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Salty Food Intake and Risk of *Helicobacter pylori* Infection

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To clarify the risk factors for *Helicobacter pylori* infection, which is considered to play an etiologic role in atrophic gastritis, duodenal ulcer and gastric cancer, various parameters including diet and socioeconomic characteristics were compared between *H. pylori*-infected and non-infected men. In a cross-sectional study of 634 men aged 40 to 49 years selected randomly from five areas with different rates of gastric cancer mortality, 474 of 628 men evaluated were positive for IgG antibody against *H. pylori*. After logistic regression analysis adjusted for area, the results showed a significant association between frequent intake of pickled vegetables and prevalence of *H. pylori* antibody (odds ratios against men who consume <1 day/week were 1.19 for 1–2 days/week, 1.92 for 3–4 days/week, 1.90 for 5–7 days/week; *P* for trend = 0.02). Daily consumption of miso soup was also associated with an increased risk (odds ratio against non-daily consumer = 1.60, 95% confidence interval = 1.03–2.49). Occupation, number of siblings, education, smoking and alcohol drinking, and other dietary habits were not significantly associated with the prevalence of infection in this population. Although there are limitations in a cross-sectional study such as this, consumption of salty foods appears to increase the risk of *H. pylori* infection, which could be a marker of salty food intake or an intermediate risk factor in the etiologic sequence between salty food intake and gastric cancer.

Key words: Cross-sectional study — *Helicobacter pylori* — Salty food — Diet — Risk factor

Infection with *Helicobacter pylori* is considered to play an etiologic role in atrophic gastritis and duodenal ulcer,[1] and recently an association with gastric cancer has been reported in three prospective studies.[2–4] An international correlation study suggested that a ten-fold difference in the rate of gastric cancer was partially due to differences in prevalence of *H. pylori* infection in 17 populations from 13 countries.[5] In Japan, both mortality from gastric cancer and prevalence of *H. pylori* infection were notably high. The prevalence of *H. pylori* infection in a high-risk area in Japan was 70% in men as young as 25–34 years of age and increased to 90% in those aged 55–64 years.[5]

If *H. pylori* infection is directly related to the development of gastric cancer, its prevention or eradication should be given high priority, especially in Japan. However, little is still known about the risk factors for *H. pylori* infection or its mode of transmission. A low socioeconomic status is a consistent epidemiologic characteristic of *H. pylori*-infected populations, and person-to-person contact is suggested to be the primary mode of transmission.[1]

In order to find any risk factor for *H. pylori* infection, we analyzed various lifestyle factors, including dietary habit and socioeconomic characteristics, in relation to the presence of *H. pylori* IgG antibody in a cross-sectional study.

SUBJECTS AND METHODS

The subjects investigated were the participants in our cross-sectional study, which aimed to identify the causes of geographic variations in several types of cancer; the methods employed have been described in detail elsewhere.[6,7] Briefly, out of 880 randomly selected men aged 40 to 49 years living in five areas of Japan with different rates of gastric cancer mortality, 634 agreed to participate. Each participant was interviewed about his sociodemographic characteristics and lifestyle including dietary habit, and provided blood samples.

Specific anti-*H. pylori* IgG antibodies in sera, stored at −80°C, were measured with an enzyme-linked immunosorbent assay (ELISA) kit using an acid-extracted antigen (Helico G, Porton Cambridge, Oxford). All samples were assayed in duplicate with negative and positive quality control samples on each plate. The serum samples were assayed blindly without any knowledge of background characteristics, and samples from all five areas were always assayed on each plate at the same time. The antibody concentration was determined from the optical density reading in relation to a standard curve, which was obtained through a calibrator using the kit. A threshold of 10 units/ml was used to discriminate *H. pylori*-positive from *H. pylori*-negative subjects. The sensitivity and specificity of the assay were 96% and 86%, respectively, upon comparison with gastric biopsy findings.[8] Six subjects could not be examined for *H. pylori* IgG antibodies because the serum sample volumes were in-

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sufficient. Four hundred and seventy-four out of the 628 men evaluated were found to be positive for anti-*H. pylori* IgG antibody. The number of subjects and prevalence of *H. pylori* antibody in each area are summarized in Table I.[9]

Lifestyle factors including socio-demographic situation, personal and family history, smoking and drinking history, and dietary patterns were obtained by questionnaire in an interview conducted by a trained public health nurse or nutritionist. Family history of peptic ulcer or gastric cancer was considered positive if any parent or sibling had a history. Weekly ethanol consumption was calculated by multiplying the typical amount of ethanol (g) consumed in a day by the frequency of drinking in a week. The intake frequency per week was assigned to one of four categories (less than 1 day/week, 1–2 days/week, 3–4 days/week, 5 days or more/week) for the following food items: rice, miso (soybean paste) soup, Japanese pickles, Japanese green tea, Chinese tea, black tea, coffee, noodles, bread, orange juice, other juices, fresh fruit, green vegetables, yellow vegetables, white and other vegetables, mushrooms, potatoes, seaweed, beef, pork, chicken, bacon, liver, green meat fish, red meat fish, white meat fish, cuttle fish and octopus, crab and shrimp, shellfish, soybeans and their products, other beans and peas, egg, milk and its products, cheese and vitamin supplements.

The prevalence of *H. pylori* infection was compared among the categories for the above factors. Odds ratio and 95% confidence intervals (CI) were used as measures of association to compare categories. These were estimated from the antilogarithm of the regression coefficient and its standard error in logistic regression models. Since the prevalence of *H. pylori* antibody differed among areas of residence, adjustments were conducted using logistic regression models that incorporated variables related to area of residence at the same time. Since age had no significant effect for the presence of *H. pylori* antibody among the subjects within a 10-year range, adjustment for age was not conducted. Trends were tested by assigning a value of 0 to 3 to each of the four categories and evaluating the significance of the standard logistic regression coefficient. All the statistical analyses were performed using the SAS statistical software package (SAS Institute Inc., Cary, NC).

Table I. Number of Subjects Showing Positivity ($\geq$10 units/ml) for *Helicobacter pylori* IgG Antibody According to Area

	No. tested	No. positive	Prevalence (%)
Yokote, Akita	133	114	85.7
Katsushika-kita, Tokyo	118	90	76.3
Saku, Nagano	118	85	72.0
Ninohe, Iwate	131	104	79.4
Ishikawa, Okinawa	128	81	63.3
Total	628	474	75.5

RESULTS

The prevalences of *H. pylori* antibody are shown in Table II in relation to socio-demographic factors. The prevalence in men with well skilled occupation was slightly lower than in men with other occupations. The prevalence tended to be lower as the number of siblings increased. The prevalence among college and university graduates was slightly lower. However, none of these factors was statistically significant.

The prevalences of *H. pylori* antibody are shown in Table III in relation to medical and family history of gastric diseases. Although the prevalence in men with a medical history of peptic ulcer was slightly higher, a family history of gastric diseases did not change the prevalence. Table IV shows the prevalences of *H. pylori* antibody in relation to smoking and drinking status. The prevalences were almost identical in any category of smoking and alcohol drinking, although slight and non-significant decreases of odds ratios were found in mild

Table II. Prevalence of *Helicobacter pylori* IgG Antibody in Relation to Socio-demographic Factors

	No. tested	Prevalence (%)	Area-adjusted odds ratio (95% CI)
Occupation[a]			
Well skilled[b]	92	66.4	1.00
Labor[c]	276	75.7	1.64 (0.97–2.76)
Clerical and sales	178	78.7	1.64 (0.92–2.91)
Agricultural	75	80.0	1.61 (0.75–3.42)
No. of siblings			
0, 1	73	80.8	1.00
2, 3	212	77.8	0.83 (0.42–1.63)
4, 5	175	73.7	0.67 (0.34–1.32)
$\geq$6	168	72.0	0.69 (0.35–1.39)
	P value for trend		0.24
Education[d]			
Junior high school	207	75.4	1.00
High school	282	77.0	1.00 (0.65–1.54)
College, University	130	72.3	0.81 (0.48–1.34)
	P value for trend		0.45

a) Seven men had no occupation at the time of interview.
b) Well skilled: Professional and technical work, managerial or official.
c) Labor: Transport, craftsman, process worker or laborer.
d) Seven men were classified into other categories and 2 men did not provide their educational level.

Table III. Prevalence of *Helicobacter pylori* IgG Antibody in Relation to Medical and Family History of Gastric Diseases

	No. tested	Prevalence (%)	Area-adjusted odds ratio (95% CI)
Medical history of peptic ulcer (−)	526	74.3	1.00
(+)	102	81.4	1.33 (0.77–2.30)
Family history of peptic ulcer (−)	538	75.1	1.00
(+)	90	77.8	1.12 (0.65–1.92)
Family history of gastric cancer (−)	573	75.6	1.00
(+)	55	74.6	0.85 (0.44–1.64)

Table IV. Prevalence of *Helicobacter pylori* IgG Antibody in Relation to Smoking and Alcohol-drinking Status

	No. tested	Prevalence (%)	Area-adjusted odds ratio (95% CI)
Smoking			
Never smoked	135	74.1	1.00
Ex-smoker	131	76.3	1.10 (0.62–1.95)
Smoker ≤20/day	192	74.0	0.93 (0.56–1.55)
>20/day	170	77.7	1.16 (0.67–2.00)
P value for trend			0.76
Alcohol drinking			
Non-drinker	119	77.3	1.00
Drinker <100 g/week	158	71.5	0.72 (0.41–1.26)
100–249 g/week	147	78.2	0.96 (0.53–1.74)
≥250 g/week	204	75.5	0.74 (0.43–1.29)
P value for trend			0.51

Table V. Prevalence of *Helicobacter pylori* IgG Antibody in Relation to Dietary Intake of Salty Food

	No. tested	Prevalence (%)	Area-adjusted odds ratio (95% CI)
Pickled vegetables			
<1 day/week	101	63.4	1.00
1–2 days/week	94	68.1	1.19 (0.65–2.19)
3–4 days/week	103	80.6	1.92 (0.98–3.79)
5–7 days/week	330	79.7	1.90 (1.10–3.30)
P value for trend			0.015
Miso soup			
<5 days/week	131	65.7	1.00
5–7 days/week	497	78.1	1.60 (1.03–2.49)

(<100 g/week) and heavy (≥250 g/week) alcohol drinkers.

Among the dietary factors assessed by the questionnaire, only intake of pickled vegetables and miso soup was significantly associated with the prevalence of *H. pylori* antibody (Table V). The prevalence among men consuming pickled vegetables on 5 days or more during a week was 80%, and the adjusted odds ratio compared with the category of less than 1 day a week was 1.90 (95% CI=1.10–3.30). The test for trend also gave a significant (P=0.015) result across the four categories of intake frequency. The prevalence among men who consume miso soup almost every day was 78%, whereas it was 66% among less frequent consumers, and the adjusted odds ratio was 1.60 (95% CI=1.03–2.49). These associations were still significant after excluding men with a medical history of peptic ulcer or any cancer, and also after excluding men living in Okinawa, where consumption of pickled vegetables and miso soup is fairly low.

DISCUSSION

This cross-sectional study conducted in Japan revealed a significant association between the prevalence of *H. pylori* IgG antibody and frequent intake of pickled vegetables and miso soup. Both pickled vegetables and miso soup are indicators of the level of salty food intake. The levels of estimated salt intake per day were significantly correlated with the intake frequency of pickled vegetables among 207 men who voluntarily participated in a 3-day dietary record survey (r=0.24, P<0.001), although these indicators may not be appropriate for estimating actual level of salt intake. The values of average salt intake were 12.2 g/day (n=23) for men who consumed pickled vegetables <1 day/week, 12.3 g/day (n=32) for 1–2 days/week, 13.3 g/day (n=38) for 3–4 days/week and 14.2 g/day (n=114) for 5–7 days/week. A similar association was also found with the intake frequency of miso soup, the values of average salt intake being 12.2 g/day (n=46) for non-daily consumers and 13.9 g/day (n=161) for daily consumers (t test: P=0.002) (unpublished data). These findings suggest that frequent intake of salty foods increases the risk of *H. pylori* infection.

The accumulated findings from several prospective and retrospective epidemiologic studies have suggested that both salty foods and infection with *H. pylori* are closely linked to gastric carcinogenesis.[10] Positive geographic correlations between salt intake and gastric cancer mortality were found in an international study[11] and in the present Japanese population.[7,12] The serological prevalence of *H. pylori* IgG antibody was also correlated with gastric cancer mortality in an international study[5] and in 46 Chinese populations.[13] The correlation coefficient of gastric cancer mortality with prevalence of *H. pylori* antibody in the present five populations[9] was 0.74, whereas that with the level of urinary salt excretion was

0.98.[12] Consequently the correlation coefficient between prevalence of *H. pylori* and the level of urinary salt excretion was 0.63. These findings indirectly support the hypothesis that salty foods are a risk factor for *H. pylori* infection.

Dietary administration of salt (at 10% in the diet) induces mucosal damage such as diffuse erosion and degeneration, and destroys the mucosal barrier in the glandular stomach of rats.[14] These changes in the gastric mucosa may be associated with an increased chance of persistent infection with *H. pylori*. Furthermore, salty food itself may be a source of *H. pylori*.

Socioeconomic condition is a consistent epidemiologic determinant of *H. pylori* infection,[1, 15, 16] although we did not find any association with occupation or educational level in Japan, where the variation of socioeconomic status is expected to be narrow in comparison with developing or multi-ethnic countries. Low socioeconomic status is likely to be associated with low availability of refrigerators, and thus may be linked to frequent intake of salty foods.

The positive correlation with socioeconomic condition also suggests possible person-to-person transmission of *H. pylori* by the fecal-oral route.[1] However, this alone cannot explain the extremely high prevalence (70% among men as young as 25 to 34 years of age living in one of the high-risk areas for gastric cancer[5]) of *H. pylori* infection in Japan, where diseases communicable by the fecal-oral route are rare. Additional factors other than the presence of the bacterium itself should therefore be considered to explain persistent infection with *H. pylori*. One of these cofactors may be mucosal damage caused by salty foods, which are a typical part of the diet of most Japanese.

Since this study is a cross-sectional one, any temporal relationship between frequent intake of salty foods and development of *H. pylori* infection is unclear. However, manifestations caused by bacterial infection, such as active gastritis, are less likely to increase the frequency of salty foods, and therefore underestimation of odds ratios is a possibility. The major proportion of men positive for *H. pylori* IgG antibody would be expected to have been infected for at least several years, so that dietary habit in their youth should be considered in a future study.

If salty food intake is causally associated with gastric cancer, this may confound the relationship between *H. pylori* infection and gastric cancer. However, the epidemiologic studies that showed a positive association between *H. pylori* infection and gastric cancer did not control for the possible confounding by salty food intake.[2–5, 13] *H. pylori* infection could be a marker of salty food intake or an intermediate risk factor in the etiologic sequence between salty food intake and gastric cancer.

Although there are some limitations to cross-sectional studies such as this one, it appears that consumption of salty food may increase the risk of *H. pylori* infection. Confirmation of this must await prospective as well as experimental studies.

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