SEROPREVALENCE OF HELICOBACTER PYLORI AMONG EGYPTIAN NEWBORNS
AND THEIR MOTHERS: A PRELIMINARY REPORT

SAMIR BASSILY, ROBERT W. FRENCK, EMAD W. MOHAREB, THOMAS WIERZBA, STEPHEN SAVARINO,
ERIC HALL, AMIRA KOTKAT, ABDOLLAH NAFICY, KENNETH C. HYAMS, AND JOHN CLEMENS
U.S. Naval Medical Research Unit No. 3, Cairo, Egypt; High Institute of Public Health, Alexandria, Egypt;
National Institutes of Health, Bethesda, Maryland; U.S. Naval Medical Research Institute, Bethesda, Maryland

Abstract. Helicobacter pylori is one of the most common human bacterial infections in the world and children in the
developing countries acquire H. pylori infection early in life. We prospectively evaluated the prevalence of serum
antibodies to H. pylori in a cohort of pregnant women and their offspring. Mothers’ sera were collected during the
third trimester of pregnancy and sera from their offspring were collected when they were 7–9 months and 18 months
of age. Pylori-Stat®, a commercially available ELISA kit, was used to detect antibodies to H. pylori in the serum of
the subjects tested. Sera from 169 mothers were available for testing and 88% of these samples were positive for
anti-H. pylori IgG. Of the 169 children tested, 13% of the infants 7–9 months of age and 25% of the children 18
months of age had serologic evidence of H. pylori infection. These data indicate that infection with H. pylori is
common in Egypt and acquisition of infection occurs at a very young age.

Identification of the gram-negative, spiral gastric bacteria Helicobacter pylori occurred only a little more than a decade
ago. Despite the initial skepticism regarding the pathogenic importance of this organism, it is now recognized that in-
fec tion with H. pylori is associated with some of the most common clinical problems in medicine. Helicobacter pylori
is a cause of chronic-active gastritis and a majority of cases of peptic ulcer disease. It is also associated with the de-
velopment of gastric adenocarcinoma, the fourth most common malignancy in the world. Numerous studies have
demonstrated that H. pylori infection is ubiquitous, with approximately 50% of the world’s population infected. How-
ever, the prevalence, timing of acquisition, and the symptoms and sequelae of infection differ in developed compared
with developing countries.

In the developed world, infection during childhood is uncommon. Less than 5% of children less than five years of
age in the United States are infected with H. pylori, and by adolescence only about 10% of the population is infect-
ed. After adolescence, the prevalence of H. pylori infection increases 0.5–1% per year and peaks at approximately 50–
60% by 60 years of age in the United States.

In contrast, H. pylori infections in the developing world appear to occur earlier in life and with a higher frequen-
cy. Approximately half of the children living in developing areas are infected by five years of age, and infection
rates as high as 90% have been reported by early adulthood. While data regarding the prevalence of H. pylori
infection have been collected from many geographic regions, no information exists regarding infection rates in Egypt. The
current study is the first known report describing the sero-
prevalence of H. pylori infection in Egypt among mothers and their children.

MATERIALS AND METHODS

The study was designed to use banked sera and epide-
miologic data collected in 1992 during a prospective study of the immunogenicity of hepatitis B recombinant vaccine
among Egyptian newborns.

Study population. The population was comprised of clin-
ically healthy pregnant women receiving prenatal care at a
Ministry of Health Center for Maternal and Child Health Care in Alexandria, Egypt. All women receiving care at the Center were eligible for enrollment into the vaccine trial after providing informed consent. Subjects were excluded from the study if 1) they had evidence of past infection with hepatitis B virus or 2) they were unable or did not agree to have their infants vaccinated or have blood collected from their infants as per guidelines of the protocol.

Five hundred ninety mothers and their infants were in-
cluded in the original study. More than 90% of the subjects adhered to protocol requirements and were followed for 7–
9 months. Approximately 60% of the vaccinated children completed the entire 18-month follow-up period. Informed
consent was obtained from all subjects. The study was per-
formed according to the guidelines of the Committee for the Protection of Human Subjects at the U.S. Naval Medical
Research Unit No. 3 in Cairo, Egypt.

Demographic information. A standardized questionnaire
was administered to all expectant mothers when they en-
rolled in the hepatitis B study. Information collected includ-
ed maternal age, socioeconomic status, education level, cur-
rent living conditions, the number of past pregnancies, num-
ber of prior live births, number of currently living children,
and the planned method of feeding of the infant.

Specimen collection and testing. Blood was collected
from mothers during the third trimester of pregnancy. Infants
had blood collected at 7–9 months of age and at 18 months
of age. After collection, the blood was allowed to clot, and
the serum was separated and stored at −70°C until labora-
tory testing was performed.

Helicobacter pylori testing was performed whenever suf-
ficient sera existed from both the mother and her infant at
7–9 and 18 months. Of the 421 women entered in the origi-
 nal hepatitis B study, H. pylori testing could be performed on 169 women and their infants.

Detection of antibodies to H. pylori. Serum IgG antibodi-
es against H. pylori urease were detected using a commer-
cial ELISA. All testing was performed according to the man-
ufacturer’s instructions (Pylori-Stat® kit; BioWhittaker,
Walkersville, MD). All sera were tested blindly and data
were analyzed anonymously without linkage to personal
identification.
The predicted index value (PIV) of test samples were determined automatically with an ELISA plate reader using the measured optical density from a standard curve. Samples with a PIV $\geq 1.0$ were considered positive, while a PIV $< 0.80$ was considered negative. Samples with a PIV between 0.8 and 0.99 were considered equivocal. All equivocal samples were retested. Equivocal sera giving positive results on retesting were considered positive; those with negative or equivocal results on retesting were classified as negative. Compared with gastric biopsy results, the Pylori-Stat test kit has been found to have a sensitivity of 96%, a specificity of 94%, a positive predictive value of 90%, and a negative predictive value of 98%.

Definitions. Mothers and children $\geq 18$ months of age were considered infected with \textit{H. pylori} if they were seropositive by ELISA testing. Children 7–9 months of age were considered infected with \textit{H. pylori} if antibodies to \textit{H. pylori} in their serum were defined as indeterminant due to the possibility that the antibody was due to transplacental passage from the child’s mother.

Statistical methods. The chi-square test, or Fisher’s exact test when data were sparse, were used to examine associations between seropositivity and categorical variables. A multivariate logistic regression model was used to test the association between binary outcomes and independent variables that were statistically significant on univariate analysis. All statistically significant relationships were two-tailed and evaluated at $P < 0.05$. Analyses were conducted using either Epi-Info version 6.0\textsuperscript{19} or SAS version 6.12.\textsuperscript{20}

RESULTS

Four hundred twenty-one women and their children were enrolled in the original hepatitis B study. From this group, serum was available from 169 mother/infant pairs for \textit{H. pylori} testing. Review of the demographics of the untested group showed that they were similar to the group that was tested. The median age of mothers was 25 years (range = 17–42 years). Including the most recent pregnancy and delivery, their median gravidity was three pregnancies (range = 2–8), with a median of two children living at home (range = 1–6). All the women were married, typically of the middle socioeconomic class, and resided in Alexandria, Egypt. Sixty-three percent (107 of 169) of the women had at least a primary school education. The remaining 37% were illiterate. All women in the study lived in homes with municipal pipe water, which was used for drinking and cooking.

Of the 169 mothers tested, 148 (88%) were seropositive for \textit{H. pylori} IgG antibodies. Although maternal age, number of pregnancies, and number of past deliveries were not associated with the serostatus of the mother, maternal level of education was related (Table 1). Ninety-three percent of the educated mothers were infected with \textit{H. pylori} compared with 79% of the mothers without formal education ($P = 0.01$). The significant relationship between maternal education and \textit{H. pylori} serostatus remained after adjusting for age of the mother.

At 7–9 months of age, 13% (22 of 169) of the children were positive for antibodies to \textit{H. pylori}; by 18 months of age, positivity had increased to 25% (42 of 169). Forty-five percent of the children with antibodies to \textit{H. pylori} at 7–9 month of age were seronegative at 18 months. In contrast, 20% of the children who were seronegative at 7–9 months had become infected by 18 months of age.

Multiple variables were examined in an attempt to determine predictors of \textit{H. pylori} infections among the 18-month-old children. While not statistically significant, there was a trend between maternal serostatus and her baby becoming infected with the \textit{H. pylori} during infancy. At 18 months after delivery, 27% (40 of 148) of the babies born to seropositive mothers were infected compared with 9.5% (2 of 21) of babies born to seronegative mothers ($P = 0.08$). Factors not associated with early childhood infection with \textit{H. pylori} included maternal age, the gravidity and parity of the mother, and the gender of the child.

DISCUSSION

This study provides the first data regarding the seroprevalence of \textit{H. pylori} infections in Egypt. The finding that 88% of the women tested had antibody to \textit{H. pylori} was consistent with the high prevalence of infection in other developing areas.\textsuperscript{12} Infection rates of 85% were noted in a study from Nigeria,\textsuperscript{21} and rates of 80–90% have been documented in studies from Algeria and Ivory Coast. These high infection rates are in marked contrast to infection rate in the United States.\textsuperscript{22}

Our study also demonstrated that Egyptian children appear to acquire infections with \textit{H. pylori} early in life and the number of infected children increases rapidly with age. Serologic evidence as a marker for infection with \textit{H. pylori} is reasonable for epidemiologic studies. However, since the test does not provide direct evidence of current infection, results may at times be difficult to interpret. A major problem arises when evaluating serum of newborns. Due to the transplacental passage of IgG, babies born to infected mothers will also have antibodies to \textit{H. pylori} in their blood at birth. Maternal antibodies to \textit{H. pylori} tend to disappear quickly in children and by four months of age few children still possess maternally acquired antibody.\textsuperscript{23} However, maternal antibody may wane more slowly in some infants. Therefore, in the present study, while the 13% seroprevalence for antibodies to \textit{H. pylori} in 7–9-month-old children may indicate a high infection rate, it was impossible to conclusively differentiate between passively acquired and actively produced antibodies to \textit{H. pylori}. Spontaneous acquisition and elimination of \textit{H. pylori} infection, especially in young infants may explain the

<table>
<thead>
<tr>
<th>Table I</th>
<th>A comparison of maternal characteristics and \textit{Helicobacter pylori} serologic status</th>
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<tbody>
<tr>
<td>Maternal characteristics</td>
<td>\textit{H. pylori} infection</td>
</tr>
<tr>
<td>Median age in years (range)</td>
<td>Seronegative (n = 21$^*$)</td>
</tr>
<tr>
<td>25.0 (19–39)</td>
<td>25.0 (17–42)</td>
</tr>
<tr>
<td>Median gravidity (range)</td>
<td>3 (2–6)</td>
</tr>
<tr>
<td>Median parity (range)</td>
<td>2 (1–5)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Formal (n = 107)</td>
<td>8 (7%)</td>
</tr>
<tr>
<td>None (n = 62)</td>
<td>13 (21%)</td>
</tr>
</tbody>
</table>

* One was equivocal on initial testing.
† Four were equivocal on initial testing.
‡ P = 0.01.
seroconversion in 10 of 22 seropositive infants from 7–9 months to 18 months of age.\textsuperscript{24,25} To definitively diagnose \textit{H. pylori} infection in children 7–18 months old, more sophisticated studies, including gastric biopsy or urea breath testing, would be needed and this was beyond the scope of our study. However, the 25% prevalence rate for antibodies against \textit{H. pylori} in the 18-month-old children represents true infection and parallels similar high rates of infection noted in children from other parts of the developing world.\textsuperscript{12,21}

In addition to determining seroprevalence, we were able to examine potential risk factors for acquiring \textit{H. pylori}.\textsuperscript{26,27} We found that increased education was significantly associated with an increased risk of infection among mothers. This finding is in contrast to a previous report from Saudi Arabia in which 77% of non-college graduates were infected with \textit{H. pylori} compared with 54% of college graduates.\textsuperscript{28} A potential explanation for our results is increased transmission from Egyptian schools where average classroom size is up to 60 children. The association between crowding and increased prevalence of \textit{H. pylori} infection has been demonstrated in many studies. In both the United States and Bangladesh, crowding in the home was significantly associated with \textit{H. pylori} infection.\textsuperscript{22,29} Another study demonstrated that there was a positive association between infection with \textit{H. pylori} in adulthood and a lower socioeconomic standard of living during the childhood years, again suggesting the importance of crowding and transmission of \textit{H. pylori}.\textsuperscript{30}

An important trend in the present study was the relationship between maternal \textit{H. pylori} serostatus and the risk of infection in early childhood. Of the 148 children born to mothers infected with \textit{H. pylori}, 40 (27%) were infected at 18 months of age compared with two (9.5%) of the 21 children born to uninfected mothers. While the results fell short of statistical significance, the trend is noteworthy and warrants further evaluation. The literature is varied regarding the relationship between \textit{H. pylori} infection in mothers and their children. One study found that 82% of the children born to mothers infected with \textit{H. pylori} also became infected compared with 14% of the children with infection if their mothers were seronegative.\textsuperscript{31} However, other studies have not demonstrated an association between maternal and infant infection.\textsuperscript{22,23,32} A possible explanation for the conflicting results is that maternal seropositivity is only a surrogate marker for true risk factors, such as maternal premastication of food, family density, or poor hygienic conditions.\textsuperscript{29,34,35} Additional research is thus required to determine how maternal-infant transmission occurs.

In summary, we have demonstrated that \textit{H. pylori} infection is common in Egypt and that infection occurs early in life. Potential predictors of infection have been identified and will need to be further evaluated in future prospective studies.

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