Increased Susceptibility to *Helicobacter pylori* Infection in Pregnancy

S. Lanciers,^{1,2} B. Despinasse,¹ D.I. Mehta,³ and U. Blecker^{2,3}

¹Division of Pediatric Gastroenterology, Louisiana State University Medical Center,
New Orleans, LA

²Division of Pediatric Gastroenterology, Academic Children's Hospital, Free University of
Brussels, Belgium

³Division of Pediatric Gastroenterology, Alfred I. duPont Hospital for Children, Wilmington, DE

ABSTRACT

Objective: *Helicobacter pylori* plays a major role in abdominal symptoms and gastroduodenal pathology, including gastric cancer. Pregnancy has been associated with changes in both humoral and cell-mediated immunity. These changes include alterations in the various classes of antibodies during different gestational periods. It has been previously suggested that these alterations may expose pregnant women to an increased risk of infection with this microorganism.

Methods: To further investigate this hypothesis, we assayed sera from 229 asymptomatic pregnant women for the presence of *H. pylori*-specific immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies by means of a commercially available serum ELISA test (Malakit™, Biolab, Belgium). Both tests were previously validated in large series of *H. pylori*-positive and -negative subjects. While the presence of *H. pylori*-specific IgG antibodies is only a marker for a "chronic" infection with this bacterium and therefore no indicator of the time of acquisition of the infection, specific IgM antibodies are a more specific marker for a recently acquired infection with *H. pylori*. Results were compared with those previously obtained in asymptomatic, healthy, nonpregnant individuals.

Results: One hundred twenty of 229 women (52.4%) and 55/118 nonpregnant subjects (46.6%) were seropositive for *H. pylori*-specific IgG antibodies ($P > 0.3$). Out of these 120 IgG-antibody-positive women, 36 (30%) were positive for *H. pylori*-specific IgM antibodies, as were 25/109 (22.9%) in the IgG-antibody-negative group ($P > 0.3$). Overall, 61/229 (26.6%) of the pregnant women had recently been infected with *H. pylori*, compared with 11% of the healthy, nonpregnant population ($P > 0.01$).

Conclusions: Our observations confirm the possibility of an increased susceptibility to *H. pylori* infection in pregnancy. Additional studies are necessary to further understand the immune response to *H. pylori* in pregnancy. Infect. Dis. Obstet. Gynecol. 7:195–198, 1999.

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KEY WORDS

Helicobacter pylori; pregnancy; serology; IgM; IgG; ELISA; infection

Helicobacter pylori has been found to be the major cause for gastroduodenal pathology, both in adults^{1,2} and in children,^{3, 4} a finding that resulted in a new understanding of and approach to

chronic active gastritis, duodenal ulcers, and, to a lesser degree, gastric ulcers.

The exact route of transmission of *H. pylori* is still not well understood. We know that the human

Correspondence to: Uwe Blecker, MD, Department of Gastroenterology, Alfred I. duPont Hospital for Children, 1600 Rockland Road, P.O. Box 269, Wilmington, DE 19899. E-mail: ublecker@nemours.org

body is the only natural reservoir for *H. pylori* and that, therefore, person-to-person transmission is the most likely method of transmission.⁵ A number of factors, such as crowding index,⁶ low socioeconomic status,⁷ an infected family member,⁸ and ethnicity,⁹ have all been linked to a higher incidence of *H. pylori* infection.

Recently it has been suggested that this bacterium might play an important role as a cofactor in the development of gastric adenocarcinoma^{10,11} and lymphoma.^{12,13} *H. pylori* infection increases with advancing age.¹⁴ We previously demonstrated that *H. pylori* infection is also present in symptom-free subjects, both in children¹⁵ and adults.¹⁶

Pregnancy has been associated with changes in both humoral and cell-mediated immunity. Although not yet completely understood, these changes include alterations in the various classes of antibodies during different gestational periods, which may lead to an increased susceptibility to certain infections.¹⁷ Our study was designed to explore whether pregnant women are at an increased risk for acquiring *H. pylori* infection due to immunological changes that occur during pregnancy.

To minimize potential differences in risk factors between the investigated groups, all subjects were pooled from the same population and matched for age and socioeconomic background.

METHODS

Patients

We investigated 229 healthy pregnant women (ages 20 to 40 years) and 118 healthy nonpregnant women (ages 18 to 40 years) for the presence of *H. pylori*-specific antibodies. The subjects were Caucasians of middle to upper socioeconomic class and background and were matched for age. Both groups were asymptomatic with regard to gastrointestinal symptoms and were not taking any antibiotics, H₂-blockers, or proton pump inhibitors for at least 6 weeks. Pregnant women were tested at routine prenatal visits during their second trimester. The control group was comprised of women who were tested during routine prenatal screening. As mentioned above, the exact route of transmission and risk factors for *H. pylori* infection are still not quite understood. To minimize the impact of any such risk factors, all investigated subjects were drawn from the same population.

Serology

The sera were tested using the Malakit™ *Helicobacter pylori* series (Biolab S.A., Limal, Belgium), a solid-phase (microwells) two-step indirect ELISA method based on the sandwich principle for the detection of specific immunoglobulin M (IgM) or immunoglobulin G (IgG) antibodies to *H. pylori* in human sera. This assay uses fractionated and purified antigens for *H. pylori*. During the first step, samples and controls are diluted 1:200 and incubated in microwells at 37°C for 45 minutes to form an *H. pylori* antigen/anti-*H. pylori*-antibody complex. The unbound components are washed off. In the subsequent incubation (at 37°C for 45 minutes), a rabbit anti-human-IgM peroxidase conjugate is added to react with the *H. pylori* antigen/anti-*H. pylori*-antibody complexes. Unreacted conjugate is washed off. After the addition of azinobenzthiazoline sulfonate (ABTS) and a last incubation step (at 37°C for 60 minutes), the enzymatic reaction is stopped with a fixator (NaOH).

The intensity of the green coloration is measured at 405 nm and is directly proportional to the amount of anti-*H. pylori* antibodies in the sample. A positive control giving an absorbency higher than 1,000 is used to ensure that the entire test protocol is working properly.

A positive result for *H. pylori*-specific IgM antibodies by this ELISA technique was defined as an IgG level two or more standard deviations above the mean of all negative IgG and IgM titers previously obtained by the company (company's unpublished data) and our group.^{18,19}

Statistics

The Fisher exact test was used for statistical calculations.

RESULTS

One hundred twenty of 229 pregnant (52.4%) and 55/118 (46.6%) nonpregnant women were positive for *H. pylori*-specific IgG antibodies ($P > 0.3$). Out of the 120 IgG-antibody-positive pregnant women, 36 (30%) were positive for *H. pylori*-specific IgM antibodies, as were 25/109 (22.9%) in the IgG-antibody-negative group ($P > 0.3$).

In the nonpregnant control group, 8/55 (14.5%) IgG-positive and 5/63 (7.9%) IgG-negative subjects were positive for *H. pylori*-specific IgM antibodies.

Overall, 61/229 (26.6%) of the pregnant women

had recently been infected with *H. pylori*, as defined by positivity for specific IgM antibodies, compared with 13/118 (11%) in the nonpregnant population ($P > 0.01$). This reflects a relative risk of 2.21 (95% confidence interval, 2.02–2.40) of becoming infected with *H. pylori* during pregnancy ($P > 0.01$).

DISCUSSION

Pregnancy is associated with a number of modifications and adaptations. Although it has been well established that immunoregulation and immunomodulation occur during pregnancy, it is important to fully understand the effects these changes have on a pregnant woman's susceptibility to infectious agents. In this study we sought to elucidate whether pregnant women are at an increased risk for acquiring *H. pylori* infection.

Prior studies have confirmed the prevalence of *H. pylori* seropositivity in asymptomatic children and adults.^{15,16} *H. pylori* has been linked to chronic gastritis, peptic ulcer disease and, to a lesser extent, gastric adenocarcinoma and gastric lymphoproliferative disease, specifically low-grade B-cell lymphoma.^{1,10,12,20} In view of the important pathogenesis of *H. pylori*, it is important to investigate the maternal history of *H. pylori* infection in *H.-pylori*-positive pregnant women.

Recently, we investigated the role of passive immunity and the evolution of *H. pylori* infection in children born to mothers with active *H. pylori* infection from parturition to twelve months of age. We were able to demonstrate that these infants do not appear to have an increased risk of developing *H. pylori* infection during their first year of life.²¹

Looking at asymptomatic women in both the pregnant and control groups, the pregnant women in our study had a significantly higher relative risk of acquiring the disease. Therefore, this study confirms the possibility of an increased risk of acquiring *H. pylori* infection during pregnancy.

The presence of *H.-pylori*-specific IgG has not been shown to be protective. In addition, both groups had comparable prevalences for anti-*H.-pylori* IgG antibodies. This excludes the possibility of IgG titers as a cause for the increased incidence of specific IgM antibodies in our pregnant population.

During pregnancy, physiologic alterations occur that increase the potential for gastrointestinal

symptoms; in late pregnancy the rise in serum progesterone levels causes lower esophageal sphincter tone to decrease.¹⁷ Additionally, intragastric pressure increases and the intraesophageal pressure decreases while gastric pH and gastric acid output remain unchanged.¹⁷ But pregnancy may also convey a relative protective effect against the formation of peptic ulcer disease. With the above noted, there remains the possibility that the well-known increased incidence of gastrointestinal symptomatology during pregnancy²² is related to *H. pylori* disease. Recently it has been suggested that *H. pylori* infection may cause hyperemesis gravidarum.²³

Follow-up studies are needed to delineate the pregnant women's complete immune response in the face of infection with *H. pylori*. As we better understand the pregnant host's immune response, it will aid in the prevention of future disease through possible prenatal screening exams and vaccination programs, as well as possible pharmacotherapy and immunotherapy alternatives.

Based on our findings of an increased incidence of *H. pylori* infection during pregnancy, further studies may be required to investigate the indication of screening for *H. pylori* in pregnant women.

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