

Coinfection: *Helicobacter pylori*/Human Immunodeficiency Virus

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To compare *H. pylori* infection prevalence and gastric mucosa damage in HIV-infected and non-HIV-infected patients, gastric biopsies were systematically taken in 209 individuals who underwent upper GI endoscopy (102 HIV-infected and 107 non-HIV-infected). *H. pylori* was found in 42 (41.1%) HIV-infected patients and in 53 (49.5%) non-HIV patients ($P = 0.22$, $\chi^2 = 1.47$, NS). In HIV-positive patients infected with *H. pylori* the mean CD4 count was higher than in HIV-positive patients without *H. pylori* (364 and 228 cells/mm³, respectively; $P = 0.0001$). *H. pylori* gastritis was more severe in the HIV-positive group ($\chi^2 = 15.02$, $P = 0.0001$). The frequency of *H. pylori* in gastric mucosa in HIV-infected and non-HIV patients was similar. HIV-infected patients with *H. pylori* had a higher mean CD4 count than HIV-infected individuals without *H. pylori*. Gastric lesions associated with *H. pylori* were more severe in the HIV-positive population.

KEY WORDS: HIV; AIDS; *Helicobacter pylori*; gastritis.

Helicobacter pylori is a causative organism for gastric damage (1–4). After its identification in 1982, it has been linked to many diseases, including gastritis, peptic ulcer, and gastric malignancies (5, 6). The reported prevalence in unselected populations ranges from 30 to 60% (7, 8). Studies in Argentina have shown a frequency of *H. pylori* in urban area residents of 35 to 55% (9, 10).

The prevalence of *H. pylori* in patients infected with human immunodeficiency virus (HIV) has been reported to be remarkably lower than that found in non-HIV-infected individuals (11–16). Reasons for these lower rates remain unclear (11, 17–19). Some studies (20–22) have indicated that the CD4/CD8 ratio in gastric mucosa is different in subjects with and without *H. pylori* infection. Therefore, CD4 lymphocytes, which are depleted in AIDS patients, might be associated with a different presentation of

H. pylori infection (22–24). Also, the frequent use of antibiotics by AIDS patients could lead to *H. pylori* eradication from gastric mucosa, explaining the lower prevalence described in this population (11, 25).

Our objective in this study was to compare the prevalence of *H. pylori* infection and histologic damage of gastric mucosa in HIV-infected and non-HIV-infected patients referred for upper GI endoscopy at our hospital.

PATIENTS AND METHODS

This prospective cross-sectional study was carried out at the Gastroenterology Division of the Hospital Fernández, a major referral center for assistance of HIV-infected individuals in the city of Buenos Aires, Argentina. From May 2001 to April 2003, 102 HIV-positive patients (Table 1) who underwent upper GI endoscopy were included in the study. Symptoms that led to endoscopy were upper abdominal pain, heartburn, nausea, vomiting, weight loss, early satiety, postprandial distension, and anorexia. Patients with GI bleeding, dysphagia, or chronic diarrhea were not included. This sample was age-matched with 107 non-HIV-infected subjects (48 males; mean age, 33 years) whose endoscopy indications were the same as noted above.

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TABLE 1. DATA ON HIV-INFECTED PATIENTS

| | n (%) |
|-----------------------------|---------------------------|
| <i>n</i> | 102 |
| Males | 62 (60.9) |
| Mean age | 36 years |
| Heterosexual | 48 (47.1) |
| Homosexual | 37 (36.3) |
| Intravenous drug addicts | 17 (16.7) |
| Mean CD4 count | 282 cells/mm ³ |
| On HAART | 63 (61.7) |
| Viral load > 100,000 copies | 44 (43.6) |
| 100,000–20,000 copies | 7 (6.9) |
| 20,000–50 copies | 26 (25.7) |
| < 50 copies | 24 (23.8) |
| Previous OI | 30 (29.4) |

Patients gave their written informed consent to participate in the research. They all answered a questionnaire about symptoms and consumption of medications, including antibiotics, anti-inflammatory drugs, and acid secretion inhibitors; if HIV positive, they were also asked about risk factors for HIV infection and whether they were on antiretroviral therapy (HAART). CD4 count and HIV viral load were accepted as valid if the blood sample for their determination had been taken within 1 month before or after the entrance to the study.

Video endoscopes (Olympus GIFV or Pentax 3400) were used for the procedure. Two random gastric biopsies, from the antrum and fundus, were always taken. Specimens were processed, then stained with hematoxylin–eosin and modified Giemsa colorants. When histologic gastritis was diagnosed, the degree of activity was graded according to a modified Sydney classification (4).

STATA Intercool 8 software was used to introduce data. Independent sample *t*-test and chi-square or Fischer tests were used for the analyses. A *P* value < 0.05 was regarded as statistically significant. Odds ratios (OR) and 95% confidence intervals (CI) were estimated.

RESULTS

H. pylori was found in 42(41.1%) HIV-infected patients and in 53 (49.5%) non-HIV patients (*P* = 0.22; NS).

Among the HIV-positive population coinfecting with *H. pylori*, the mean CD4 count was higher than in those HIV-infected individuals without *H. pylori*, 364 and 228 cells/mm³, respectively (*P* = 0.0001; OR = 0.44; 95% CI, 0.28–0.69) (Table 2).

Only 10 opportunistic infections (OI) were detected in HIV-infected patients with *H. pylori* infection (1 *Cryptosporidium* and 1 cytomegalovirus in gastric mucosa and

TABLE 2. HIV-INFECTED PATIENTS AND *H. pylori* (Hp) STATUS RELATED TO CD4 COUNT AND CONCOMITANT OPPORTUNISTIC INFECTIONS (OI)

| | <i>Hp</i> present | <i>Hp</i> absent | <i>P</i> value |
|---------------------|-------------------|------------------|----------------|
| CD4/mm ³ | 364 | 228 | 0.0001 |
| OI | 10 (23.8%) | 27 (45%) | 0.02 |

TABLE 3. *H. pylori*-ASSOCIATED GASTRIC LESIONS IN HIV-INFECTED PATIENTS (HIV+) AND IN CONTROLS (HIV–)

| | HIV+ | HIV– |
|------------------------|------|------|
| <i>n</i> | 42 | 53 |
| Hp Only in antrum* | 5 | 5 |
| only in fundus* | 7 | 4 |
| In antrum & Fundus* | 30 | 44 |
| Lymph follicles* | 21 | 23 |
| Intestinal metaplasia* | 6 | 6 |
| Atrophy* | 7 | 2 |
| Mild Gastritis† | 2 | 12 |
| Moderate* | 17 | 33 |
| Severe‡ | 23 | 8 |

*NS.

† $\chi^2 = 4.62$; *P* = 0.03; OR = 0.17; 95% CI, 0.02–0.89.

‡ $\chi^2 = 15.02$; *P* = 0.0001; OR = 6.81; 95% CI, 2.36–20.24.

8 esophageal candidiasis), while in HIV-infected patients without *H. pylori*, 27 OI were diagnosed (*P* = 0.02; OR = 0.38; 95% CI, 0.19–0.99) (Table 2).

Gastric lesions were more severe in HIV-positive patients infected with *H. pylori* than in HIV-negative patients with *H. pylori* ($\chi^2 = 15.02$, *P* = 0.0001). The findings of atrophy, intestinal metaplasia, and lymphatic follicles in gastric mucosa were similar in both groups (Table 3).

There was no statistically significant difference between *H. pylori* presence in gastric mucosa and symptoms, medications (including antibiotics, antiinflammatories, and HAART), risk factors for HIV infection, and HIV viral load.

DISCUSSION

In the present study we demonstrated that the prevalence of *H. pylori* infection in HIV-infected patients at our hospital was similar to that found in HIV-negative individuals. Previous reports (26–27, 28) seem to have underestimated the prevalence of *H. pylori* infection in HIV-positive patients. Marano *et al.* (13) concluded that in HIV-infected patients with histologic chronic active gastritis, *H. pylori* is found at a much lower frequency than in HIV-negative patients, and they added that impaired acid secretion in AIDS may reduce the colonization of gastric mucosa by the bacteria. Benz *et al.* (19) also reported that, although in HIV-positive patients active chronic gastritis is predominantly related to *H. pylori* infection, its prevalence is significantly reduced compared to that in HIV-negative controls.

Our results seem to be comparable to those reported by Nielsen and Anderesen (12) and by Sud *et al.* (18), who found evidence of *H. pylori* infection in 48% of a series of 73 HIV-infected subjects.

In Argentina high rates of *H. pylori* infection are related to poor social and economic conditions, low levels of education, and older age, with the highest frequency in the fifth decade of life (9, 10). Since HIV-infected and non-HIV-infected individuals assisted at our hospital come from the same urban area and belong to the same social class, we only had to match them according to age to demonstrate that the prevalence of *H. pylori* infection was equivalent in both groups, regardless of the HIV condition.

A low CD4 count, more than HIV status itself, has been linked to less frequent *H. pylori* infection (21, 29). In agreement with previous publications (17–19), we found that HIV-infected patients with a *H. pylori* have a higher mean CD4 count than HIV-infected patients without *H. pylori* (364 and 228 cells/mm³, respectively; $P = 0.0001$). The *H. pylori* group also had fewer OI ($P = 0.02$; Table 2).

It is well known that CD4 cells play a role in inducing gastritis and that this gastritis may be a mechanism by which *H. pylori* colonization is enhanced (21). Adults with HIV infection and/or a low CD4 count would then lose this mechanism by which *H. pylori* colonization is sustained, and infection intensity would diminish. Low CD4 counts are apparently associated with low-grade *H. pylori* infection (20, 21, 26, 27).

The T-cell response to the organism could serve to induce or perpetuate tissue and epithelial damage. In AIDS patients, the deteriorated T-cell function would induce a decreased incidence of *H. pylori* gastritis (30–32). HIV-positive subjects with high CD4 levels should display the same prevalence of *H. pylori* infection as the general population in that particular geographic area.

Despite *H. pylori* infection, HIV-infected individuals, as children, might be protected from the development of diseases, such as gastric or duodenal ulcers. This is probably the consequence of lower IFN- γ secretion capacity of their mucosal lymphocytes (3, 21, 33, 34). In our series, there was only one HIV-infected patient with peptic ulcer, and three in the control group (NS).

Although inflammation of the gastric mucosa was always present when *H. pylori* was detected, gastritis was more severe in HIV-positive patients (Table 3). We do not have a clear explanation for these findings, and further studies on gastric mucosa immunologic system changes in HIV and *H. pylori* coinfection would be of great interest.

Finally, the frequent use of antibiotics in AIDS has been implicated in the lower rate of *H. pylori* infection observed (11, 30). These drugs would lead to eradication of the bacteria; however, the antibiotics most commonly used in AIDS patients are not always efficacious against *H. pylori*, and they could only be responsible for ameliorating the infection, not eradicating it (11, 30). We found no statistic

association between previous antibiotic ingestion and *H. pylori* status in our patients.

CONCLUSIONS

The frequency of *H. pylori* in the gastric mucosa of HIV-infected patients who underwent upper endoscopy at our hospital was similar to that found in non-HIV patients. The group of HIV-infected patients with *H. pylori* had a statistically significant higher mean CD4 count than those without *H. pylori*. Gastric lesions related to *H. pylori* were found at the same frequency in both groups, though gastritis was more severe in the HIV group.

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