

Review Article

Helicobacter pylori in the Era of Highly Active Antiretroviral Therapy (HAART): A Review

Ethel Zimberg Chehter^{1*}, Wilson Roberto Catapani¹, Fernando Beani Margeotto², Demetrius Germini³, Alexandre Cruz Henriques² and Jaques Waisberg^{2,3}

¹Department of Medicine, Division of Gastroenterology, ABC Medical School, Brazil

²Department of Surgery, Division of Digestive Surgery, ABC Medical School, Brazil

³Department of Surgery, Division of Digestive Surgery, Hospital for State Civil Servants, Brazil

***Corresponding author**

Ethel Zimberg Chehter, Department of Medicine, Division of Gastroenterology, ABC Medical School, Avenida Principe de Gales, 821 – Bairro Principe de Gales, Santo André - São Paulo, SP 09060-650, Brazil, Tel: +55-11-99962-9456; Fax: +55-11-49935416; Email: chehter.ops@terra.com.br

Submitted: 18 February 2014

Accepted: 26 February 2014

Published: 06 June 2014

Copyright

© 2014 Chehter et al.

OPEN ACCESS**Keywords**

- *Helicobacter pylori*
- HIV
- Acquired immunodeficiency syndrome
- Antiretroviral therapy highly active
- Dyspepsia
- Peptic Ulcer
- Gastritis

Abstract

Human Immunodeficiency Virus (HIV) infection predisposes to a multitude of opportunistic infections, many of them resulting in gastrointestinal symptoms. There were doubts about the pattern of the incidence of *H.pylori* in HIV infected patients: one group argues that the immunodeficiency allows the increased replication of the bacteria and in the other hand others argues that there is no inflammation in the stomach for the *H.pylori* replication. So we aimed to find out the answer for this question, with a review of the literature. We find that the incidence of *H.pylori* infection is lower among patients with Acquired Immunodeficiency Syndrome (AIDS) compared to matched HIV-infected and -uninfected controls. This event suggests a correlation between the improvement of immunity as a result of more efficient antiviral therapy and the decrease in the frequency of digestive diseases in AIDS, mainly opportunistic pathologies. *H.pylori* infection and dyspepsia in HIV-infected patients have increased in the High Active Antiretroviral Therapy (HAART) era. *H.pylori* infection in HIV-infected patients in the post-HAART era has a low prevalence of the bacteria in patients with count of CD4 cells $< 200/\text{mm}^3$ than in patients with CD4 cells count $\geq 200/\text{mm}^3$. The knowledge of this fact allow us to make different guidelines in dyspepsia in HIV infected patients based on CD4 levels: above $200/\text{mm}^3$ we can think in opportunistic agents and in patients with CD4 cells count $\geq 200/\text{mm}^3$ we can think in differential diagnosis in dyspepsia like uninfected patients. On the other hand, the managements and the protocols in the presence of dyspepsia in HIV-infected patients or patients in which AIDS are installed resemble the guidelines established for the general population.

CORE TIP

Human Immunodeficiency Virus (HIV) seropositive patients frequently experience upper gastrointestinal tract symptoms that cause considerable morbidity and are due to multiple etiologies. HIV infection predisposes to a multitude of opportunistic infections, many of them resulting in gastrointestinal symptoms. The role of *H.pylori* infection in gastroduodenal lesions might be different between the general population and Acquired Immunodeficiency Syndrome (AIDS) patients, and it remains unclear up to now if upper gastrointestinal symptoms, mainly dyspepsia, are common adverse effects in patients under Highly Active Antiretroviral Therapy (HAART).

INTRODUCTION

The involvement of the gastrointestinal tract has been associated with infection with Human Immunodeficiency Virus

(HIV) since the first cases reported in the United States in the early 1980s [1,2]. This involvement may occur because the Gut-Associated Lymphoid Tissue (GALT) represents the largest reservoir of HIV in the body and/or as a result of the side effects of medications used for the prevention or control of HIV infection as forming part of the High Active Antiretroviral Therapy (HAART) [3,4].

HIV seropositive patients frequently experience upper-gastrointestinal- tract symptoms that cause considerable morbidity and are due to multiple etiologies. HIV infection predisposes to a multitude of opportunistic infections, many of them resulting in gastrointestinal symptoms [5].

Helicobacter pylori (*H.pylori*) is a causative organism for chronic gastritis and is associated with peptic-ulcer disease. Infection may be asymptomatic as well [6-8]. The prevalence of

H.pylori varies among continents and countries around the world, and its prevalence varies from 9% to 82% [6,9]. The relationship between the bacteria and clinical manifestations is well known. It is clear that, among the several types of *Helicobacter pylori* only the carriers of the Cag A gene, that signalizes a pathogenicity island, with a myriads of pathogenic genes such as Bab A, OIp A and many others and also the carriers of the VaC A gene can induce the disease. So, only CagA and also VaC A gene carriers will develop disease such as ulcers. All the others genes combinations will not develop any disease and are asymptomatic [10-12].

The role of *H.pylori* infection in gastroduodenal lesions might be different between the general population and acquired immunodeficiency syndrome (AIDS) patients [10,11] and it remains unclear up to now [12].

In contrast to the established role of *H.pylori* in gastritis and duodenal ulcers in general, conflicting results have been reported in patients with Human Immunodeficiency Virus (HIV) infection and the acquired immunodeficiency syndrome [13,14]. It is well known that the acute and chronic gastritis are asymptomatic, in general population, but could the HIV patients be more susceptible for diseases. Could they be infected for more than one cepa of *Helicobacter pylori*? As they are immunocompromised, could these patients have more amounts of *Helicobacter pylori*? Could they have greater chance of developing a duodenal or gastric ulcer, MALT lymphoma or atrophic gastritis?

Gastrointestinal (GI) discomfort is a common complaint among patients infected with HIV. GI symptoms can be caused by a myriad of factors, including, but not limited to, co-infections, antiretroviral therapy, medications for opportunistic infections, and nutritional status [1,3,4]. Some researchers have hypothesized that *H.pylori* infection may be more common among HIV-infected patients as a result of immune suppression [15-18]. An increased incidence of *H.pylori* infection would contribute to the prevalence of GI complaints in this population [1]. Several epidemiologic studies have examined the relationship between *H.pylori* infection and HIV [12,13,19,20].

Since the advent of Highly Active Antiretroviral Therapy (HAART) for the treatment of HIV/AIDS in 1996, the incidence of most opportunistic disorders in the developed world has dramatically declined but definitely not disappeared [2,4]. The number of new yearly HIV infections (about 55,000) and the total number of infections (more than 1.1 million) in the USA remains very significant [9,21]. Post-HAART GI symptoms and biopsy results are still common, especially in large inner-city hospitals [21]. Also, upper-gastrointestinal symptoms, mainly dyspepsia, are common adverse effects in patients under HAART [4,21].

There is great controversy about the prevalence of patients co-infected with HIV and *H.pylori*, especially after the advent of the use of HAART to control HIV infection [22,23]. Studies have shown an increased prevalence of this bacteria in people infected with HIV relied on the CD4 count: more than 200 cells/mm³ and is decreased in HIV/AIDS patients with less than 200 cells/mm³.

The aim of this review is find out the answer for the question: the incidence of *H.pylori* is increased (because the immune suppression) or decreased (because of the inappropriate environment with low inflammation)? We search the literature

(Pubmed) using the words: *H.pylori*, HIV, AIDS, gastroduodenal diseases. The inclusion criteria were the presence of HIV infection and *H.pylori* searched in any method, one or more diagnostic tests. Then we make the description of these studies in chronologic appearance (Table 1).

PRE - HAART STUDIES (UNTIL 1996)

The first paper found was a controlled study was conducted by Battan et al. [10] on HIV-infected patients referred for upper endoscopy procedure evaluation regarding the prevalence of *H.pylori* infection. Four different stains and cultures for *H.pylori* were performed on biopsy specimens from the gastric antrum. Sixteen (40%) of 40 patients with AIDS or AIDS-Related Complex (ARC) were diagnosed to be infected with *H.pylori*, versus 14 (39%) of 36 age-matched control patients. Eight of 15 AIDS/ARC patients without AIDS-related esophagogastroduodenal findings (53%) were infected with *H.pylori* versus 8 of 25 (32%) with endoscopic findings typical of AIDS. No invasion of the *lamina propria* by *H.pylori* was noted in any patient. Active chronic gastritis was present in 60% of AIDS/ARC patients and 61% of controls. Fifty-eight and 59%, respectively, of active-chronic-gastritis cases were infected with *H.pylori*. All the *H.pylori* infections, except one, were found in patients with chronic gastritis. These authors concluded that in AIDS/ARC patients, *H.pylori* infection and active chronic gastritis are as common as in other patients referred for upper endoscopy. Cell-mediated immune deficiency does not appear to increase the risk of infection with *H.pylori*.

Then in the early 90s, Edwards et al. [18] using a retrospective study design determined the prevalence of *H.pylori*-associated histologic gastritis in 201 patients with AIDS. The authors found an unexpectedly low prevalence rate of *H.pylori* in the AIDS patients when compared with HIV-negative controls. These authors have already speculated that it may be a consequence of antimicrobial therapy, specific HIV-related host factors, including hypochlorhydria or an inadequate mucosal inflammatory response, which may impair successful colonization of *H.pylori*.

In 1993, Marano et al. [11], in a cross-sectional study, evaluated the prevalence of *H.pylori* in AIDS patients and the association with chronic gastritis, erosions, and ulcer disease. Seventy-three AIDS patients referred for the evaluation of gastrointestinal symptoms underwent upper endoscopy and antral gastric biopsy. Histological grading of gastritis was diagnosed and the degree of activity was graded on a hematoxylin-eosin stain. *H.pylori* organisms were identified by an acridine orange stain. A single pathologist evaluated the biopsy specimens. *H.pylori* was found in 15% (11 of 73) of AIDS patients. Histological changes of chronic active gastritis were evident in 94.5% (69 of 73) of the study group. *H.pylori* was identified in 15.9% (11 of 69) of biopsy specimens with chronic active gastritis. The organism was more common in biopsy specimens with a higher grade of activity in the chronic gastritis. Endoscopic erosions or ulcers were noted in 11 patients (seven gastric, four duodenal). *H.pylori* was present in 18% (2 of 11) of AIDS patients with erosions or ulcers. The authors stated that the prevalence of *H.pylori* in AIDS patients with histological changes of chronic active gastritis is much lower than the prevalence previously reported for HIV-negative patients with similar pathology. The low prevalence observed

Table 1: *Helicobacter pylori* infection in HIV-infected patients.

Authors	Study population	Method for identifying <i>H.pylori</i> infection	Result
Battan et al. [10]- 1990	40 AIDS/ARC 36 Matched controls	Histology, culture	N.S.
Manaroet al. [11] - 1993	73 AIDS	Histology	15.9%
Benz et al [15] - 1993	41 HIV (+) 47 Uninfected	Histology, culture	HIV (+) 73% Uninfected 100%*
Quiróset al. [13]- 1994	101 HIV (+) 170 Controls	Serology	HIV (+) 53% Controls 33.5% *
Vaira et al. [19]-1995	111 HIV (+) (73 AIDS) 219 Uninfected	Histology, urease, serology	HIV (+) 49% Uninfected 61% *
Nielsen et al. [14]- 1995	102 HIV (+) 94 Controls	Serology	HIV (+) 30% Controls 25% (N.S.)
Eidtet et al. [24]- 1995	77 HIV (+) 77 Uninfected	Histology	HIV (+) 30% Uninfected 68% *
Cacciarelliet al. [25]- 1996	48 HIV (+) A = CD4 > 200 B = CD4 < 200 C = 24 uninfected	Histology	A 69%, B 13%, C 63% * (B x C)
Fabris et al. [26]-1997	19 HIV (+) 48 AIDS	Serology, histology	CD4 < 100 = 43% CD4 100–200 = 56% CD4 > 200 = 78% *
Varskyet al. [27]-1998	497 HIV (+) (23 withulcers)	Histology	HIV (+)/ Ulcer 31% HIV (+)/ Non Ulcer 60% HIV (+)/ Non Ulcer 69% (N.S.)
Fernando et al. [28]-2001	61 HIV (+) 115 Uninfected	Serology	HIV (+) 75% Controls 87% *
Lichterfeldet al. [29]- 2002	60 HIV (+) 30 Uninfected	Serology, ureabreathtest	HIV (+) 23% Controls 27% (N.S.)
Sudet al. [5]- 2002	73 HIV (+)	Serology	HIV (+) 47.9% AIDS (N.S.)
Alimohamedet al. [12]- 2002	52 HIV (+) 52 Controls	Histology, urease	HIV (+) 73.1% Controls 84.6% (N.S.)
Chiuet al. [30]- 2004	52 HIV (+) 104 Uninfected	Histology	HIV (+) 17.3% Controls 63.5% *
Olmos et al. [22]- 2004	102 HIV (+) 107 Uninfected	Histology	HIV (+) 41.1% Controls 49.5% (N.S.)
Werneck-Silva and Prado [4]- 2007	528 HIV (+)/AIDS	Histology	32.4% Hp (+) < in AIDS *
Panos et al. [20]- 2007	58 HIV (+) 58 Uninfected	Histology, urease	HIV (+) 20.7% Control 65% *
Lvet al. [6]- 2007	122 HIV (+) 29 Uninfected	Histology	HIV (+) 22.1% Controls 44.8% *
Mach at al. [31] -2007	94 HIV (+) 47 CD4 < 200 47 CD4 > 200 52 Uninfected	Histology, urease	CD4 < 200 40%, C 69% CD4 > 200 72% Uninfected 69% *
Huppmannet al. [21]- 2010	152 HIV (+)	Histology	15.2%
Nkuizeet al. [3]- 2010	706 HIV (+) 239 without HAART (A) 238 with "early" HAART (B) 229 with "recent" HAART (C)	Histology	A 11%, B 32.71%, C 39.57% * (AxB)
Fialho et al. [33]- 2011	113 HIV (+) 141 Uninfected	Histology, urease	HIV (+) 37% Controls 75.2% *
Hestviket al. [34]- 2011	236 HIV (+)	Fecal antigenest	22.5%
Nkuizeet al. [23]- 2012	145 HIV (+)	Histology	33%

Abbreviations: AIDS: Acquired Immunodeficiency Syndrome; ARC: AIDS-Related Complex; N.S: Non Significant; HIV: Human Immunodeficiency Virus; (+)-Positive Hp= *Helicobacter Pylori*
p value*= Significant P value

does not implicate *H.pylori* as the causal agent in most chronic active gastritis in the AIDS population. Impaired acid secretion may reduce colonization of gastric mucosa and explain the low rate of *H.pylori* observed.

In the same year of 1993, the histology of gastritis, status of *H.pylori* infection, and parameters of humoral and cellular-mediated immune response were investigated by Benz et al. [15] in 41 HIV-positive and 47 HIV-negative patients, who were subjected to upper endoscopy for the evaluation of gastrointestinal symptoms. In HIV- positive patients, 37% had active chronic gastritis against 62% of the HIV- negative patients. In 73% of HIV-positive cases of active chronic gastritis, *H.pylori* was detected by bacteriological culture and/or Warthin-Starry stain. In HIV-negative patients, active chronic gastritis was always associated with *H.pylori* infection. The production of antibodies as measured by two commercially available ELISA tests was significant in HIV-positive and HIV- negative patients and both tests correlated well with *H.pylori* detection by culture or direct microscopy. Immunoglobulin class-specific immunoblots corresponded to the ELISA results in HIV-negative patients but to a lesser extent in the HIV-positive group which was assumed to be related to unspecific polyclonal activation in these patients. Systemic cellular immunity was investigated by proliferation assays of peripheral blood mononuclear cells. Proliferative response to the unspecific mitogen PHA was reduced in HIV-positive patients. A sonicated *H.pylori* antigen failed to induce lymphocyte proliferation. The antimitogenic effect was also seen in the case of co-incubation with PHA. This observation was independent of *H.pylori* and HIV- infection status. These results showed that in HIV-positive as in HIV-negative patients, active chronic gastritis is predominantly related to *H.pylori* infection. The prevalence of *H.pylori*-associated gastritis in HIV-positive patients is significantly reduced ($p < 0.025$) compared to HIV-negative controls. Benz et al. [15] concluded that decreased susceptibility to *H.pylori* infection in HIV positive patients may not be explained by the abnormal reactivity of their humoral- or cellular-mediated immune response.

Quirós et al. [13] compared antibody titers in 612 serum samples from 570 individuals considered at risk for *H.pylori* infection; 170 of them were control sera from 110 adults and 60 children with no gastric alterations. The study groups were 93 institutionalized mentally handicapped children, 40 heterosexual couples, 101 HIV-seropositive patients, 86 patients with chronic renal failure and 40 individuals (20 adults and 20 children) with symptoms associated with gastritis or gastroduodenal ulcer disease. In the adult and child control groups, 33.5% and 11.6% of the individuals had circulating anti-*H.pylori* antibodies. Significantly more adults (80%) and children (75%) with gastric symptoms had detectable circulating antibody titers.

Vaira et al. [19] in 1995, have carried out a large prospective study of the frequency of *H.pylori* infection and HIV-1 status in a community of ex-drug abusers including subjects with (N = 210) and without (N = 259) upper- gastrointestinal symptoms, utilizing both endoscopy and serology. Control groups were patients with upper-gastrointestinal symptoms not at high risk of HIV-1 infection (N = 219) and asymptomatic blood donors (n = 322). *H.pylori* was present in 52% of symptomatic community

residents having endoscopy and 55% of the control patients with symptoms but not at high risk of HIV-1 infection. *H.pylori* was less common in HIV-1-positive patients (40%) than those who were negative (66%; $P < 0.001$). In patients with AIDS (33%), the frequency of *H.pylori* infection was reduced compared to HIV-1-positive patients without AIDS (53%; $P = 0.05$). All the residents with AIDS had upper- gastrointestinal symptoms. In community residents, peptic ulcers were always associated with *H.pylori* infection. In *H.pylori* serology tests, there was no difference in the frequency of infection in asymptomatic residents (56%), whether HIV-1 positive (55%) or HIV-1 negative (58%) as compared with those residents with symptoms. Overall, *H.pylori* was less common in HIV-1-positive residents (49%) than in those who were HIV-1 negative (61%; $p < 0.05$). This difference was due mainly to the low frequency of infection in residents with AIDS (33%). These results suggest that *H.pylori* infection is common in HIV-1- positive patients, and only slightly reduced when compared with at-risk HIV-1-negative subjects.

In 1995, Nielsen et al. [14] retrospectively studied 102 HIV-infected patients with early infection who were in most cases asymptomatic. Serological IgG-antibody response to *H.pylori* was assessed by ELISA. Compared with an age-matched control group the seroprevalence of *H.pylori* positivity was not significantly different (19% vs. 25%). The authors observed no association with CD4 counts, p24 antigen, antibiotic prophylaxis with sulfamethoxazole/trimethoprim, or antiretroviral treatment. In 54 of 83 patients initially seronegative, a second examination was performed after a median of 24 months, and two patients had *H.pylori* seroconverted, indicating an incidence of new infection of 2%/year. Nielsen et al. [14] stated that previous reports have underestimated the prevalence of *H.pylori* infection in HIV patients, which seems to be similar to that in an HIV-negative population.

There is conflicting evidence concerning the prevalence of *Helicobacter pylori* gastritis in HIV-infected patients. Furthermore, a possible influence of immunodeficiency on the acquisition of Mucosa-Associated Lymphoid Tissue (MALT) in the antral mucosa remains to be elucidated [1,6,10].

Eidt et al. [24] analyzed 77 consecutive HIV-1-infected patients and compared them in a prospective study with 77 HIV-1-negative age-matched patients, using immunohistochemical staining. These authors observed that *H.pylori* was found in 30% of HIV-1- infected patients and 68% of controls ($p < 0.01$). They found that the degree of inflammation and the number of lymphoid follicles and intraepithelial B lymphocytes observed in the gastric antral tissue was lower in HIV-1-infected patients than in control subjects. The authors concluded that the lower incidence of *H.pylori* in HIV-1-infected patients may be a consequence of reduced inflammatory response found in the gastric tissue. This event may explain the lower incidence of MALT (mucosal-associated lymphoid tissue) in HIV-1-infected patients.

EARLY HAART STUDIES (FROM 1996 TO 2002)

In 1996, Cacciarelli et al. [25] evaluated the prevalence of *H.pylori* and peptic-ulcer disease in relation to absolute CD4 counts in HIV-seropositive patients with GI symptoms. Seventy-

two patients (48 HIV-positive and 24 HIV-negative) with GI symptoms were evaluated with upper endoscopy and gastric antral biopsy. Samples were prepared with Giemsa stain and reviewed by a single pathologist to determine the status of *H.pylori* infection. The patients were stratified on the basis of HIV status and CD4 count: group A, HIV-positive patients with a CD4 count greater than 200; group B, HIV-positive patients with CD4 counts less than 200; and group C, an HIV-negative control group. The prevalence of *H.pylori* infection in the three groups was as follows: group A, 69% (11/16); group B, 13% (4/32), and group C, 63% (15/24). Peptic-ulcer prevalence in group A was 19% (3/16); in group B, 3% (1/32); and group C, 25% (6/24). The prevalence of *H.pylori* in HIV-positive patients with a CD4 count less than 200 was found to be significantly lower ($p < 0.001$) than that found in HIV-negative patients. The number of peptic ulcers in the HIV-positive group with $CD4 < 200$ was significantly less ($P = 0.035$) than that of the HIV-negative patients. The authors concluded that these results suggest a role of CD4 cell and immune function in sustaining *H.pylori* infection and *H.pylori*-related peptic-ulcer disease.

Fabris et al. [26] in 1997, analyzed 67 consecutive patients infected with the HIV, 72% of which had overt AIDS. They were examined by upper endoscopy due to various indications and evaluated for the prevalence of *H.pylori* infection. The infection was studied by performing both histological examination of gastric biopsies and serological testing for anti-*H.pylori*IgG antibodies. The *H.pylori* prevalence rate was 55% in histology; no significant differences were observed in HIV-infected subjects and those with overt AIDS (52% vs. 63%, respectively; $P = NS$). Positive histological testing appeared to be directly related to the peripheral CD4 lymphocyte count (minimum rates of 43% were detected in patients with $CD4 < 100 \times 10^6/liter$ and maximum rates of 78% in patients with $CD4 > 200 \times 10^6/liter$, respectively; $P < 0.05$) and inversely related to the frequency of antibiotic treatments performed over the six months prior to endoscopy. Low CD4 counts were also apparently associated with low-grade *H.pylori* infection. Serological testing was positive for anti-*H.pylori* IgG antibodies in 39% of patients; compared to histology, serology displayed a sensitivity of 57% and a specificity of 81%. The discrepancy between histological- and serological- positive results for *H.pylori* was noted to be higher in the more advanced phases of HIV infection. The authors suggest that the serological testing for anti-*H.pylori*IgG antibodies seems to require cautious interpretation in HIV-positive patients.

In the next year, 1998, Varsky et al.[27] analyzed 497 HIV-positive patients with upper- digestive tract symptoms and found 23 (5%) with Gastroduodenal Ulcers (GDU) at upper endoscopy. To establish the causes of GDU in this setting, 16 of these patients who had had comprehensive histological evaluation (group I) were compared with 20 HIV-positive subjects with upper-gastrointestinal symptoms but without ulcer (group II), and with 16 seronegative patients with GDU (group III). Eighty-one percent of group I subjects and 90% of group II patients had C3 AIDS. The presence of gastritis and *H.pylori*, fungi, mycobacteria, viruses (especially cytomegalovirus and herpes simplex), and parasites was determined in all three groups by histopathological and microbiological studies. The prevalence of chronic active gastritis was 13/16 (81%) in group I, 12/20 (60%) in group II,

and 15/16 (94%) in group III. It was associated with *H.pylori* in group III, with opportunistic pathogens in groups I and II, and with none in group III. *H.pylori* was detected in 5/16 patients (31%) in group I, in 12/20 (60%) in group II, and 11/16 (69%) in group III. Cytomegalovirus was histologically diagnosed in 8/16 patients (50%) in group I and in 1/20 (5%) in group II. This virus was the only factor shown to be significantly associated with GDU in these cases ($P = 0.0046$). Cryptosporidium was found in 2/16 (12.5%) patients in group I, in 1/20 (5%) in group II, and in none in group III. Differences between groups I and II were not statistically significant and other organisms were observed in the three groups. These authors concluded that gastroduodenal ulcers were infrequent in HIV-positive subjects with upper digestive tract symptoms, and CMV was the only organism significantly associated with GDU in HIV-positive patients. Among HIV-positive patients, *H.pylori* was an uncommon cause of ulcers. Among HIV-positive subjects with ulcers, chronic active gastritis was more common than, *H.pylori* and it was associated with other pathogens. They stated that HIV-positive patients with GDU should have endoscopic biopsies to detect opportunistic infections, especially CMV, because *H.pylori* infection is uncommon.

We find the next published study only in 2001 were Fernando et al. [28] studied 221 adults drawn from an impoverished urban population with high HIV seroprevalence (35%) to determine the prevalence of gastroduodenal pathology and its relationship to serological markers of *H.pylori* virulence proteins and other potential environmental and immunological determinants of disease, including HIV infection. Eighty-one percent were *H.pylori* seropositive, and 35% were HIV seropositive. Urban upbringing and low CD4cell count were associated with a reduced likelihood of *H.pylori* seropositivity rate, as was current *Ascaris* infection, in keeping with recent evidence from an animal model. One hundred ninety-one adults underwent gastroduodenoscopy, and 14 had gastroduodenal pathology. Mucosal lesions were a major cause of abdominal pain in this population. While the majority of patients with gastroduodenal pathology (12 of 14) were seropositive for *H.pylori*, none were seropositive for HIV. Smoking was associated with increased risk of macroscopic pathology, and a history of *Mycobacterium bovis* BCG immunization was associated with reduced risk. Antibodies to *H.pylori* lipopolysaccharide were associated with pathology. HIV infection was associated with protection against mucosal lesions, suggesting that fully functional CD4 lymphocytes may be required for the genesis of gastroduodenal pathology.

Lichterfeld et al. [29]- 2002, studied whether the decreased frequency of infections in HIV patients might be associated with the stage of the underlying HIV disease or concomitant drug regimens the patients had received. Thus, 60 randomly selected HIV outpatients were stratified according to the stage of their HIV infection, their CD4 cell count, and the drug regimens they were given. Within these subgroups of patients, *H.pylori*-infection prevalence was separately investigated by serological and ^{13}C -urea breath testing for bacterial overgrowth. Data were compared to a reference population of 30 healthy volunteers. No difference in *H.pylori*-infection prevalence was found between the HIV-infected patients in general and the reference cohort. A significantly lower proportion of *H.pylori*-infected individuals

was observed among those HIV patients who had AIDS-defining diseases. Furthermore, a substantial but insignificant decrease of *H.pylori*-infection prevalence was noted in HIV-positive patients with an extensive decline of CD4 cell count ($< 100/\mu\text{l}$). HIV-positive patients who had received antimicrobial or H2-antagonizing drugs within 12 months prior to the study commencement also were found to have a remarkably decreased frequency of *H.pylori* infections independently of their CD4 cell count. No association between *H.pylori*-infection prevalence and the patient's age, sex, risk group, or the type of their antiretroviral treatment was found. The authors concluded from these results that the decreased *H.pylori*-infection prevalence in HIV-infected patients may, apart from frequent antibiotic treatment, be correlated to the stage of HIV-mediated immune suppression.

In the same year of 2002, Sud et al. [5] investigated the prevalence of *H.pylori* co-infection with HIV and its correlation with gastrointestinal symptoms in HIV-infected patients. Seventy-three consecutive HIV-infected patients were included in the study. Antibodies (IgG) to *H.pylori* were tested by ELISA. Eleven patients presented with gastrointestinal symptoms. Thirty-five of the 73 (47.9%) patients had serological evidence of *H.pylori* infection. Six of them had gastrointestinal symptoms. Twenty-four patients with *H.pylori* infection had AIDS. The authors observed that there was no difference in the prevalence of *H.pylori* infection between patients with and without AIDS.

Another paper in 2002, Alimohamed et al.[12] performed a hospital-based prospective case-control study to analyze the prevalence of *H.pylori* gastric mucosal infection and the pattern of upper gastrointestinal endoscopic findings in HIV-seropositive patients. Fifty-two HIV-seropositive patients with upper-gastrointestinal symptoms were recruited (as well as 52 HIV-seronegative age- and gender- matched controls). Both cases and control subjects underwent upper-gastrointestinal endoscopy, and biopsies were taken according to standard protocol. *H.pylori* detection was done by the rapid urease test and histology, and *H.pylori* gastric-mucosal infection was considered to be present in the circumstance of a positive detection by both tests; biopsies were also taken for tissue diagnosis and CD4 peripheral lymphocyte counts were determined using flow cytometry. *H.pylori* prevalence was 73.1% [95% CI 59.9-83.8] in HIV- positive subjects and 84.6% [95% CI 72.9-92.6] in HIV-negative controls ($p=0.230$). Prevalence of *H.pylori* decreased with decreasing peripheral CD4 lymphocyte counts. Median CD4 lymphocyte count was 67 cells per mm^3 in HIV-positive patients. On endoscopy, the most common lesion in HIV-positive patients was esophageal candidiasis (occurring in 51.9%), which was often associated with the presence of oral candidiasis and, together with erosions, ulcers and nodules in the esophagus, occurred exclusively in these patients. The authors stated that *H.pylori* prevalence was not significantly different between HIV-positive and HIV-negative subjects, and it decreased in HIV-positive subjects with decreasing CD4 cell counts.

RECENT HAART STUDIES (FROM 2003 TO 2012)

In 2004, Chiu et al. [30] compared the prevalence of *H.pylori* and Cytomegalovirus (CMV) infection in AIDS patients and HIV-negative controls, and the impact of CD4 lymphocyte counts on *H.pylori* and CMV infection in the same subjects was also assessed.

One hundred and fifty-six patients (52 HIV-positive, 104 HIV-negative) with gastrointestinal symptoms were evaluated with upper gastrointestinal endoscopy and biopsy. Comparison of the prevalence of *H.pylori* and CMV infection was made by dividing AIDS patients into two groups: those with CD4 counts $>100/\text{mm}^3$ and those with CD4 counts $<100/\text{mm}^3$, and ulcer and non-ulcer patients. The results showed that in comparison with HIV-negative controls, AIDS patients had a lower prevalence of *H.pylori* infection ($P < 0.0001$) but a higher prevalence of CMV infection ($P < 0.0001$). Cytomegalovirus infection was frequently found in AIDS patients with CD4 count $<100/\text{mm}^3$, in comparison with those with a CD4 count $>100/\text{mm}^3$. In AIDS patients, CMV was more frequently detected in subjects with peptic ulcers ($P = 0.0125$). Conversely, the prevalence of *H.pylori* infection in AIDS patients was not different between those with and without peptic ulcers. The conclusion of the authors was that the low prevalence of *H.pylori* infection and peptic ulcers in AIDS patients suggests a different role of *H.pylori* infection in peptic ulcers or even a different mechanism of peptic ulcerogenesis in HIV-positive subjects. Cytomegalovirus, rather than *H.pylori*, may be the main causative pathogen of peptic ulcers in AIDS patients.

To compare *H.pylori*-infection prevalence and gastric-mucosa damage in HIV-infected and non-HIV-infected patients, Olmos et al. [22] (2004) analyzed gastric biopsies systematically taken in 209 individuals who underwent upper-gastrointestinal endoscopy (102 HIV-infected and 107 non-HIV-infected). The results showed that *H.pylori* was found in 42 (41.1%) HIV-infected patients and in 53 (49.5%) non-HIV patients ($P = 0.22$). In HIV-positive patients infected with *H.pylori*, the mean CD4 cell count was higher than that of HIV-positive patients without *H.pylori* (364 and 228 cells/ mm^3 , respectively; $P = 0.0001$). *H.pylori* gastritis was more severe in the HIV-positive group ($P = 0.0001$). They concluded that the frequency of *H.pylori* in gastric mucosa in HIV-infected and non-HIV patients was similar. Also, HIV-infected patients with *H.pylori* had a higher mean CD4 cell count than HIV-infected individuals without *H.pylori*. The authors stated that gastric lesions associated with *H.pylori* were more severe in the HIV-positive population.

In 2007, Werneck-Silva and Prado [4] did a prospective study of the prevalence and the etiology of endoscopic lesions in a large cohort of dyspeptic adult HIV-infected patients under HAART, according to their immunological status. They studied 528 (334 men and 194 women) HIV-infected patients under HAART with epigastric pain and/or nausea and vomiting who underwent upper endoscopy. Patients were classified into two groups, according to CD4 cell count (>200 cells/ mm^3 or ≤ 200 cells/ mm^3). Gastric and duodenal biopsies were taken from normal mucosa and from any lesion found in this procedure. Gastric mucosa alterations were seen in 61.74% of patients (40.71% erythema, 18.38% erosion and 2.65% ulcer). Duodenum-mucosa alterations were seen in 25.37% of patients, mainly erosions (19.50%) and ulcer (3.59%). There was no difference in endoscopic findings according to CD4 cell count groups. Chronic active gastritis was shown in 459 patients (86.93%). *H.pylori* infection was seen in 32.38%, and it was more prevalent in the group with CD4 > 200 ($p < 0.01$). Opportunistic infections and malignancies were seen exclusively in patients with CD4 ≤ 200 . The authors concluded that most of the endoscopic lesions

in dyspeptic HIV-infected patients under HAART were not related to AIDS. Upper endoscopy was more helpful in dictating clinical treatment in patients with low CD4 counts ($<$ or $=$ 200) and should be done earlier in this group.

In the year of 2007, Panos et al. [20] performed a case-control study to evaluate the prevalence and morbidity of *H.pylori* in HIV-infected patients. HIV-seropositive patients were infected by *H.pylori* less often than HIV-seronegative controls [12/58 (20.7%) versus 38/58 (65.5%), $p < 0.001$]. The mean CD4 count was lower for *H.pylori*-negative than *H.pylori*-positive HIV-infected patients ($p < 0.007$). Also, among HIV patients, prior use of antibiotics or proton pump inhibitors was more common in those without *H.pylori* infection; however, this difference was not statistically significant ($P = 0.06$). The grading of the density of *H.pylori* infection and the grading of the histomorphological features according to the Sydney classification were similar between HIV-seropositive and -seronegative patients with *H.pylori* infection.

Again in 2007, Lv et al. [6] compared the prevalence of *H.pylori*-infection, peptic ulcers, Cytomegalovirus (CMV) infection and candida esophagitis in HIV-positive and HIV-negative patients, and evaluated the impact of CD4 lymphocyte on *H.pylori* and opportunistic infections. A total of 151 patients (122 HIV-positive and 29 HIV-negative) with gastrointestinal symptoms were examined by upper endoscopy and biopsy. Samples were assessed to determine the prevalence of *H.pylori*-infection, CMV, candida esophagitis and histologic chronic gastritis. The results showed that the prevalence of *H.pylori* was less common in HIV-positive patients (22.1%) than in HIV-negative controls (44.8%; $P < 0.05$), and the prevalence of *H.pylori* displayed a direct correlation with CD4 count stratification in HIV-positive patients. In comparison with the HIV-negative group, HIV-positive patients had a lower incidence of peptic ulcers (20.7% vs. 4.1%; $P < 0.01$), but a higher prevalence of chronic atrophy gastritis (6.9% vs. 24.6%; $P < 0.05$). Unlike the HIV-negative group, *H.pylori* infection had a close relationship to chronic active gastritis ($P < 0.05$). The authors concluded that In HIV-positive patients, chronic active gastritis was not significantly different between those with *H.pylori* infection and those without. Furthermore, the lower prevalence of *H.pylori* infection and peptic ulcers in HIV-positive patients with gastrointestinal symptoms suggests a different mechanism of peptic ulcerogenesis and a different role of *H.pylori*-infection in chronic active gastritis and peptic ulcers. The pathogenesis of chronic active gastritis in HIV-positive patients may be different from the general population that is closely related to *H.pylori* infection.

As the HIV infection causes progressive immune-defense-system dysfunction, including in the gastrointestinal tract, Mach et al. [31] evaluated the morphological changes in the upper-gastrointestinal tract mucosa in HIV-infected patients in relation to the degree of immunodeficiency, presence of *H.pylori*, fungal colonization, and antiretroviral treatment (HAART). One hundred forty-six patients (94 HIV-positive, 52 HIV-negative) with dyspeptic symptoms were evaluated by upper-gastrointestinal endoscopy and biopsy. The HIV-infected were divided into two groups: 47 patients with CD4 count $>200/\text{mm}^3$ and 47 with severe immunodeficiency (CD4 count $<200/\text{mm}^3$); 42 of the total patients were treated with HAART. Gastric

mm^3); 42 of the total patients were treated with HAART. Gastric biopsies for histopathology and urease test, esophageal swabs, and gastric aspirates for mycological evaluation were taken. The results disclosed that the HIV-infected patients with severe immunodeficiency had a lower prevalence of *H.pylori* infection and active chronic gastritis in the gastric antrum compared with the other HIV-infected patients and controls (*H.pylori* in 40%, 72%, and 69%, respectively; $p < 0.05$). The authors stated that mycotic esophagitis and mycotic colonization of the stomach were more frequent in patients with severe immunodeficiency. The prevalence of gastric mucosa changes was not different between the patients treated and not treated with HAART, and *H.pylori* infection was less frequent in HIV-infected patients treated with HAART. In severely immunodeficient patients with dyspeptic symptoms, the prevalence of *H.pylori* and active chronic gastritis in the gastric antrum is much lower than in HIV-negative patients.

A significant number of HIV-1 patients experience poor immune reconstitution despite long-term viral suppression with HAART. In 2010, Magen et al. [32] determined whether eradication of *Helicobacter pylori* could facilitate a better immune reconstitution in these patients. They evaluated 49 immunological non-responder HIV-1 symptomatic patients by ^{13}C -urea breath test for the presence of active *H.pylori* infection. The ^{13}C -urea breath test was positive in 26 (53%) of them. Eleven patients (group 1) were treated with a combination of antibiotics. Eight weeks later, successful eradication was proven by a repeat negative ^{13}C -urea breath test in all 11 patients. The remaining 15 (group 2) refused the *H.pylori* eradication treatment. All 26 patients were followed for 24 months and evaluated for blood CD4 and CD8 cell counts and percentages and for plasma HIV-1 viral load. At the time of *H.pylori* diagnosis and eradication (baseline), CD4 and CD8 cell counts were similar in both study groups. There were no significant changes in either CD4 or CD8 cell counts in group 2 patients. None of the patients of group 1 demonstrated virological failure, while four (26.7%) group 2 patients experienced virological failure requiring change of HAART regimen. The authors stated that triple therapy for *H.pylori* eradication is associated with a significant, although possibly transient immune reconstitution in HAART-treated HIV-1 patients with viral suppression without immunological response.

In 2010, Kelly et al. [17] found evidence of a specific effect of HIV on gastric pH which was readily reversed by anti-retroviral therapy and not mediated by gastric atrophy.

As the HIV infection causes progressive immune-defense-system dysfunction, including in the gastrointestinal tract, Mach et al. [32] evaluated the morphological changes in the upper-gastrointestinal tract mucosa in HIV-infected patients in relation to the degree of immunodeficiency, presence of *H.pylori*, fungal colonization, and antiretroviral treatment (HAART). One hundred forty-six patients (94 HIV-positive, 52 HIV-negative) with dyspeptic symptoms were evaluated by upper-gastrointestinal endoscopy and biopsy. The HIV-infected were divided into two groups: 47 patients with CD4 count $>200/\text{mm}^3$ and 47 with severe immunodeficiency (CD4 count $<200/\text{mm}^3$); 42 of the total patients were treated with HAART. Gastric

biopsies for histopathology and urease test, esophageal swabs, and gastric aspirates for mycological evaluation were taken. The results disclosed that the HIV-infected patients with severe immunodeficiency had a lower prevalence of *H.pylori* infection and active chronic gastritis in the gastric antrum compared with the other HIV-infected patients and controls (*H.pylori* in 40%, 72%, and 69%, respectively; $p < 0.05$). The authors stated that mycotic esophagitis and mycotic colonization of the stomach were more frequent in patients with severe immunodeficiency. The prevalence of gastric mucosa changes was not different between the patients treated and not treated with HAART, and *H.pylori* infection was less frequent in HIV-infected patients treated with HAART. In severely immunodeficient patients with dyspeptic symptoms, the prevalence of *H.pylori* and active chronic gastritis in the gastric antrum is much lower than in HIV-negative patients

In 2010, a review of 706 HIV-infected patients who underwent GI endoscopy was undertaken by Nkuize et al.[3]. The cohort was divided into three groups: group 1 (G1), pre-HAART, consisting of 239 patients who underwent endoscopy between January 1991 and December 1994; group 2 (G2), early HAART, consisting of 238 patients who underwent endoscopy between January 1999 and December 2002; and group 3 (G3), recent HAART, consisting of 229 patients who underwent endoscopy between January 2005 and December 2008. Parameters studied included age, gender, opportunistic chemoprophylaxis, antiretroviral therapies, CD4 cell counts, symptoms, observations at the first UGI endoscopy, and histology. When G1, G2 and G3 were compared, significant increases were seen over time in the following parameters: the percentage of women, the mean CD4 cell count, and the frequencies of reflux symptoms, gastroesophageal reflux disease, gastritis, gastric ulcers, and *H.pylori* infection. Significant decreases were seen in the frequencies of the administration of anti-opportunistic infection prophylaxis, odynophagia/dysphagia, acute/chronic diarrhea, candida esophagitis, nonspecific esophageal ulcer and Kaposi sarcoma. No significant change was observed in the other parameters, i.e., digestive bleeding, duodenal ulcers or inflammatory duodenopathy. The authors stated that these results suggest a correlation between the improvement of immunity as a result of more efficient antiviral therapy and the decrease in the frequency of digestive diseases in AIDS, mainly opportunistic pathologies. However, *H.pylori* infection, reflux symptoms, and gastroesophageal reflux disease have increased in the HAART era.

Fialho et al. [33] conducted a study in northeastern Brazil, evaluating the prevalence of *H.pylori* infection and the presence of gastritis in HIV-infected patients. There were 113 HIV-positive and 141 age-matched HIV-negative patients included, all of whom underwent upper-gastrointestinal endoscopy for dyspeptic symptoms. *H.pylori* status was evaluated by urease test and histological examination. The prevalence of *H.pylori* infection was significantly lower ($p < 0.001$) in HIV-infected (37.2%) patients than in uninfected (75.2%) patients. There were no significant differences between *H.pylori* status and gender, age, HIV viral load, antiretroviral therapy, and the use of antibiotics. A lower prevalence (not significant) of *H.pylori* was observed among patients with CD4 cell count below $200/\text{mm}^3$. Chronic active antral gastritis was observed in 87.6% of the HIV-

infected patients and in 78.4% of the control group ($P = 0.11$). These results suggested that *H.pylori* infection was significantly associated with chronic active gastritis in the antrum in both groups, but it was not associated with corpus chronic active gastritis in the HIV-infected patients. The authors concluded that the prevalence of *H.pylori* was significantly lower in HIV-positive patients compared with those who were HIV-negative.

In 2011, Hestvik et al. [34] determined the prevalence of and factors associated with *H.pylori* colonization in HIV-infected, HAART-naïve Ugandan children aged 0-12 years. In a hospital-based survey, 236 HIV-infected children were tested for *H.pylori* colonization using a faecal antigen test. A standardized interview with socio-demographic information and medical history was used to assess risk factors. A cluster of differentiation 4 (CD4) cell percentages was prevalent in most children. The overall prevalence of *H.pylori* in the HIV-infected children was 22.5%. Age-specific prevalence was as follows: up to one year, 14.7%; 1-3 years, 30.9%; and 3-12 years, 20.7%. HIV-infected children who were more seriously affected by their disease (low CD4 cell percentage or WHO clinical stage II-IV) were less likely to be colonized with *H.pylori*. There was a trend for a lower prevalence of *H.pylori* in children who had taken antibiotics for the preceding two weeks (21.6%) than in those who had not taken antibiotics (35.7%). There was no statistically significant difference in prevalence by gender, housing, congested living, education of the female caretaker, drinking water, or toilet facilities. HIV-infected, HAART-naïve Ugandan children had a lower prevalence of *H.pylori* colonization compared with apparently healthy Ugandan children (44.3%). Children with a low CD4 cell percentage and an advanced clinical stage of HIV had an even lower risk of *H.pylori* colonization. These authors speculated that the treatment with antibiotics due to co-morbidity with infectious diseases is a possible explanation for the relatively low prevalence.

In 2012, Nkuize et al.[23] evaluated demographic characteristics in HIV-positive patients receiving HAART who had upper-gastrointestinal symptoms requiring gastrointestinal endoscopy and compared the findings in patients with and without *H.pylori*-infection. The authors prospectively observed all HIV-infected patients treated with antiretroviral therapy that underwent gastrointestinal endoscopy for the first time and were tested for *H.pylori* from January 2004 to December 2008. Data collected included the following: demographics (age, gender, ethnicity, Body Mass Index [BMI], tobacco use, alcohol intake, and HIV risk behavior); comorbidity (viral hepatitis B or C, any organ dysfunction, or opportunistic disease); medication, including antibiotics, H2 blockers, proton pump inhibitors, and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); CD4 cell counts, viral load; symptoms; and endoscopic and histologic diagnoses. Patients were compared according to *H.pylori* status (presence vs. absence). The results showed that 145 patients were evaluated. Compared to patients without *H.pylori* infection ($n = 97$), those with *H.pylori* infection ($n = 48$) had a significantly higher CD4 cell count ($P = 0.008$), had a greater incidence of duodenal ulcers ($P = 0.005$), were more likely to be heterosexual ($P = 0.047$), had a higher BMI ($P = .027$), had lower viral loads ($P < 0.01$), were less likely to have received macrolide antibiotics in the last 3 months ($P < 0.001$), and had less comorbidity ($P = 0.03$). They were also more frequently Black African than Caucasian. In multivariate

analysis, being heterosexual and having a low viral load were independently associated with an increased risk of having *H.pylori* co-infection. The authors' conclusion was that in the antiretroviral therapy era, HIV-*H.pylori* co-infection is associated with a greater incidence of duodenal ulcers and higher CD4 counts, higher BMI, less comorbidity, and less frequent use of macrolides.

SUMMARY AND FUTURE PERSPECTIVES

After the advent of potent antiviral therapy (HAART), it has shown an increase in the incidence of *H.pylori* and its complications [2-4,21,23,29,34] in HIV-infected patients. The trend found in most published studies on *H.pylori* infection in HIV-infected patients in the post-HAART era is the low prevalence of the bacteria in patients with a low count of CD4 cells (< 200/mm³). In patients with CD4 cell count ≥ 200/mm³, rates of infection with the bacteria resemble those of the general population [4,6,12,15,22,23,26,28,32]. It does appear that the incidence of *H.pylori* infection is lower among patients with AIDS compared to matched HIV-infected and -uninfected controls. These results suggest a correlation between the improvement of immunity as a result of more efficient antiviral therapy and the decrease in the frequency of digestive diseases in AIDS, mainly opportunistic pathologies. However, *H.pylori* infection and dyspepsia in HIV-infected patients have increased in the HAART era. But, in patients without AIDS and with increasing infection by *H.pylori*, was not observed a rise of bacteria-induced infection including gastric or duodenal ulcer, MALT lymphoma and atrophic gastritis. We can assume that the *Helicobacter* does not change its behavior in patients without AIDS and their dyspepsia can be drug-induced or have other causes. So it is very important to look for causes other than *Helicobacter* infection in HIV dyspeptic patients.

Thus, the managements and the protocols in the presence of dyspepsia in HIV-infected patients or patients in which AIDS are installed resemble the guidelines established for the general population. Moreover, in HIV-infected patients with more intense immunodeficiency, the presence of opportunistic infections is most common and is usually responsible for the dyspeptic complaints of these patients [2,6,18,21,27,30].

AUTHORS CONTRIBUTIONS

Chehter EZ contributed to conception and design the article, reviewed literature and wrote the manuscript draft; Catapani WR revising the draft and final approval of the version; Fernando Beani Margeotto edited the final draft; Demetrius Germini performed the review of the literature; Alexandre Cruz Henriques performed the review of the literature and revising the draft; Jaques Waisberg contributed to conception and design the article and final approval of the version.

REFERENCES

- Romanelli F, Smith KM, Murphy BS. Does HIV infection alter the incidence or pathology of *Helicobacter pylori* infection? *AIDS Patient Care STDS*. 2007; 21: 908-919.
- Raufman JP. Declining gastrointestinal opportunistic infections in HIV-infected persons: a triumph of science and a challenge for our HAARTs and minds. *Am J Gastroenterol*. 2005; 100: 1455-1458.
- Nkuize M, De Wit S, Muls V, Arvanitakis M, Buset M. Upper gastrointestinal endoscopic findings in the era of highly active antiretroviral therapy. *HIV Med*. 2010; 11: 412-417.
- Werneck-Silva AL, Prado IB. Dyspepsia in HIV-infected patients under highly active antiretroviral therapy. *J Gastroenterol Hepatol*. 2007; 22: 1712-1716.
- Sud A, Ray P, Bhasin DK, Wanchu A, Bamberg P, Singh S. *Helicobacter pylori* in Indian HIV infected patients. *Trop Gastroenterol*. 2002; 23: 79-81.
- Lv FJ, Luo XL, Meng X, Jin R, Ding HG, Zhang ST. Low prevalence of *H.pylori* and endoscopic findings in HIV-positive Chinese patients with gastrointestinal symptoms. *World J Gastroenterol*. 2007; 13: 5492-5496.
- Tonkic A, Tonkic M, Lehours P, Mégraud F. Epidemiology and diagnosis of *Helicobacter pylori* infection. *Helicobacter*. 2012; 17: 1-8.
- Sonnenberg A. Review article: historic changes of *Helicobacter pylori*-associated diseases. *Aliment Pharmacol Ther*. 2013; 38: 329-342.
- Bashinskaya B, Nahed BV, Redjal N, Kahle KT, Walcott BP. Trends in peptic ulcer disease and identification of *Helicobacter pylori* as a causative organism: population-based estimates from the US nationwide inpatient sample. *J Glob Infect Dis*. 2011; 3: 366-370.
- Battan R, Raviglione MC, Palagiano A, Boyle JF, Sabatini MT, Sayad K, et al. *Helicobacter pylori* infection in patients with acquired immune deficiency syndrome. *Am J Gastroenterol*. 1990; 85: 1576-1579.
- Marano BJ Jr, Smith F, Bonanno CA. *Helicobacter pylori* prevalence in acquired immunodeficiency syndrome. *Am J Gastroenterol*. 1993; 88: 687-690.
- Alimohamed F, Lule GN, Nyong'o A, Bwayo J, Rana FS. Prevalence of *Helicobacter pylori* and endoscopic findings in HIV seropositive patients with upper gastrointestinal tract symptoms at Kenyatta national hospital, Nairobi. *East Afr Med J*. 2002; 79: 226-231.
- Quirós A, Quirós E, González I, Bernal MC, Piedrola G, Maroto MC. *Helicobacter pylori* seroepidemiology in risk groups. *Eur J Epidemiol*. 1994; 10: 299-301.
- Nielsen H, Andersen LP. Serodiagnosis of *Helicobacter pylori* infection in patients with human immunodeficiency virus infection. *APMIS*. 1995; 103: 689-692.
- Benz J, Hasbach H, Brenden M, Eidt S, Fätkenheuer G, Schrappe M, et al. Humoral and cellular immunity in HIV positive and HIV negative *Helicobacter pylori* infected patients. *Zentralbl Bakteriol*. 1993; 280: 186-196.
- Lake-Bakaar G, Elsakar M, Hagag N, Lyubsky S, Ahuja J, Craddock B, et al. Changes in parietal cell structure and function in HIV disease. *Dig Dis Sci*. 1996; 41: 1398-1408.
- Kelly P, Shawa T, Mwanamakondo S, Soko R, Smith G, Barclay GR, et al. Gastric and intestinal barrier impairment in tropical enteropathy and HIV: limited impact of micronutrient supplementation during a randomised controlled trial. *BMC Gastroenterol*. 2010; 10: 72.
- Edwards PD, Carrick J, Turner J, Lee A, Mitchell H, Cooper DA. *Helicobacter pylori*-associated gastritis is rare in AIDS: antibiotic effect or a consequence of immunodeficiency? *Am J Gastroenterol*. 1991; 86: 1761-1764.
- Vaira D, Miglioli M, Menegatti M, Holton J, Boschini A, Vergura M, et al. *Helicobacter pylori* status, endoscopic findings, and serology in HIV-1-positive patients. *Dig Dis Sci*. 1995; 40: 1622-1626.
- Panos GZ, Xirouchakis E, Tzias V, Charatsis G, Bliziotis IA, Doulgeroglou V, et al. *Helicobacter pylori* infection in symptomatic HIV-seropositive and -seronegative patients: a case-control study. *AIDS Res Hum Retroviruses*. 2007; 23: 709-712.

21. Huppmann AR, Orenstein JM. Opportunistic disorders of the gastrointestinal tract in the age of highly active antiretroviral therapy. *Hum Pathol.* 2010; 41: 1777-1787.
22. Olmos M, Araya V, Pskorz E, Quesada EC, Concetti H, Perez H, et al. Coinfection: *Helicobacter pylori*/human immunodeficiency virus. *Dig Dis Sci.* 2004; 49: 1836-1839.
23. Nkuize M, De-Wit S, Muls V, Ntounda R, Gomez-Galdon M, Buset M. Comparison of demographic characteristics and upper gastrointestinal endoscopy findings in HIV-positive, antiretroviral-treated patients with and without *Helicobacter pylori* coinfection. *Helicobacter* 2012; 17: 153-159.
24. Eidt S, Schrappe M, Fischer R. Analysis of antral biopsy specimens for evidence of acquired mucosa-associated lymphoid tissue in HIV1-seropositive and HIV1-negative patients. *Scand J Gastroenterol.* 1995; 30: 635-639.
25. Cacciarelli AG, Marano BJ Jr, Gualtieri NM, Zuretti AR, Torres RA, Starpoli AA, et al. Lower *Helicobacter pylori* infection and peptic ulcer disease prevalence in patients with AIDS and suppressed CD4 counts. *Am J Gastroenterol.* 1996; 91: 1783-1784.
26. Fabris P, Bozzola L, Benedetti P, Scagnelli M, Nicolin R, Manfrin V, et al. *H.pylori* infection in HIV-positive patients. A serohistological study. *Dig Dis Sci.* 1997; 42: 289-292.
27. Varsky CG, Correa MC, Sarmiento N, Bonfanti M, Peluffo G, Dutack A, et al. Prevalence and etiology of gastroduodenal ulcer in HIV-positive patients: a comparative study of 497 symptomatic subjects evaluated by endoscopy. *Am J Gastroenterol.* 1998; 93: 935-940.
28. Fernando N, Holton J, Zulu I, Vaira D, Mwaba P, Kelly P. *Helicobacter pylori* infection in an urban African population. *J Clin Microbiol.* 2001; 39: 1323-1327.
29. Lichterfeld M, Lorenz C, Nischalke HD, Scheurlen C, Sauerbruch T, Rockstroh JK. Decreased prevalence of *Helicobacter pylori* infection in HIV patients with AIDS defining diseases. *Z Gastroenterol.* 2002; 40: 11-14.
30. Chiu H, Wu M, Hung C, Suhn C, Lin J. Low prevalence of *Helicobacter pylori* but high prevalence of cytomegalovirus-associated peptic ulcer disease in AIDS patients: Comparative study of asymptomatic subjects evaluated by endoscopy and CD4 counts. *J GastroenterolHepatol.* 2004; 19: 423-428.
31. Mach T, Skwara P, Biesiada G, Ciesla A, Macura A. Morphological changes of the upper gastrointestinal tract mucosa and *Helicobacter pylori* infection in HIV-positive patients with severe immunodeficiency and symptoms of dyspepsia. *Med SciMonit.* 2007; 13: 14-19.
32. Magen E, Elbirt D, Agmon-Levin N, Mishal J, Stoeber Z. Eradication of *Helicobacter pylori* can facilitate immune reconstitution in HIV-1-infected immunological non-responders. *Int J Infect Dis.* 2010; 14: e322-327.
33. Fialho AB, Braga-Neto MB, Guerra EJ, Fialho AM, Fernandes KC, Sun JL, et al. Low prevalence of *H.pylori* infection in HIV-positive patients in the northeast of Brazil. *BMC Gastroenterol.* 2011; 11: 13.
34. Hestvik E, Tylleskar T, Ndeezi G, Grahnquist L, Olafsdottir E, Tumwine JK, et al. Prevalence of *Helicobacter pylori* in HIV-infected, HAART-naïve Ugandan children: a hospital-based survey. *J Int AIDS Soc.* 2011; 14: 34.

Cite this article

Chehter EZ, Catapani WR, Margeotto FB, Germini D, Henriques AC, et al. (2014) *Helicobacter pylori* in the Era of Highly Active Antiretroviral Therapy (HAART): A Review. *JSM Gastroenterol Hepatol* 2(3): 1026.