloric sphincter function. More than half of the patients with eso-gastro-duodenal inflammatory conditions were infected with HP. Thus, of the 1525 investigated patients, 1241 (81.38%) patients presented esophagitis lesions, of which 852 (68.65%) were HP positive, 1122 (73.5%) presented various forms of gastritis, of which 791 (70.5%) were HP positive; 238 patients presented gastroduodenitis, of which 178 (73.11%) were HP positive.

At present, worldwide, there is considered that the most frequent cause of chronic infection is HP infection [39]. This bacterium causes progressive lesions of the gastric mucosa and it is now accepted that it plays a causal part in various important diseases, such as gastric ulcer, duodenal ulcer, gastric adenocarcinoma and gastric lymphoma [40, 41]. Therefore, it is considered that HP induced gastritis is the most important risk factor for peptic ulcer and its complications, as well as for gastric ulcer.
Conclusions

The clinical and paraclinical examination of the 1525 patients with dyspeptic disorders showed that 63.67% were HP infected. The lesions of the upper digestive tract and the HP infection started quite early, 29 patients being aged less than 20 years old, which shows that the bacteria transmission from one person to another takes place during childhood or adolescence. The prevalence of HP infection increased with age, most HP-positive patients being recorded in the age group of 50–59 years old. The endoscopic evaluation of the patients showed that most of the patients presented associated esogastric, gastro-duodenal or esogastic duodenal lesions. There were not recorded any significant percentage differences of the HP infection between the patients from the urban area and the ones from the rural area. In the studied group, the esogastr-duodenal lesions were dominated by the inflammatory processes (esophagitis, gastritis, duodenitis) that represented 98.75%, while the proliferative processes represented only 1.25%.

Conflict of interests

The authors declare that they have no conflict of interests.

References


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