# The presence of Helicobacter pylori in cervical preinvasive lesions

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**Summary**

*Purpose: Helicobacter pylori (H. pylori)* is believed to play a role in several gynecological and obstetric pathologies since the cervical mucosa resembles the gastric environment. The microorganism is expected to infect the upper genital tract via the oral-genital and fecal-genital routes. *Methods:* We studied 35 cases with benign, ASCUS, ASC-H, LSIL and HSIL pap-smear results. The presence of *H. pylori* in the uterine cervix and active infection were investigated with the H. pylori stool antigen test. Biopsy specimens were stained with hematoxylin-eosin and Warthin-Starry stains to find *H. pylori* in cervical tissue. Seroprevalence was investigated by using ELISA for *H. pylori* IgG and IgA. *Results:* The *H. pylori* seroprevalence was 65.7%; further, 17.1% of the cases had an active infection. *H. pylori* was not found in the cervix or the cervicovaginal secretions. *Conclusion:* The cervix is not a reservoir for *H. pylori*, and the microorganism does not appear to be transmitted through the fecal-genital route.

*Key words:* Helicobacter pylori; Cervix.

## Introduction

*Helicobacter pylori (H. pylori)* infects more than half the human population all over the world [1]. Its prevalence differs according to socioeconomic status, geography, ethnicity, age, and hygienic precautions [2, 3]. In developing countries the rate of infection among children under eight years of age is 10% per year and 70-90% of adults are already infected with the bacteria. Population studies in Turkey revealed that *H. pylori* seropositivity is 60% among the age group of six months to two years and 86% among the two to five year-old age group [4].

*H. pylori* is detected within the gastric fluid, saliva, feces, dental plaques, and nails [5-9]. Animals, food, and water are the other sources of infection [10]. Bacteria are transmitted through the oral-oral and iatrogenic (e.g., endoscopy, laryngoscopy) routes and due to environmental factors [11, 12].

Gürbüz *et al.* observed 90% *H. pylori* positivity in dental plaque and 86% positivity in the stomachs of chronic dyspepsia patients [13]. The persistence of the bacteria in dental plaque following the eradication from the stomach was an important finding of this study.

*H. pylori* seropositivity at an early age is one of the major factors in the etiopathogenesis of peptic ulcers, gastric adenocarcinoma, and gastric primary B-cell lymphoma [14-17]. The Eurogast study has revealed a correlation between the prevalence of *H. pylori* seropositivity and the incidence and mortality of gastric cancer [14].

*H. pylori* locomotes with its flagella and can pass through the mucosa to colonize under this layer. This new environment with a high pH level protects the microorganism from the bactericidal effect of gastric acid. High amounts of urease produced by the bacteria lead to bicarbonate and ammonium accumulation, which facilitate the colonization by further increasing the pH of the environment.

The female genital tract has been investigated for the presence of *H. pylori* a few times previously. Because it has structural similarities to the stomach, we aimed to investigate the presence of *H. pylori* in cervical preinvasive lesions in this study.

## Materials and Methods

This study was performed at the Uludag University Medical Faculty, Department of Obstetrics and Gynecology, and approved by the ethical committee of the university. Informed written consent was obtained from the patients. Thirty-five patients with indications for colposcopy were included in the study. The presence of *H. pylori* in the cervix was investigated by brush cytology and histopathology. The *H. pylori* stool antigen test (Premier Platinum HpSA; Meridian, Bioscience, USA) was used to determine the presence of active infection, and the standardized test was used to investigate the presence of bacteria in cervicovaginal secretions for possible fecal transmission. Serum *H. pylori* IgA EIA and IgG EIA (IBL, Hamburg) antibodies were measured by ELISA to determine the status of bacterial infection.

Colposcopy was performed for all patients and biopsy specimens were taken from suspicious areas. Hematoxylin-eosin and Warthin-Starry stains were used for histopathological diagnosis and *H. pylori* detection by 100× immersion microscopy. Endocervical samples were obtained with a brush, and smears were prepared on two separate slides for examination with the same stains.

Statistical analysis was performed by using the Statistics Package for Social Sciences (SPSS 13.0), and $p \leq 0.05$ was accepted as significant.

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## Results

The mean age of the patients was 36.54 ± 8.73 years (± SD), and the mean age of marriage was 20.17 ± 2.45 years (± SD). The mean gravida was 2.05 ± 1.16 (± SD) and the mean parity was 1.57 ± 0.91 (± SD).

Twenty-four (66.5%) of the patients were using the following contraceptive methods: 55% were using coitus interruptus; 33%, condoms; 9%, oral contraceptives; 4%, tubal ligation; and 4%, intrauterine devices.

Regarding the cervical smears, 23% were benign; 46%, atypical cells of undetermined significance (ASCUS); 8%, high-grade ASC (ASC-H); 14%, low-grade squamous intraepithelial lesion (LSIL); and 9%, high-grade (H) SIL. Of the histopathological specimens, 23 (66%) were chronic cervicitis; two (6%), cervical intraepithelial neoplasia (CIN) 1; two (6%), CIN 2; two (6%), CIN 2-3; one (3%), invasive squamous carcinoma; and five (13%) had no abnormality.

The distribution of the histopathological results according to the cytology results is shown in Table 1.

Table 1. — *Cytological and histopathological results of the patients.*

| Cytology | Histopathology | N | % |
|---|---|---|---|
| Benign | No abnormality | 3 | 37.5 |
| (n = 8) | Chronic cervicitis | 5 | 62.5 |
| ASCUS | No abnormality | 2 | 12.5 |
| (n = 16) | Chronic cervicitis | 12 | 75 |
| | CIN 1 | 1 | 6.2 |
| | CIN 2 | 1 | 6.2 |
| ASC-H | Chronic cervicitis | 2 | 66.7 |
| (n = 3) | Invasive carcinoma | 1 | 33.3 |
| LSIL | Chronic cervicitis | 4 | 80 |
| (n = 5) | CIN 2 | 1 | 20 |
| HSIL | CIN 1 | 1 | 33.3 |
| (n = 3) | CIN 2–3 | 2 | 66.7 |

Patients with histopathological diagnoses of CIN 1, CIN 2, and CIN 2-3 were treated with the loop electrosurgical excision procedure (LEEP), and one with the histopathological diagnosis of invasive carcinoma underwent radical hysterectomy. One of the CIN 1 patients who underwent LEEP had the postoperative diagnosis of *in situ* carcinoma with positive margins. She subsequently underwent cold-knife conization, and she was pronounced surgical-margin free. Two other patients who underwent LEEP with the histopathological diagnosis of CIN 2-3 had the same postoperative diagnosis; however, they too needed cold-knife conization to achieve surgical margins free of disease. Three patients were treated with cryotherapy.

The overall *H. pylori* seroprevalence was 65.7%; further, 17.1% of the patients were found to have active infection (Table 2).

Pearson's chi-square test revealed a significant association between the presence of active infection and the IgA antibodies ($p = 0.005$) (Table 3).

*H. pylori* could not be detected within the cervical smears, histopathological samples, endocervical mucosa, or the cervicovaginal secretions.

Table 2. — *Helicobacter pylori serum antibody and stool antigen test results of the patients.*

| Test | N | % |
|---|---|---|
| *Helicobacter pylori serum* | | |
| IgG (+) | 23 | 65.7 |
| IgG (–) | 12 | 34.3 |
| *Helicobacter pylori serum* | | |
| IgA (+) | 12 | 34.3 |
| IgA (–) | 23 | 65.7 |
| *Helicobacter pylori stool* | | |
| Antigen (+) | 6 | 17.1 |
| Antigen (–) | 29 | 82.9 |

Table 3. — *Helicobacter pylori serum IgA and stool antigen test results of the patients.*

| | Serum H. pylori IgA (+) | Serum H. pylori IgA (-) | Total |
|---|---|---|---|
| *H. pylori* stool antigen test (+) | 5 | 1 | 6 |
| *H. pylori* stool antigen test (–) | 7 | 22 | 29 |
| Total | 12 | 23 | 35 |

## Discussion

In developing countries, *H. pylori* is one of the most common infections. The cervix has a structure similar to that of the stomach with respect to mucinous columnar cells and the surrounding acidic environment. Particularly, the ectopic endocervical columnar epithelium may be a perfect harbor for *H. pylori*.

Another common microorganism, the human papilloma virus (HPV), is known to be transmitted through oral sex and causes esophageal neoplasia and nasopharyngeal papillomatosis [18]. Similar to HPV, *H. pylori* can infect the cervix during oral or anal sex or viral shedding during defecation.

Most of the studies regarding the sexual transmission of *H. pylori* are concentrated on oral-to-oral transmission among homosexual males. Aceti *et al.* has demonstrated that the sexual behavior of homosexual males facilitates the colonization of *H. pylori* and that heterosexual males with similar behaviors are also at increased risk of *H. pylori* infection [19]. It has been demonstrated that the partner of an infected individual has a higher prevalence of *H. pylori* than does the general population [20-23].

*H. pylori* has been isolated in saliva, dental plaque, feces, and nails [6-9]. Eslick has classified the sexual transmission routes of *H. pylori* as oral-oral, oral-anal, and oral-genital as also through masturbation and the usage of sex toys [24]. Figura *et al.* investigated infertile couples for the presence of *H. pylori* infection [25]. They found a significantly increased prevalence of infection in infertile couples as compared with the control group. Among the infected patients in the study group, all follicular fluid samples and 50% of the sperm samples were positive for *H. pylori* antibodies. Only a minority had such antibodies in vaginal secretions.

Infected sexual partners may create a problem for the fetus during gestation. Previous studies have reported that *H. pylori* can infect the fetus during gestation via vertical transmission [26-28]. Raymond *et al.* isolated *H. pylori* in

a newborn infant suffering from vomiting and weight loss on the sixth day of life [29]. Fijumuro *et al.* detected *H. pylori* DNA in the feces of 30% of a group of 50 3-day-old newborns [30].

In our study, in order to detect the active infection, we used the *H. pylori* stool antigen test, which has a sensitivity and specificity greater than 90% [31]. We detected active infections in 17.1% of our patients. We used brush cytology, which has 98% sensitivity and 96% specificity, to detect *H. pylori* in the endocervical canal [32]; however, there were no positive findings. Although there have been a couple of studies focused on the detection of *H. pylori* in the vagina, none of these have investigated cervical lesions for the presence of the organism. Histopathological methods have been reported as 95-99% specific and 93-99% sensitive for *H. pylori* [33]. In our study, we performed colposcopy-directed biopsies to look for the bacteria in the histopathology of the suspicious areas but detected no *H. pylori* infection.

## Conclusion

We were unable to detect *H. pylori* in cervical cytology and histopathological samples. Moreover, the standardized stool *H. pylori* antigen tests for cervicovaginal secretions were negative. We concluded that *H.pylori* does not appear to colonize the cervix with preinvasive lesions.

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