ASSOCIATION BETWEEN SEROPOSITIVITY OF ANTIBODIES AGAINST HEPATITIS A VIRUS AND HELICOBACTER PYLORI

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Abstract. Helicobacter pylori and hepatitis A virus (HAV) are documented to share common transmission routes including fecal-oral. This study examined the association between seropositivity of antibodies against H. pylori (anti-HP) and HAV (anti-HAV) via a community-based survey of 40 randomly selected kindergartens in 10 urban and 10 rural areas. Serum samples from 2,047 healthy preschool children and 104 teachers were screened for anti-HP by enzyme-linked immunosorbent assay, and for anti-HAV by microparticle enzyme immunoassay. In children, a low prevalence of anti-HAV (0.44%) was found, in contrast to a high prevalence in their teachers (78.8%); anti-HP seroprevalence was 6.4% for children and 30.8% for teachers. Anti-HAV and anti-HP seropositivities were significantly associated in teachers after adjustment for age, sex, and residential area through multiple logistic regression analysis (multivariate-adjusted odds ratio = 7.3; 95% confidence interval [CI] = 1.4–36.8, \( P < 0.001 \)). Our findings suggest that HAV and H. pylori may have shared transmission routes in central Taiwan 15 years or more ago, but not any recently.

INTRODUCTION

Helicobacter pylori infection is related to chronic antral gastritis, which is associated with duodenal or gastric ulcer and probably also gastric adenocarcinoma.\(^1\) Close person-to-person contact under crowded living conditions during early childhood is considered a prime determinant of H. pylori infection in the very young.\(^2\)\(^-\)\(^3\) Several methods of transmission for H. pylori have been proposed, including fecal-oral and oral-oral routes.\(^4\)\(^-\)\(^6\) In developing countries, it is transmitted mainly by fecal-oral.\(^6\) However, studies in developed countries are rare.\(^7\)

Hepatitis A virus (HAV) is transmitted predominantly through the fecal-oral route. Taiwan was a hyperendemic area for HAV infection before the late 1980s.\(^11\) The seroprevalence of HAV infection was greater than 90%; most HAV infection occurred during childhood.\(^12\) A striking decline in the prevalence of HAV infection was observed among children in Taiwan.\(^13\)\(^-\)\(^15\)

If crowding and poor living conditions are the major determinant of H. pylori infection,\(^6\) then the association between H. pylori infection and other infection transmitted also through the fecal-oral route, such as HAV, deserves further investigation. HAV infection, a known sensitive marker of infection,\(^6\) then the association between seropositivity of antibodies against H. pylori (anti-HP) and HAV (anti-HAV) have been documented, suggesting a shared fecal-oral transmission common for H. pylori and HAV.\(^4\)\(^-\)\(^6\)\(^-\)\(^8\) It is the aim of this study to investigate the association between seroprevalence of H. pylori and HAV in young preschool children and their teachers.

MATERIALS AND METHODS

Study population and subject selection. In central Taiwan, including Taichung County, Taichung City, Miaoli County, Changhua County, and Nantou County, a total of 40 kindergartens in 10 urban and 10 rural areas were randomly selected; 2,047 kindergarten children and 104 teachers were recruited on a voluntary basis. A blood sample was collected from each subject, and serum specimens were kept at \(-70^\circ\)C until laboratory examination. Laboratory examination. Serum antibodies against HAV (anti-HAV) were analyzed by means of a commercially available microparticle enzyme immunoassay (AxSYM HAVAB, Abbott Laboratories, Abbott Park, IL) on an AxSYM analyzer. Serum samples with S/CO (sample rate/cutoff rate) values in the range of 0 to 1 were considered reactive for hepatitis A antibodies. Serum samples were also screened for antibodies against H. pylori (anti-HP) by enzyme-linked immunosorbent assay (ELISA). The ELISA procedure for Pyloriset EIA-G (Orion Corporation, Orion Diagnostica, Espoo, Finland) assay was performed according to the manufacturer’s instructions.\(^19\) A sample was considered positive for IgG antibodies to H. pylori if the absorbance of the serum sample was equal to or higher than that of the reference serum with the lowest positive titer. Otherwise, the sample was considered negative.

Statistical analysis. The association between seroprevalence of anti-HP and anti-HAV was examined for the statistical significance by Fisher’s exact test method. Odds ratio (OR) with its 95% confidence interval (CI) was also calculated to indicate the magnitude of the association. Multiple logistic regression analysis was used to derive multivariate-adjusted OR and its 95% CI.

RESULTS

Kindergarten children had much lower seroprevalences of anti-HP and anti-HAV than their teachers as shown in Table 1. The seroprevalence of anti-HP was similar in males and females, while females had higher anti-HAV than males. The seroprevalences of anti-HP and anti-HAV were similar in urban and rural areas.
A lack of 9 anti-HAV-seropositive kindergarten children (0%) and 132 out of 2,038 anti-HAV-seronegative kindergarten children (12.7%) were seropositive for anti-HP (OR = 0.8, 95% CI = 0.04–13.1) as shown in Table 2. However, 30 out of 82 anti-HAV-seropositive teachers (36.6%) and 2 out of 22 anti-HAV-seronegative teachers (9.1%) were anti-HP-seropositive showing an OR of 5.8 with a 95% CI of 1.4–38.6. The association between seropositivity of anti-HP and anti-HAV among teachers remained statistically significant after adjustment for residence area, age as a continuous variable, and sex through multiple logistic regression analysis (multivariate-adjusted OR = 7.3, 95% CI = 1.4–38.6).

DISCUSSION

Kindergarten children in this study were not immunized with HAV vaccine. The seropositivity of anti-HAV may reflect their accumulated incidence of HAV infection. The seroprevalence of anti-HAV among schoolchildren in Taiwan was as high as 28% in 1984.26 It was found to decrease rapidly from 89% in 1975 to 10% in 1991 among adolescents in Taipei City.24 In this study, a low prevalence of anti-HP and anti-HAV was identified among kindergarten children. Teachers born before 1980 when Taiwan was a hyperendemic area for HAV, had a much higher prevalence of anti-HAV and anti-HP. The difference in seroprevalence of anti-HAV between children and teachers was much greater than that of anti-HP suggesting that the existence of H. pylori transmission routes in early childhood that are not related to those of HAV.

Hepatitis A virus infection is a sensitive marker of fecal exposure.15 If the fecal-orale route is also significant in the transmission of H. pylori, the seroprevalence status of this bacterium should correlate with that of HAV. As shown in Table 2, there was no association between H. pylori and HAV infections in kindergarten children. The finding further suggests that there are independent transmission routes for H. pylori and HAV for children born after 1990, a finding similar to previous studies.18,21–23 On the contrary, there was a significant correlation between the seroprevalence of anti-HP and anti-HAV (P < 0.001) among teachers who were born before 1980. Showing a seven-fold risk after adjustment for age, sex, and area, anti-HP-positive teachers were more likely to be anti-HAV-seropositive than those who were anti-HP negative. This suggests that for those who were born before 1980, H. pylori infection was transmitted at least partly through the same transmission routes as HAV. However, since the seroprevalence of anti-HAV was much higher than that of anti-HP, the transmission of HAV through these common routes may be more efficient than that of H. pylori.

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