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Helicobacter pylori infection: relationship between seroprevalence and dietary preference in a rural area.

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Abstract

In order to evaluate the relationship between Helicobacter pylori (H. pylori) infection and dietary preference, a cross-sectional study was performed among 626 residents in a rural area of Japan. Seropositive rates were 88.7% in males and 71.4% in females, and these increased with age for both sexes [male $P < 0.05$ and female $P < 0.01$]. The relationship between H. pylori-seropositivities and salted-food intake, after adjustment for age, demonstrated a significant result in the "almost every day" group in males with an odds ratio (OR) of 8.39 and with 95% confidence intervals (CI) of 1.02-69.30. As regards an association between seropositivities of H. pylori and levels of serum pepsinogens for the screening of chronic atrophic gastritis (low pepsinogen values used were a pepsinogen I level below 70 ng/ml and a pepsinogen I/pepsinogen II ratio below 3.0), the ORs of H. pylori-seropositivities for low pepsinogen cases were 6.32 [95% CI: 1.42-28.03] in males and 12.72 [95% CI: 4.57-35.46] in females. With regard to the relationship between low pepsinogen cases and light-colored vegetables intake, a significant low OR for the low pepsinogen cases was obtained in the "almost every meal" group in females after adjustment for age and seropositivities of H. pylori with an OR of 0.37 and with 95% CI of 0.15-0.92.

KEYWORDS: Helicobacter pylori, chronic atrophic gastritis, dietary preference

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Helicobacter Pylori Infection: Relationship Between Seroprevalence and Dietary Preference in a Rural Area

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In order to evaluate the relationship between *Helicobacter pylori (H. pylori)* infection and dietary preference, a cross-sectional study was performed among 626 residents in a rural area of Japan. Seropositive rates were 88.7% in males and 71.4% in females, and these increased with age for both sexes [male $P < 0.05$ and female $P < 0.01$]. The relationship between *H. pylori*-seropositivities and salted-food intake, after adjustment for age, demonstrated a significant result in the "almost every day" group in males with an odds ratio (OR) of 8.39 and with 95% confidence intervals (CI) of 1.02-69.30. As regards an association between seropositivities of *H. pylori* and levels of serum pepsinogens for the screening of chronic atrophic gastritis (low pepsinogen values used were a pepsinogen I level below 70 ng/ml and a pepsinogen I/pepsinogen II ratio below 3.0), the ORs of *H. pylori*-seropositivities for low pepsinogen cases were 6.32 [95% CI: 1.42-28.03] in males and 12.72 [95% CI: 4.57-35.46] in females. With regard to the relationship between low pepsinogen cases and light-colored vegetables intake, a significant low OR for the low pepsinogen cases was obtained in the "almost every meal" group in females after adjustment for age and seropositivities of *H. pylori* with an OR of 0.37 and with 95% CI of 0.15-0.92.

Key words: *Helicobacter pylori*, chronic atrophic gastritis, dietary preference

Helicobacter pylori (H. pylori) is a curved, microaerophiric, gram-negative bacterium that was first isolated in 1983 from stomach biopsy specimens of patients with chronic gastritis (1). This discovery has resulted in a revised view of the human stomach as an environment for bacterial growth and has revolutionized our understanding of illness of the upper gastrointestinal tract of humans. Possibly, the bacterium, the host, and the environment all play important roles in the outcome of an infection. The reservoir for *H. pylori* infection is probably humans. However, the sources and the modes of transmission of *H. pylori* are not well understood, although it is suspected that the organism is passed directly from one person to another *via* feces, saliva, or vomitus. The rate of *H. pylori* acquisition is higher in developing countries than in industrialized countries (2-7). In addition, the prevalence of *H. pylori* infection varies between races and ethnic groups (4, 5, 8). The variation in prevalence of *H. pylori* infection suggests that other factors related to lifestyle are involved.

In order to determine risk factors for *H. pylori* infection and chronic atrophic gastritis (CAG), this study focused on lifestyle factors, including dietary preference, and examined the presence of immunoglobulin (Ig) G antibody to *H. pylori*; it also measured serum pepsinogen levels in a cross-sectional study. Improved dietary preference may be related to the decline in prevalence of infection and the prevention of CAG. Several studies have demonstrated that levels of serum pepsinogens can be utilized for the screening of CAG (9, 10). The tested hypothesis is whether dietary preference is associated with *H. pylori*-seropositivity and the development of CAG. We carried out a seroepidemiological study of adults in the asymptomatic rural population.

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Materials and Methods

Study population. The rural area (population 16,000) studied is located in the western part of Japan. The study subjects were 626 volunteers between the ages of 40 and 64 years residing in this area. Subjects were comprised of 171 males (27.3%) and 455 females (72.7 %). This study was conducted from August to October in 1993. Each subject completed a self-administered questionnaire, the results of which were reviewed by trained public health nurses. All subjects were also questioned about their history of diseases: whether they had ever had cancer, stroke, diabetes mellitus, or hyperlipemia, and whether they were currently under treatment. Sociodemographic information was obtained directly from each individual through a self-administered questionnaire that requested various personal details, including age, sex, height, weight, dietary preference, occupation, smoking habits, alcohol consumption, and family history. Each dietary interview was performed by a dietician. This interview asked about the consumption of rice, miso soup, soybean curd (tofu), pickled vegetables (salted food), green-colored vegetables, light-colored vegetables, fruits, meat, fish, egg, milk, and daily products. Informed consent was obtained from each subject before that person participated in the study.

Serological methods. Analysis for *H. pylori* IgG was carried out in a single laboratory using an enzyme immunoassay (EIA) kit (Enteric Products Co., Italy) with duplicate measurements. The sensitivity and specificity of this test was 98.7% and 99.0%, respectively (11). Seropositive cases of *H. pylori* were defined as a test result that showed the presence of anti-*H. pylori* IgG. The levels of serum pepsinogen I (PG I) and pepsinogen II (PG II) were measured using a competitive binding double-antibody radioimmunoassay kit (Dainabot Co., Tokyo, Japan) (12). Cut-off values recommended for the screening of CAG from PG I and PG II were adopted the PG I level as 70 ng/ml and a PG I/PG II ratio as 3.0 (9, 10). Cases with a low pepsinogen level (low-PG I cases) were defined as those having lower values for both of them. The sensitivity and specificity of these cut-off values for gastric cancer (GC) were found to be 64.0% and 87.0%, respectively (10).

Statistical methods. We categorized the subjects into 5 age groups. The Chi-squared test or the Mantel-Haenszel Chi-squared test was used to examine the relationship between *H. pylori*-seropositivities or low-PG I cases and age by sex. The logistic regression model was applied to analyze the relationship between *H. pylori*-seropositivities and low-PG I cases. The same model was also used to analyze the relationship between *H. pylori*-seropositivities or low-PG I cases and each dietary factor, as well as smoking habits and alcohol consumption. The age adjusted odds ratios (OR) and their 95% confidence intervals (CI) were determined using unconditional logistic regression models to evaluate the strength of the association. Probability values less than 0.05 were considered significant. The data were analysed using the SAS program (SAS Institute, Cary, NC, USA).

Results

Table 1 shows the seropositive rates of *H. pylori* by age and sex. Out of 626 subjects, 463 *H. pylori*-

Table 1 Seropositivities of *Helicobacter pylori* by age and sex

Group	Males			Females		
	Number of sera	Number of seropositive cases	%	Number of sera	Number of seropositive cases	%
40-44 (years)	23	15	65.2	52	35	67.3
45-49	22	14	63.6	59	40	67.8
50-54	25	22	88.0	81	48	59.3
55-59	34	28	82.4	119	92	77.3
60-	67	59	88.1	144	110	76.4
Total	171	138	88.7	455	325	71.4
P value for trend			$P < 0.01$			$P < 0.05$

seropositivities were confirmed. The seropositive rate was higher in males (88.7%) than in females (71.4%) and a sex difference was observed ($P < 0.05$). Seropositive rates of *H. pylori* increased with age for both sexes, with $P < 0.01$ for males and $P < 0.05$ for females.

Table 2 shows the relationship between seropositivities of *H. pylori* and the degree of eating salted-food per week. The frequency of salted-food intake per week was divided into 3 categories. Regarding the relationship between *H. pylori*-seropositivities and salted-food intake, an OR was found to be significantly high among the "almost every day" group in males [OR = 8.39, 95% CI: 1.02–69.30] after adjustment for age. There was, however, no statistically significant difference in females. In addition, no significant difference was observed between *H. pylori*-seropositivities and the other dietary factors for both sexes.

Table 3 shows the cases with low pepsinogen level stratified by age and sex. The low-PG I cases were 23.3 %, 28.1% in males and 21.5% in females, and conse-

Table 2 Relationship between seropositivities of *Helicobacter pylori* and salted-food intake

Frequency of intake	Number of cases	Number of seropositive cases	%	Odds ratio	95% confidence interval
Males					
< 1 day per week	51	39	76.5	1.00	
1–3 days per week	75	58	77.3	1.19	0.50– 2.84
Almost every day	29	28	96.6	8.39*	1.02–69.30
Females					
< 1 day per week	186	141	75.8	1.00	
1–3 days per week	158	112	70.9	0.80	0.49– 1.30
Almost every day	67	43	64.2	0.62	0.34– 1.13

Odds ratio was adjusted for age. Cases (16 males and 44 females) with hypertension under treatment (salt reduced-food intake) were excluded. *$P < 0.05$.

Table 3 Cases with low pepsinogen level (low-PG I cases) stratified by age and sex

Group	Males			Females		
	Number of cases	Number of low-PG I cases	%	Number of cases	Number of low-PG I cases	%
40–44 (years)	23	2	8.7	52	10	19.2
45–49	22	4	18.2	59	11	18.6
50–54	25	5	20.0	81	18	22.2
55–59	34	11	32.4	119	24	20.2
60–	67	26	38.8	144	35	24.3
Total	171	48	28.1	455	98	21.5
P value for trend			$P < 0.01$			$P = 0.38$

quently the sex difference could not be said to be statistically significant. Low-PG I cases significantly increased with age in males ($P < 0.01$), but not in females.

Table 4 shows the relationship between *H. pylori*-seropositivities and low-PG I cases. There were significant associations between *H. pylori* seropositivity and low pepsinogen level in males ($P < 0.05$) and in females ($P < 0.01$). The ORs of *H. pylori*-seropositive cases for low-PG I cases were 6.32 (95% CI: 1.42–28.03) in males and 12.72 (95% CI: 4.57–35.46) in females. No relation was found between *H. pylori*-seropositivities and smoking habits or alcohol consumption. There was no association between low-PG I cases and smoking habits; nor was there an association between low-PG I cases and alcohol consumption.

Table 5 shows the relationship between low-PG I cases and the frequency of eating light-colored vegetables per week. The intake frequency of light-colored vegetables was divided into 3 groups. After adjustment for age and *H. pylori*-seropositivities, a significantly low OR for low-PG I cases was observed among the "almost every meal" group in females (OR = 0.37, 95% CI: 0.15–0.92). In addition, there was likely to be an inverse trend between low-PG I cases and the frequency of eating

Table 4 Relationship between seropositivities of *Helicobacter pylori* (*H. pylori*) and cases of low pepsinogen level (low-PG I cases)

Seropositive cases of *H. pylori*	Number of cases	Number of low-PG I cases	%	Odds ratio	95% confidence interval
Males					
Seronegative	33	2	6.1	1.00	
Seropositive	138	46	33.3	6.32*	1.42–28.03
Females					
Seronegative	130	4	3.1	1.00	
Seropositive	325	94	28.9	12.72**	4.57–35.46

Odds ratio was adjusted for age.
$^*P < 0.05$; $^{**}P < 0.01$.

Table 5 Relationship between cases of low pepsinogen level (low-PG I cases) and light-colored vegetables intake

Frequency of intake	Number of cases	Number of low-PG I cases	%	Odds ratio	95% confidence interval
Males					
< 3 days per week	50	12	24.0	1.00	
Almost every day	98	29	29.6	1.22	0.54–2.78
Almost every meal	15	4	26.7	0.91	0.23–3.57
Females					
< 3 days per week	108	31	28.7	1.00	
Almost every day	278	59	21.2	0.68	0.40–1.16
Almost every meal	58	7	12.1	0.37*	0.15–0.92

Odds ratio was adjusted for age and *Helicobacter pylori*-seropositivities.
$^*P < 0.05$.

light-colored vegetables. However, there was no statistically clear association between low-PG I cases and the other variables in both males and females.

Discussion

The role of dietary preference in *H. pylori*-associated gastrointestinal diseases remains unclear. Factors other than the presence of the bacterium itself should therefore be considered as causes of the persistent infection with *H. pylori*. The main purpose of this epidemiological study was to determine whether dietary preference might be a risk factor for *H. pylori* infection. In this study, we measured levels of PG I and PG II, which are indirectly related to CAG diagnosed by endoscopic findings. The low-PG I cases were those with a PG I level below 70 ng/ml and a PG I/PG II ratio below 3.0 (9, 10). The low PG I level has been shown to be closely associated with CAG. Several case-control studies have been carried out and the results have indicated an association between *H. pylori* infection and GC (13-15). CAG is known to be an important risk factor for GC (16). *H. pylori* has been classified as a Group I carcinogen by the International Agency for Research on Cancer (17). A few studies provide epidemiologic evidence demonstrating an association between *H. pylori* infection and CAG (18-20) and our results were also consistent with these previous observations. Therefore, determination of the PG I level and the PG I/PG II ratio would replace endoscopic CAG in mass screening.

As to the relationship between sex and age, a significant sex difference in seropositive rates of *H. pylori* was observed; no significant sex-related difference was found in CAG cases. Concerning CAG cases, males have a lower rate than females in the age range of 40-44. It was, however, difficult to explain why males in the age range of 40-44 experienced a lower rate than females in CAG cases in this study.

Positive geographic correlations between salt intake and GC mortality were found in the Japanese population (21, 22) and in international studies (23-25). The dietary administration of salt induces mucosal damage such as diffuse erosion and degeneration, and destroys the mucosal barrier in the glandular stomach (26). In our study, salted-food intake alone demonstrated a significant association in the "almost every day" group in *H. pylori*-male seropositivities. An inverse but insignificant trend was observed in female seropositivities. With respect to the contrasting results between sexes, these facts suggest that other factors are associated with *H. pylori* infection in addition to salted-food intake.

A few studies have been conducted to evaluate risk factors for CAG. An adequate intake of antioxidant micronutrients, particularly vitamin C, was negatively associated with *H. pylori*-seropositivity (19, 27, 28). The prevalence of histologically determined CAG was found to be lower in frequent consumers of light-colored vegetables in the United States (19, 29). In this study, the "almost every meal" response to consumption of light-colored vegetables was associated with a significant lower risk for CAG in females. A low risk for CAG was also found in the "almost every meal" group of males, although it was not statistically significant. These facts seem to indicate that light-colored vegetables are likely to possess a preventive factor for CAG. However, although dietary habits are likely to influence acquisition of infection, dietary preferences alone may not be the only factors in determining clinical outcome of *H. pylori* infection. The possible effects of light-colored vegetables on the development of CAG deserve further attention.

In conclusion, this survey of randomly selected adults indicates that risks of *H. pylori* infection and low PG I level are influenced by a few dietary factors. Salted-food intake may contribute to *H. pylori* infection. Light-colored vegetables intake is likely to be effective in the prevention of CAG. However, several other factors certainly play a role in the complex process that leads to GC. The major proportion of Japanese seropositivities for *H. pylori* would be expected to have been infected in childhood; it follows that dietary preference in their youth should then be considered in a future study. Therefore, a larger prospective cohort study is needed to determine the association among these factors. Further studies are necessary to determine the association with dietary preference.

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