

# Helicobacter pylori infection and risk of gastric cancer in Changle County, Fujian Province, China

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**Subject headings** Helicobacter pylori; stomach neoplasm; risk factors; case control studies

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## Abstract

**AIM** To evaluate the effects of *Helicobacter pylori* infection on and other environmental factors on the development of gastric cancer.

**METHODS** A population-based case-control study was conducted in Changle County, Fujian Province. The primary gastric cancer cases were histologically confirmed or diagnosed by surgery between January 1996 and March 1998. Healthy controls were randomly selected and matched by age, sex, and neighborhood of residence. A total of 101 pairs were included in the study. Specially trained interviewers conducted face-to-face interviews with the subjects according to a standardized questionnaire. *Helicobacter pylori* infections were measured by serum IgG antibody to *Helicobacter pylori*. Conditional Logistic Regression analysis was used.

**RESULTS** The presence of IgG antibody to *Helicobacter pylori* was 63.7% in study subjects, 56.0% in patients with cardiac cancer, and 60.5% in patients with non-cardiac gastric cancer. The risk factors of gastric cancer in Changle County were identified such as low educational level [OR=3.864; 95% confidence interval (95% CI) 1.604-9.311], low consumption of fresh vegetables (OR=4.925; 95% CI 1.356-17.885), high intake of fish sauce (OR = 10.587; 95% CI 2.821-39.738), unscheduled meals (OR = 4.254; 95% CI 1.445-

12.552), and *Helicobacter pylori* infection (OR = 3.453; 95% CI 0.901-13.224).

**CONCLUSION** *Helicobacter pylori* infection may be important in the etiology of gastric cancer, but major risk factors other than *Helicobacter pylori* are responsible for the high gastric morbidity in Changle County.

## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) infection is associated with gastric cancer<sup>[1-4]</sup>. However, only a small proportion of individuals developed gastric cancer in comparison with the relatively high prevalence of *H. pylori* infection in the general population. In this study we evaluated the effects of *H. pylori* infection and other environmental risk factors on the development of gastric cancer in Changle County, one of the areas with highest morbidity of gastric cancer in the world.

## MATERIALS AND METHODS

### Study subjects

One hundred and one gastric cancer patients (87 males and 14 females) and the same number of normal controls, individually matched with region, sex and age ( $\pm 3$  years) were included in the study. The studied subjects must have resided in Changle County for more than 20 years. The primary gastric cancer patients were histologically confirmed or diagnosed by operation during January 1996 - March 1998. Those who have ever been diagnosed as having gastric diseases in the past 3 years were not eligible as controls.

### Data collection

Trained interviewers interviewed the patients and controls. A standardized questionnaire was used to obtain information on basic demographic characteristics (gender, race, year and place of birth, and education), dietary habits, personal habits (smoking and drinking), medical history and so on.

### H. pylori assay

The presence of anti-*H. pylori* - IgG was assessed using the commercially available high-molecular-weight cell-associated protein *H. pylori* -immuno-

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assay (Enteric Products Inc, Westbury, New York). The assay was done in 96-well microtiter plates. Sera diluted 1:101 were added, and peroxidase conjugated anti-human IgG was used as the detector. The absorbance of the solution was measured at 450 nm.

### Statistical analysis

Data were handled by Epi-info. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated by Conditional Logistic Regression using STATA software

## RESULTS

A total of 101 pairs were included in the study. They were all Han nationality. The age of the patients ranged from 32 years to 78 years, averaging 58.93 years. The educational level was higher in controls than in the patients. The serum samples of 101 patients and 100 controls were tested for antibodies against *H. pylori*. Among them, 128(63.68%) were *H. pylori* positive. The prevalence of *H. pylori* infection was not significantly different in different age (above 30 years) and sex groups. The demographic characteristics as well as the distributions of prevalence of *H. pylori* infection in different sex and age groups are presented in Table 1 and Table 2.

**Table 1 Demographic characteristics as well as Helicobacter pylori infection in patients and controls**

	Patients		Controls		P value
	n	%	n	%	
Age (years)					
30-39	4	(4.0)	5	(5.0)	
40-49	18	(17.8)	18	(17.8)	
50-59	25	(24.8)	22	(21.8)	
60-69	34	(33.7)	38	(37.6)	
≥70	20	(19.8)	18	(17.8)	0.9597
Gender					
Males	87	(86.1)	87	(86.1)	
Females	14	(13.9)	14	(13.9)	1.0 000
Education					
College	1	(1.0)	1	(1.0)	
High school	17	(16.8)	68	(67.3)	
Elementary school	65	(64.4)	24	(23.8)	
Illiterate	18	(17.8)	8	(7.9)	0.0 000
<i>H. pylori</i>					
Positive	60	(59.4)	68	(68.0)	
Negative	41	(40.6)	32	(32.0)	0.2 064

**Table 2 Helicobacter pylori infection in study subjects**

Age group (years)	Men			Women		
	n	Hp(+)	%	n	Hp(+)	%
30-39	7	7	(100.0)	2	2	(100.0)
40-49	29	18	(62.1)	7	5	(71.4)
50-59	46	28	(60.9)	1	1	(100.0)
60-69	58	39	(67.2)	13	6	(46.2)
≥70	33	18	(54.6)	5	4	(80.0)
Total	173	110	(63.6)	28	18	(64.3)

$\chi^2 = 5.68, P = 0.2241; \chi^2 = 4.22, P = 0.3769$

No statistical difference was found in respect to presence of IgG antibody to *H. pylori* between patients and controls (Table 3). No significant difference was observed in anatomic distribution, although the prevalence of *H. pylori* infection was higher in non-cardiac gastric cancer (60.5%) than in cardiac cancer (56.0%), (Table 4).

**Table 3 Helicobacter pylori infection and gastric cancer**

Controls	Patients		Pairs
	Hp(+)	Hp(-)	
Hp(+)	39	29	68
Hp(-)	20	12	3
Pairs	59	41	100

$c^2 = 1.31, P = 0.25$

**Table 4 Helicobacter pylori infection in gastric cancer cases**

Gastric cancer	n	<i>H. pylori</i> infection	
		n	%
Cardiac	25	14	56.0
Non-cardiac	76	46	60.5

$\chi^2 = 0.04, P = 0.8395$

Further analysis was conducted using Conditional Logistic Regression. The results showed the risk factors of gastric cancer in Changle County were fish sauce intake, low consumption of fresh vegetables, unscheduled meals, low educational level and *H. pylori* infection (Table 5).

**Table 5 The results of multivariate Conditional Logistic Regression analysis**

Factors	$\beta$	$S_x$	OR	95%CI
Low educational level	1.3 517	0.4 487	3.864	1.604-9.311
Low consumption of vegetables	1.5944	0.6580	4.925	1.356-17.885
High intake of fish sauce	2.3596	0.6748	10.587	2.821-39.738
Unscheduled meals	1.4479	0.5508	4.254	1.445-12.552
<i>H. pylori</i> infection	1.2392	0.6852	3.453	0.901-13.224

## DISCUSSION

Changle County is a hyperendemic area of gastric cancer<sup>[5]</sup>. Chronic *H. pylori* infection has been identified as the most important risk factor of gastric cancer<sup>[6]</sup>. The results of our study showed that residents in Changle County had a high prevalence of *H. pylori* infection. This coincided the fact the concept of high prevalence of *H. pylori* infection in the high risk area of gastric cancer. However, no statistical significant difference was found in respect to presence of *H. pylori* infection between patients and controls. The lack of association in this study may be due to the high prevalence of *H. pylori* in Changle County. *H. pylori* infection can initiate a sequence of histological alterations in the mucosa that may finally result in the development of gastric cancer,

but not all infected subjects will eventually develop gastric cancer. *H. pylori* alone cannot account for development of gastric cancer. Apart from *H. pylori* infection, other factors may play important roles in carcinogenesis.

The development of gastric cancer is believed to be a multistep and multifactorial process. In the Correa model of gastric carcinogenesis, environmental factors are related to the evolution from normal gastric tissue through superficial gastritis, atrophic gastritis, intestinal metaplasia and dysplasia to carcinoma<sup>[7]</sup>. Environmental co-factors other than microbial agents may play roles in initiation, promotion or progression of gastric cancer.

The results of this study suggest that dietary factors, such as high intake of fish sauce and low consumption of fresh vegetables possibly increase the risk of gastric cancer. Fish sauce is a kind of traditional sauce consumed daily by Changle residents. It is usually produced from several kinds of sea fishes after long fermentation processes. The mutagenicity of fish sauce has been reported by several experimental studies<sup>[8,9]</sup>. There was a large amount of important precursors of N-nitrosamines detected in fish sauce. High intake of fish sauce was an important risk factor involved in the etiology of gastric cancer. However, consumption of diets high in vegetables is the most effective means in preventing gastric cancer. Vegetables contain many biologically active compounds that may be responsible for an anticarcinogenic effect against gastric cancer<sup>[10]</sup>. Additionally, unscheduled meals may cause injuries of gastric mucosa and potentiate the effects of carcinogens. Our study indicated that unscheduled meals might be one of the etiological factors for gastric cancer. In this study the educational level was higher in controls than in patients.

This supported the results of previous studies that socioeconomic status is a risk factor for gastric cancer, which in turn is related to diet and education.

These findings indicate that primary prevention should be focused in Changle County on reducing the etiological factors: fish sauce intake, deficiency in fresh vegetables, and *H. pylori* infection. Further elucidation of these risk factors for stomach cancer in Changle and assessment of the interaction between these risk factors and *H. pylori* infection are important for investigating the possible mechanisms of gastric carcinogenesis.

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