

HELICOBACTER PYLORI INFECTION IN HIV-POSITIVE PATIENTS

PhD Thesis Abstract

PhD student: **Nina-Ioana Şincu**

Scientific coordinator: **prof. dr. Simona Băţagă**

Helicobacter (H.) pylori is responsible for infecting more than half of the Globe's population and is associated to several gastro-intestinal diseases: acute or chronic gastritis, peptic ulcer or digestive malignancies. Human immunodeficiency virus (HIV) currently infects over 35 million persons and causes 1.6 million deaths associated to the acquired immunodeficiency syndrome (AIDS) each year. The study of *H. pylori* – HIV coinfection represents an important research issue, as these germs are responsible for two of the most significant present-day pandemics. Literature data, however, offer limited and sometimes discordant information regarding its prevalence and associated factors. Considering geographic variations in the frequency of *H. pylori* infection, connected to local social and economic factors, the study of *H. pylori* – HIV coinfection in our geographic area presents utility.

This paper builds on the premises of a complex gastro-intestinal pathology in HIV-infected patients, including *H. pylori* infection, a condition which associates peculiar factors in this category of subjects. The study of the various clinical and laboratory features of *H. pylori* – HIV coinfection represents the main purpose of this paper. Secondary objectives are represented by: establishing the frequency of *H. pylori* infection in HIV-positive subjects compared to the general population, investigating various factors associated to the presence of *H. pylori* in HIV-positive persons, analyzing the main death causes in HIV-infected patients with dyspeptic complaints, in correlation with the presence of *H. pylori* and endoscopic and pathologic monitoring of digestive tract pathology in HIV-positive patients, correlated to their immune status and antiretroviral therapy (ARVT).

In order to achieve the objectives, I have divided the paper into four interconnected studies. Data were collected from the patients' medical papers, as well as laboratory and pathology registers. The diagnosis of *H. pylori* infection was established in the Laboratory of Infectious Diseases from the Clinical County Hospital Mureş by non-invasive methods: testing for anti-*H. pylori* IgG antibodies and *H. pylori* stool antigen. Statistical analysis was performed by using GraphPad Prism 6 program.

Study 1. The frequency of *H. pylori* infection in HIV-positive versus HIV-negative dyspeptic patients. I performed an analytic, observational, case-control, retrospective study, over a 5-year period (January 1st 2009 – December 31st 2013), by comparing the frequency of *H. pylori* infection among two groups of patients with dyspeptic complaints: group A, composed of 91 HIV-positive patients monitored in the anti-HIV/AIDS Regional Center Mureş, and group B, formed by 1338 HIV-negative persons, admitted to various departments of the County Clinical Hospital Mureş.

The frequency of *H. pylori* infection was 40.66% among HIV-positive subjects and 52.16% among HIV-negative persons with dyspeptic symptoms, emphasizing a negative, statistically significant association between HIV and *H. pylori* ($p = 0.0336$, $OR = 0.6283$). The result resembles other researchers' observations. Literature data offers several hypothesis to explain this result: high frequency of digestive opportunistic infections, which inhibit the proliferation of *H. pylori* by competitive mechanism, and accidental eradication of *H. pylori* infection under antibiotic therapy prescribed for extra-digestive conditions. Besides, HIV-positive patients have several other risk factors for digestive tract illnesses, apart from *H. pylori* infection: smoking (49.45%), alcohol abuse (25.27%) and anti-inflammatory treatment (56.04%).

Study 2. Factors which influence the presence of *H. pylori* in HIV-positive patients. I performed an analytical, observational, case-control, retrospective study, over a 5 year-period (January 1st 2009 – December 31st 2014), on two groups of HIV-infected patients monitored in the anti-HIV / AIDS Regional Center Mureş: group A, composed of 37 *H. pylori*-positive patients and group B, 54 *H. pylori*-negative subjects, by comparing the presence of various factors possibly associated to *H. pylori* infection in the two groups.

H. pylori-positive HIV-infected patients had higher level of CD4+ T-lymphocytes than H. pylori-negative subjects, although the difference was not statistically significant. HIV-RNA plasma viral load (VL) was lower among H. pylori-positive patients than in H. pylori-negative persons, though not statistically significant difference was reported. Both observations concur to the tendency depicted by literature data, as better immune status associates lower frequency of digestive opportunistic infections and less frequent antibiotic treatments. I emphasized a statistically significant positive association between antiretroviral therapy (ARVT) and the presence of H. pylori, probably due to the improvement of immune status under ARVT.

Study 3. Mortality among HIV-infected patients with dyspeptic complaints. I performed an analytic, observational, case-control, retrospective study, over a 5-year period (January 1st 2009 – December 31st 2013), by comparing two groups of HIV-positive dyspeptic patients, investigating various factors involved in their evolution: group A, formed by 21 deceased patients and group B, composed of 70 survivors.

Mortality rate among HIV-infected patients with dyspepsia was 23.07% (230.7 deaths / 1000 persons), higher than the overall mortality rate reported in the general population for the same age category by World Health Organization (WHO). The main causes of death were extra-digestive opportunistic infections, especially tuberculosis due to multi-drug-resistant (MDR) strains, central nervous system neoplastic conditions and liver cirrhosis secondary to hepatitis B virus infection, similar to those generally reported among HIV-positive patients, irrespective of the presence of digestive symptoms. I emphasized statistically significant positive associations between death and the advanced clinic-immunologic stage of HIV infection (C3), CD4+ T-cells level below 200 cells/ μ L, lack of ARVT, wasting syndrome and B or C hepatitis virus coinfection. No statistically significant association was registered between H. pylori infection and death, while the main causes of death were similar among H. pylori-positive and H. pylori-negative subjects.

Study 4. Endoscopic and pathologic survey of digestive tract pathology in HIV-infected patients. I performed a retrospective, descriptive study, over an 8-year period (January 1st 2006 – December 31st 2013), on 39 HIV-infected patients with various digestive symptoms, monitored in the anti-HIV/AIDS Regional Center Mureş, who underwent upper / lower digestive endoscopy and pathologic examination of biopsy samples.

The main complaints of HIV-infected patients were nausea, vomiting, abdominal pain, dysphagia and retrosternal pain upon swallowing, diarrheic stools, loss of appetite and rectal bleeding. Endoscopic exam established the diagnosis in various digestive diseases, ranging from opportunistic infections, such as esophageal candidiasis, to non-HIV-associated conditions, similar to those encountered in the general population: reflux esophagitis, peptic ulcer, hemorrhoidal disease. Esophageal candidiasis was positively associated to CD4+ T-cells level below 200 cells/ μ L, while ARVT was negatively associated to the presence of gastro-intestinal AIDS-defining illnesses, similar to literature data. 3 out of the 11 patients who died, mostly due to extra-digestive opportunistic infections, had been previously diagnosed with a gastro-intestinal AIDS-defining condition.

Conclusions. HIV-infected patients suffer from a large range of gastro-intestinal conditions, including opportunistic infections as well as diseases similar to those encountered in the general population, depending on their immune status and the presence of ARVT.

Although the main causes of death in HIV-infected patients with gastro-intestinal symptoms are extra-digestive opportunistic infections, mostly MDR tuberculosis, diagnosing a digestive AIDS-defining condition may predict the patient's unfavorable outcome.

Low CD4+T-cells count, below 200 cells/ μ L and advanced clinic-immunologic status of HIV infection are associated with unfavorable evolution, towards death, in HIV-infected patients, while ARVT has a negative impact upon mortality. Hepatitis B or C virus coinfections and wasting syndrome are associated with poor outcome.

H. pylori infection did not significantly influence survival in HIV-positive patients, as the main causes of death (opportunistic infections) were similar among H. pylori-positive and -negative subjects.

The frequency of H. pylori infection in HIV-positive patients was lower than that registered among HIV-negative subjects. HIV- H. pylori coinfecting patients tend to have lower levels of CD4+ T-cells and HIV-RNA plasma VL, corresponding to the use of ARVT and its positive association with H. pylori infection.

Considering the increased frequency of numerous risk factors for digestive illnesses (apart from H. pylori infection) in HIV-positive patients, alternative etiologies for gastro-intestinal diseases should be investigated, besides the presence of H. pylori, in this category of patients.

Key-words: Helicobacter pylori, human immunodeficiency virus, CD4+ T-lymphocytes, HIV-RNA plasma viral load, antiretroviral therapy.