

Original

## *Helicobacter pylori* Infection among Patients Visiting a Clinic in Kasama City, Ibaraki Prefecture

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### Abstract

We examined *Helicobacter pylori* infection in patients who visited the Iso Clinic (Kasama City, Ibaraki Prefecture) with abdominal complaints, and determined the prevalence of *H. pylori* infection by age, sex, endoscopic diagnosis, abdominal complaint, gastric mucosa, and living environment. Peptic ulcer disease was observed in 23.2% of the patients examined with endoscopy, but there was no association between abdominal complaints and the prevalence of *H. pylori* infection. The prevalence of *H. pylori* infection was high among patients with peptic ulcer disease and atrophic gastritis. The prevalence of *H. pylori* infection was higher in the generation born before the start of the period of rapid economic growth (71.5%) than in the generation born afterward (64.8%). No significant difference was observed between males and females. The prevalence of *H. pylori* infection was high in those who drank well water during childhood and those who were raised in a house with a nonflushing of toilet (67.2% and 67.5%, respectively). There were no associations with river basin of residence, alcohol consumption, or smoking. The prevalence of *H. pylori* infection among patients who visited Iso Clinic was higher than that among patients seen at Tama-Nagayama Hospital, Nippon Medical School (Tama City, Tokyo). The difference is attributable to the higher prevalence of *H. pylori* infection in the elderly.

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Key words: *Helicobacter pylori*, Kasama City, well water, basin, non-flushing of toilet

### Introduction

Ever since *Helicobacter pylori* was detected in gastric biopsy specimens of patients with chronic gastritis<sup>1</sup> by Warren (a pathologist) and Marshall (an internist) in Australia, its associations with gastroduodenal diseases, such as peptic ulcer disease, gastric cancer, and gastric MALToma, and extragastric lesions, such as idiopathic

thrombocytopenic purpura (ITP), have been discussed<sup>2</sup>. Approximately 50% of the world's population (2.7 billion people) (40% in advanced countries and 70% to 80% in developing countries) are infected with *H. pylori*<sup>3</sup>. The World Health Organization and the International Agency for Research on Cancer consensus group stated in 1994 that there was sufficient epidemiologic and histologic evidence to classify *H. pylori* on the basis of recent studies<sup>4</sup>. However, there has been no direct proof

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that *H. pylori* induces gastric cancer, and randomized interventional studies are in progress throughout the world<sup>5,6</sup>. In Japan, Saito et al of the National Cancer Center planned the Japanese Intervention Trial of *Helicobacter pylori*. Prevention of the onset and progression of gastric mucosal atrophy by means of eradication of *H. pylori* has been selected as the endpoint, and the data from this trial are currently being analyzed.

A study of the prevalence of *H. pylori* infection by age group in Japan has suggested a rightward shift of the peak during long-term examination<sup>7</sup>. This shift has been explained by the cohort effect resulting from an age-related rightward shift in patients infected during childhood, and the accumulation of cases of new infection has been ruled out<sup>7</sup>. Reports on the incidence of *H. pylori* infection in mass screenings of occupational cohorts and regional cohorts, and in examinations of subjects at hospitals in local cities have occasionally been published. However, there have been no detailed studies of the status of infection among subjects examined by private-practice physicians in depopulated areas with little variation or movement of the population. Therefore, we investigated *H. pylori* infection in patients with abdominal complaints who visited Iso Clinic, which was established by the authors, with the aim of examining the status of *H. pylori* infection in patients examined at private clinics in Kasama City, Ibaraki Prefecture. Kasama City has a small population which peaked in 1945 at 36,000 and has been steadily decreasing ever since. The present population is 30,000. Our results were compared with results obtained at the Department of Gastrointestinal Endoscopy (incorporated into the Department of Gastroenterology in April 2003), Tama-Nagayama Hospital, Nippon Medical School.

#### Materials and Methods

The subjects were 220 patients with no history of *H. pylori* eradication who visited Iso Clinic (Inada, Kasama City, Ibaraki Prefecture) with various abdominal complaints from January 9, 2002 to October 14, 2003. They ranged in age from 7 to 86 years (mean age, 57.2 years). The male-to-female

ratio was 79 : 141. Endoscopy was performed in 194 patients (from 17 to 86 years of age; mean age, 59.3 years; male : female ratio, 66 : 128) and *H. pylori* infection was diagnosed in 219 patients (from 7 to 86 years of age; mean age, 57.3 years; male : female ratio, 79 : 140). For comparison of the prevalence of *H. pylori* infection, we examined data from 1,221 patients with abdominal complaints who visited Tama-Nagayama Hospital, Nippon Medical School (Tama City, Tokyo) and underwent endoscopic examination. The subjects at Tama-Nagayama Hospital, Nippon Medical School were recruited during the same period as were those at Iso Clinic. They ranged in age from 9 to 89 years, with a mean age of 53.8 years and a male : female ratio of 732 : 489. Those with a history of *H. pylori* eradication/or oral administration of anticoagulants were excluded. Histopathological diagnosis was used as the gold standard, and the sensitivity, specificity, and accuracy of the <sup>13</sup>C-urea breath test (UBT) were examined in 1,445 patients of Tama-Nagayama Hospital, Nippon Medical School (from 25 to 69 years of age; mean age, 54.1 years; male : female ratio, 839 : 606). A total of 2,886 patients were enrolled in this study.

#### 1) Questionnaire

The patients who visited Iso Clinic and agreed to participate in the study were asked to fill out a questionnaire regarding the place of residence, age, sex, drinking water (city water or well water) style of lavatory (flush or nonflush), habits of alcohol intake and smoking (adults), and abdominal complaints (Table 1). On the basis of the results, we determined the prevalence of *H. pylori* infection according to the difference in living environment.

#### 2) Diagnosis of *H. pylori* infection

For the diagnosis of *H. pylori* infection, <sup>13</sup>C-UBT was used at Iso Clinic, histopathological diagnosis by triple-site gastric biopsy<sup>8,9</sup> was used at Tama-Nagayama Hospital, Nippon Medical School. For <sup>13</sup>C-UBT, exhaled air was collected in a fasting state early in the morning, and the subjects were instructed to orally ingest <sup>13</sup>C-urea (Ubit<sup>®</sup>, 100 mg) dissolved in 100 ml of water. After oral intake, the

Table 1 Questionnaire

Date:

Please cooperate with a survey on *H. pylori* infection.

We are planning to investigate the status of *H. pylori* infection in Kasama City by asking the patients of our clinic to fill out a questionnaire. If you agree to participate, please write down your name, address and the date of birth, and answer the following questions to the best of your knowledge. We assure you that the information you provide here will never be publicly disclosed.

Nagamitsu Iso, Iso Clinic

Address

Name

Date of birth: \_\_\_\_\_ ( \_\_\_\_\_ years old )  
year/month/day

## 1. Place of residence

- 1) Until the age of 5 years ( sample: \*\* City, \*\* Prefecture; \*\* Cho, \*\* Gun, \*\* Prefecture. If your address changed more than once, please write down all of your addresses to the best of your recollection. )
- 2) From the age of 6 years until the present( If your address changed more than once, please write down all of your addresses to the best of your recollection. )

## 2. Drinking water

- 1) Until 5 years of age
  - a) City water
  - b) Well water
- 2) Between 6 and 20 years of age
  - a) City water
  - b) Well water
- 3) At present ( if you are an adult )
  - a) City water
  - b) Well water

## 3. Lavatory

- 1) Until 5 years of age
  - a) Nonflush
  - b) Flush
- 2) Between 6 and 20 years of age
  - a) Nonflush
  - b) Flush
- 3) At present ( if you are an adult )
  - a) Nonflush
  - b) Flush

## 4. Drinking habit

- 1) Drink alcohol ( since the age of \*\* years )
- 2) Drink little or no alcohol
- 3) Stopped drinking ( used to drink alcohol between the ages of \*\* and \*\* years )
- 4) Never drank alcohol

## 5. Smoking

- 1) Smoke ( since the age of \*\* years )
- 2) Stopped smoking ( used to smoke between the ages of \*\* and \*\* years )
- 3) Never smoked

## 6. Have you ever had a gastric or duodenal disease before?

- 1) No
- 2) Yes
  - a) gastric ulcer, b) gastritis, c) duodenal ulcer, d) others ( \_\_\_\_\_ )

Thank you very much for your cooperation.

subjects rinsed their mouths with water two or three times to eliminate  $^{13}\text{C}$ -urea adhering to the oral cavity. After oral rinsing, the subjects maintained the left lateral position for 5 minutes, and thereafter remained at rest in the sitting position. Exhaled air was collected 20 minutes after oral intake of  $^{13}\text{C}$ -urea, and the  $^{13}\text{CO}_2$  concentrations in exhaled air before

and after oral intake were determined with a mass spectrometer to calculate the change from the preadministration value ( $\Delta^{13}\text{C}$ : ‰) Changes of 2.5‰ or more were regarded as positive for *H. pylori*. For children 15 years or younger, the dose of Ubit<sup>®</sup> was 75 mg and changes of 3.0‰ or more were regarded as positive for *H. pylori*<sup>10</sup>. For triple site gastric

biopsy, specimens were collected from the greater curvature of the lower antrum ( #1 ) the greater curvature of the upper body ( #2 ) and the lesser curvature of the lower body of the stomach ( #3 )<sup>8</sup> and stained with hematoxylin-eosin and improved Toluidine-Blue. Immunostaining was added in cases in which the diagnosis of *H. pylori* was difficult<sup>8,9</sup>.

### 3 ) Comparison of Histopathological Diagnosis and <sup>13</sup>C-UBT Results

Different methods were used for the diagnosis of *H. pylori* at Iso Clinic( <sup>13</sup>C-UBT )and Tama-Nagayama Hospital, Nippon Medical School ( histopathological diagnosis ) Therefore, in a preliminary study comparing the prevalence of *H. pylori* infection at these institutions, histopathological diagnosis was used as the gold standard, and the sensitivity, specificity, and accuracy of <sup>13</sup>C-UBT were examined using data from the Tama-Nagayama Hospital, Nippon Medical School patients.

### 4 ) Diagnosis of Gastric Mucosa ( Endoscopic Atrophy )

Endoscopic images of gastric mucosa were assessed mainly on the basis of the degree of the appearance of blood vessels on the lesser curvature of the lower body using the criteria of Oshima, which employs findings of discoloration for classification<sup>11</sup>. Complete absence of a vascular pattern and the absence of vascular pattern solely with so-called color heterogeneity were given a score of 0. Cases with mild, moderate, and severe appearance of blood vessels were given scores of 1, 2, and 3, respectively, and were diagnosed as atrophic gastritis<sup>11</sup>. The images of the gastric mucosa of patients examined with endoscopy by the authors were checked by a coworker, and the criteria were confirmed to be identical to those used at Tama-Nagayama Hospital, Nippon Medical School.

### 5 ) Comparison of the Prevalences of *H. pylori* Infection at Iso Clinic and Tama-Nagayama Hospital, Nippon Medical School

For comparison of the prevalences of *H. pylori* infection among patients examined with endoscopy at Iso Clinic and Tama-Nagayama Hospital, Nippon

Medical School, we used data from 164 subjects matched for age (  $\pm 3$  years ) sex, and endoscopic diagnosis. These subjects were further divided into three age groups( young group, 39 years or younger; middle-aged group, 40 to 64 years of age; and elderly group, 65 years or older ) and the prevalences of *H. pylori* infection were determined.

### 6 ) Statistical Analysis

Pearson's chi-square test was used for comparison of living environments. The unpaired test was used for comparison of gastric mucosa. The McNemar test was used to compare the prevalence of *H. pylori* infection at the two institutions. A computer software program ( SPSS Ver. 12.0, SPSS Inc., USA ) was used for statistical analysis. Excel 2003 ( Microsoft ) was used to calculate odds ratios ( OR ) and 95% confidence intervals ( CI ) The level of significance was set at a P value of less than 0.05.

## Results

### 1 ) Place of Residence

The places of residence of 220 subjects who answered the questionnaire were examined. Places of residence until the age of 5 years and after the age of 6 years were examined separately. Two hundred two subjects ( 91.8% ) lived in Ibaraki Prefecture when they were 5 years younger, and all continued living in Ibaraki Prefecture from the age of 6 years until the present. Of the 220 subjects, 147 ( 66.8% ) lived in Kasama when they were 5 years younger, and 145 ( 98.6% ) continued living in Kasama City from the age of 6 years until the present.

### 2 ) Endoscopic Diagnosis

Endoscopy was performed in 194 subjects. Of the abnormal findings, peptic ulcer disease was the most common ( 23.2%; 45 subjects ), followed in descending order by ( hemorrhagic ) gastric erosion ( 15.5% ) erosive gastritis ( 11.9% ) gastric polyp ( 9.3% ) reflux esophagitis ( 6.7% ) acute gastric mucosal lesion ( 2.1% ) gastric submucosal tumor ( 2.6% ), and superficial gastritis ( 1.0% ), ( Table 2a ) Localized lesions other than atrophic gastritis were absent in 27.8% of the cases ( 54 subjects ) Of the 45

Table 2 Gastroduodenal disease and the prevalence of *H. pylori* infection in 194 patients examined with endoscope

a. Endoscopic diagnosis	Cases	b. Prevalence of <i>H. pylori</i> infection	
		Prevalence (%)	(n/N)
Peptic ulcer	45	91.1%	(41/45)
Gastric ulcer	26	92.3%	(24/26)
Duodenal ulcer	11	90.9%	(10/11)
Gastroduodenal ulcer	8	87.5%	(7/8)
( Hemorrhagic ) gastric erosion	30	53.3%	(16/30)
Erosive gastritis	23	30.4%	(7/23)
Gastric polyp	18	50.0%	(9/18)
Reflux esophagitis	13	38.5%	(5/13)
Gastric submucosal tumor	5	60.0%	(3/5)
Acute gastric mucosal lesion	4	50.0%	(2/4)
Superficial gastritis	2	0%	(0/2)
No localized lesion ( including atrophic gastritis )	54	88.9%	(48/54)

Among abnormal findings, peptic ulcer disease accounted for the largest percentage ( 23.2%; 45 subjects ) followed by ( hemorrhagic ) gastric erosion ( 15.5% ) erosive gastritis ( 11.9% ) gastric polyp ( 9.3% ) reflux esophagitis ( 6.7% ) acute gastric mucosal lesion ( 2.1% ) gastric submucosal tumor ( 2.6% ) and superficial gastritis.

The prevalence of *H. pylori* infection was the highest among patients with peptic ulcers ( 91.1%; 41/45 ) followed by patients without localized lesions other than atrophic gastritis ( 88.9%; 48/54 ) gastric submucosal tumor ( 60.0%; 3/5 ) ( hemorrhagic ) gastric erosion ( 53.3%; 16/30 ) gastric polyp ( 50.0%; 9/18 ) acute gastric mucosal lesion ( 50.0%; 2/4 ) reflux esophagitis ( 38.5%; 5/13 ) erosive gastritis ( 30.4%; 7/23 ) and superficial gastritis ( 0%; 0/2 ) The prevalences of infection among patients with peptic ulcers were as follows: gastric ulcer, 92.3% ( 24/26 ) duodenal ulcer, 90.9% ( 10/11 ) and gastroduodenal ulcer, 87.5% ( 7/8 )

Table 3 Results of histopathology and <sup>13</sup>C-UBT

		Histopathology		
		+	-	
<sup>13</sup> C-UBT	+	981	24	1,005
	-	35	405	440
		1,016	429	1,445

Sensitivity: 96.6% ( 95%CI: 95.2 ~ 97.6 )

Specificity: 94.4% ( 95%CI: 91.8 ~ 96.4 )

Accuracy: 95.9% ( 95%CI: 94.8 ~ 96.9 )

patients with peptic ulcer disease, 26 had gastric ulcers ( 57.8% ) 11 had duodenal ulcers ( 24.4% ) and 8 had gastroduodenal ulcers ( 17.8% )

### 3 ) Comparison of Endoscopic and <sup>13</sup>C-UBT Results

When histological diagnosis was used as the gold standard, the respective sensitivity, specificity, and accuracy rate of <sup>13</sup>C-UBT in 1,445 subjects were 96.6% ( 95% CI, 95.2 ~ 97.6 ) 94.4% ( 95% CI, 91.8 ~ 96.4 ) and 95.9% ( 95% CI, 94.8 ~ 96.9 ) ( Table 3 )

### 4 ) Prevalence of *H. pylori* Infection

#### a ) Age and Gender

The prevalence of *H. pylori* infection in 219 subjects who underwent <sup>13</sup>C-UBT was 65.3% ( 143/219 ) Analysis by age groups showed that the prevalence of *H. pylori* infection increased with age ( Fig. 1 ) peaked at around 60 years of age ( 76.5% ) and tended to be slightly decreased at 70 years or older. The prevalences of infection for males and females were 63.3% ( 50/79 ) and 66.4% ( 93/140 ) respectively, and were not significantly different ( P = 0.64 ) ( Table 4a )

#### b ) Disease

Table 2b shows the prevalence of *H. pylori* infection by disease. The prevalence of *H. pylori* infection was the highest among patients with peptic ulcers ( 91.1%; 41 of 45 patients ) followed by patients without localized lesions other than atrophic gastritis ( 88.9%; 48 of 54 patients ) gastric submucosal tumor ( 60.0%; 3 of 5 patients ) ( hemorrhagic ) gastric erosion ( 53.3%; 16 of 30 patients ) gastric polyp

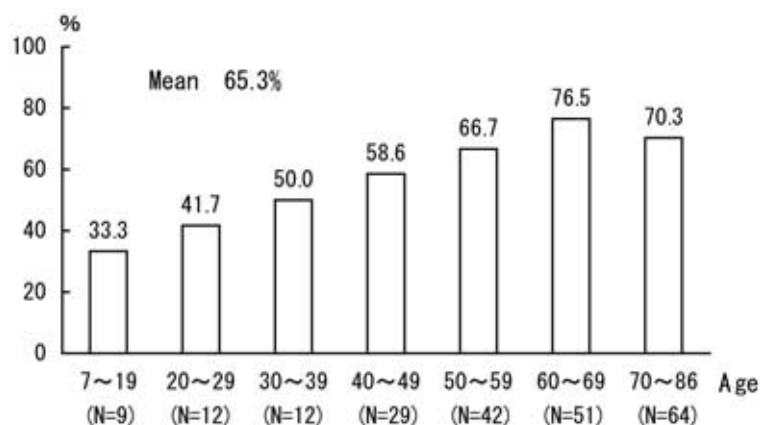


Fig. 1 The prevalence of *H. pylori* infection in 219 patients who underwent  $^{13}\text{C}$ -UBT

Analysis by age groups showed that the prevalence of *H. pylori* infection increased with age, peaked at around 60 years of age ( 76.5% ) and tended to be slightly decreased at 70 years or older.

( 50.0%; 9 of 18 patients ) acute gastric mucosal lesion ( 50.0%; 2 of 4 patients ) reflux esophagitis ( 38.5%; 5 of 13 patients ) erosive gastritis ( 30.4%; 7 of 23 patients ) and superficial gastritis ( 0%; 0 of 2 patients ) The prevalences of infection among patients with peptic ulcers were as follows: gastric ulcer, 92.3% ( 24 of 26 patients ) duodenal ulcer, 90.9% ( 10 of 11 patients ) and gastroduodenal ulcer, 87.5% ( 7 of 8 patients ) There were no significant differences among these three groups.

#### c ) Abdominal Complaints

Table 4b shows the prevalence of *H. pylori* infection according to the presence or absence of abdominal pain and abdominal fullness at the time of endoscopic examination. The prevalences of *H. pylori* infection among patients without and with abdominal pain were 65.7% ( 115/175 ) and 64.3% ( 27/42 ) respectively, with no significant difference between the groups (  $P=0.861$  ) Nor was any significant difference seen in the prevalence of *H. pylori* infection between patients without and with abdominal fullness ( 64.5%, 129/200 and 76.5%, 13/17, respectively;  $P=0.319$  )

#### d ) Gastric Mucosa

Assessment of the appearance of the gastric mucosa was possible of the 193 patients who underwent endoscopy. The prevalences of *H. pylori* infection among patients without atrophy of the lesser curvature of the lower gastric body ( score 0 )

and those with mild ( score 1 ) moderate ( score 2 ) and severe ( score 3 ) appearance of blood vessels were 26.5% ( 18/68 ) 88.1% ( 52/59 ) 90.9% ( 50/55 ) and 90.9% ( 10/11 ) respectively ( Table 5 ) There were no significant differences in the prevalences of *H. pylori* infection among patients with atrophy ( scores 1, 2 and 3 ) but the prevalence of *H. pylori* infection was significantly higher in all three groups of patients with atrophy ( scores 1, 2, and 3 ) than in patients without atrophy ( score 0 ) (  $P=0.001$ ,  $P=0.001$ , and  $P=0.001$ , respectively )

#### e ) Birth before or after Era of Rapid Economic Growth

Table 4c shows the prevalence of *H. pylori* infection in subjects born before and after the start of Japan's period of rapid economic growth. The prevalences of *H. pylori* infection in subjects born before ( 1955 or earlier ) and after the start of the period of rapid economic growth ( 1956 or later ) were 71.5% ( 118/165 ) and 64.8% ( 35/54 ), respectively, and the prevalence of *H. pylori* infection was higher in subjects born before the start of the period of rapid economic growth (  $P=0.001$  )

#### f ) Drinking Water

The prevalence of *H. pylori* infection was examined according to the type of water ( city water or well water ) the patients drank at the age of 5 years or younger, at 6 to 20 years of age, and at present ( Table 4d ) The present status was

Table 4 The prevalences of *H. pylori* infection according to gender, abdominal symptom, birthtime, drinking water, basin, lavatory, drinking, and smoking

## a. Gender

Male	Female	P value	OR	95% CI
63.3% ( 50/79 )	66.4% ( 93/140 )	0.64	0.871	0.490 ~ 1.551

## b-1. Abdominal pain

( - )	( + )	P value	OR	95% CI
65.7% ( 115/175 )	64.3% ( 27/42 )	0.861	1.065	0.527 ~ 2.153

## b-2. Abdominal fullness

( - )	( + )	P value	OR	95% CI
64.5% ( 129/200 )	76.5% ( 13/17 )	0.319	0.559	0.176 ~ 1.779

## c. Birth before or after start of period of rapid economic growth

Before	After	P value	OR	95% CI
71.5% ( 118/165 )	64.8% ( 35/54 )	0.001	0.343	0.182 ~ 0.647

## d-1. Drinking water ( before 5 years old )

City water	Well water	P value	OR	95% CI
40.0% ( 6/15 )	67.2% ( 137/204 )	0.033	3.067	1.048 ~ 8.973

## d-2. Drinking water ( 6 ~ 20 years old )

City water	Well water	P value	OR	95% CI
48.3% ( 14/29 )	67.9% ( 129/190 )	0.039	2.266	1.029 ~ 4.990

## d-3. Drinking water ( present )

City water	Well water	P value	OR	95% CI
63.3% ( 31/49 )	65.9% ( 112/170 )	0.735	1.121	0.579 ~ 2.173

## e. River basin of residence

Inada river basin	Hinuma river basin	P value	OR	95% CI
65.3% ( 124/190 )	72.2% ( 13/18 )	0.603	0.723	0.247 ~ 2.115

## f-1. Lavatory ( before 5 years old )

Flush	Nonflush	P value	OR	95% CI
30.8% ( 4/13 )	67.5% ( 139/206 )	0.007	0.214	0.064 ~ 0.721

## f-2. Lavatory ( 6 ~ 20 years old )

Flush	Nonflush	P value	OR	95% CI
40.0% ( 14/35 )	70.1% ( 129/184 )	0.001	0.284	0.135 ~ 0.599

## f-3. Lavatory ( present )

Flush	Nonflush	P value	OR	95% CI
64.3% ( 108/168 )	68.6% ( 35/51 )	0.568	0.823	0.421 ~ 1.609

## g. Drinking ( adult )

Drinker	Nondrinker	P value	OR	95% CI
59.7% ( 37/62 )	64.2% ( 70/109 )	0.555	0.825	0.434 ~ 1.565

## h. Smoking ( adult )

Smoker	Nonsmoker	P value	OR	95% CI
69.2% ( 36/52 )	66.4% ( 99/149 )	0.712	1.136	0.576 ~ 2.243

Table 5 The prevalence of *H. pylori* infection according to gastric mucosa

Gastric mucosa	0	1	2	3
Total	18/68 ( 26.5% ) <sup>1),2),3)</sup>	52/59 ( 88.1% ) <sup>1)</sup>	50/55 ( 90.9% ) <sup>2)</sup>	10/11 ( 90.9% ) <sup>3)</sup>

<sup>1)</sup> P = 0.001, <sup>2)</sup> P = 0.001, <sup>3)</sup> P = 0.001  
by unpaired t test



Fig. 2 Map of Kasama City  
Kasama City lies in west central Ibaraki Prefecture.

examined only for adults. The prevalence of *H. pylori* infection among those who drank city water at the age of 5 years or younger was 40.0% and was significantly lower than that in those who drank well water ( 67.2% ) ( P = 0.033 ) ( Table 4d-1 ). The prevalence of *H. pylori* infection among patients who drank city water at 6 to 20 years of age ( 48.3% ) was also lower than that of those who drank well water ( 67.9% ) ( P = 0.0039 ) ( Table 4d-2 ). No significant difference was observed in the prevalence of infection between the present city and well water users ( 63.3% and 65.9%, respectively ) ( P = 0.735 ) ( Table 4d-3 ). The odds ratios for city versus well water were high for the groups 5 years of age or younger and 6 to 20 years of age ( 3.067 and 2.266, respectively )

#### g) River Basins of Residence

The prevalence of *H. pylori* infection was examined separately for those who dwell in the Inada River and Hinuma River basins ( Fig. 2 ). As shown in Table 4c, the prevalence of *H. pylori*

infection was 65.3% ( 124/190 ) for residents of the Inada River and 72.2% ( 13/18 ) for residents of the Hinuma River basin, indicating no significant difference in the prevalence of *H. pylori* infection between those residing near these two rivers ( P = 0.603 ) ( Table 4e )

#### h) Style of Lavatory

The prevalence of *H. pylori* infection was examined according to the type of lavatory ( flush or nonflush ) which patients used at the age of 5 years or younger, at 6 to 20 years of age, and at present ( Table 4f ) The prevalence of *H. pylori* infection was significantly lower among the patients who used a flush lavatory at the age of 5 years or younger than among those who used the nonflush lavatory ( 30.8% and 67.5%, respectively; P = 0.007 ) ( Table 4f-1 ) A similar tendency was observed for 6 to 20 years of age ( 40.0% and 70.1%, respectively; P = 0.001 ) ( Table 4f-2 ) Comparison based on the lavatory type used at present revealed no significant difference in *H. pylori* prevalence ( 64.3% and 68.6%, respectively; P = 0.568 ) ( Table 4f-3 )

#### i) Alcohol Consumption and Smoking

The prevalence of *H. pylori* infection among drinkers ( 59.7% ) was similar to that of nondrinkers ( 64.2% ) ( P = 0.555 ) ( Table 4g ) Similar results were observed for smokers and nonsmokers ( smokers, 69.2%, 36/52; nonsmokers, 66.4%, 99/149; P = 0.712 ) ( Table 4h )

j) Comparison of Iso Clinic ( Kasama City ) and Tama-Nagayama Hospital, Nippon Medical School ( Tama City )

The prevalences of *H. pylori* infection in 164 patients matched for age, sex, and endoscopic diagnosis were 70.1% at Iso Clinic and 57.9% at Tama-Nagayama Hospital, Nippon Medical School, with the prevalence at Iso Clinic being significantly higher ( P = 0.0291, Fig. 3 ) According to age group, the prevalences in young patients were 60.0% and 40.0% ( N = 15, P = 0.3657 ) and in middle-aged patients



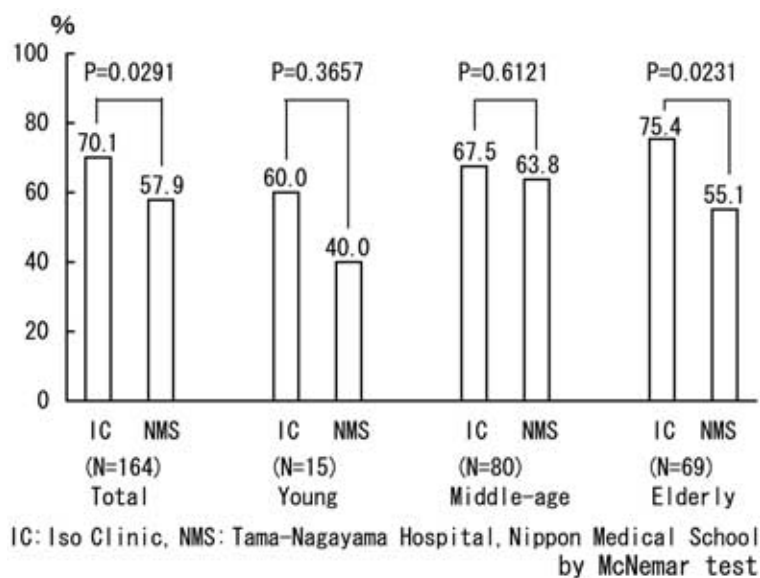


Fig. 3 Prevalences of *H. pylori* infection: comparisons between Iso Clinic and Tama-Nagayama Hospital, Nippon Medical School ( Matched for age, sex, and endoscopic diagnosis )

The prevalences of *H. pylori* infection in 164 patients matched for age, sex and endoscopic diagnosis were 70.1% at Iso Clinic and 57.9% at Tama-Nagayama Hospital, Nippon Medical School, with the prevalence at Iso Clinic being significantly higher (  $P = 0.0291$  ). According to age group, the prevalences in young patients were 60.0% and 40.0% (  $N = 15$ ,  $P = 0.3657$  ) and in middle-aged patients 67.5% and 63.8% (  $N = 80$ ,  $P = 0.3121$  ), respectively. The prevalences in the elderly were 75.4% and 55.1%, respectively. The prevalence in patients at Iso Clinic was significantly higher than that in patients at Tama-Nagayama Hospital, Nippon Medical School (  $N = 69$ ,  $P = 0.0231$  )

were 67.5% and 63.8% (  $N = 80$ ,  $P = 0.6121$  ), respectively ( Fig. 3 ) The prevalences in the elderly were 75.4% and 55.1%, respectively. The prevalence in patients at Iso Clinic was significantly higher than that in patients at Tama-Nagayama Hospital, Nippon Medical School (  $N = 69$ ,  $P = 0.0231$  )

#### Discussion

In November 2000, *H. pylori* eradication therapy for peptic ulcer disease only was approved for health insurance coverage. According to a multicenter study in Japan in which *H. pylori* positive peptic ulcer disease was followed up after eradication therapy without maintenance therapy, the recurrence rate of ulcers during a 4-year period was low ( 3% )<sup>2</sup>. Even at a rural clinic such as Iso Clinic, peptic ulcer disease was observed in 23.2% of

those who underwent endoscopy, which prompted us to recognize the importance of *H. pylori* eradication therapy. We examined *H. pylori* infection status using a questionnaire produced with the cooperation of patients who visited Iso Clinic with various abdominal complaints ( Table 1 ) although the sample size was small. Many people in our community are self-employed, and only a few people undergo mass screening conducted for regional populations. The questions asked were simple and easy to answer. However, a study of this type has never been conducted at any other clinic, and provided valuable findings that can only be obtained from areas with little movement population; when the place of residence is changed frequently, memory becomes ambiguous, and an accurate study becomes difficult. For these reasons, we believe that our study has produced accurate findings that are

difficult to obtain from other types of studies.

Invasive and noninvasive methods are available for the diagnosis of *H. pylori* infection. An invasive method, i.e., histopathological diagnosis (triple-site gastric biopsy) was mainly used for the diagnosis of *H. pylori* infection at Tama-Nagayama Hospital, Nippon Medical School<sup>8,9</sup>. This method is useful because it allows the clinician to make a four-grade (0 to 3) evaluation of the presence or absence and the degree of chronic inflammation in the gastric mucosa, neutrophilic activity, glandular atrophy and intestinal metaplasia according to the Updated Sydney system<sup>13</sup>. However, biopsy is always associated with a risk of hemorrhage. Furthermore, patients undergoing biopsy often suspect that they have a malignant disease. Therefore, a noninvasive method, <sup>13</sup>C-UBT, was used at Iso Clinic. While the intention of biopsy is to make diagnoses at certain points, UBT allows diagnoses to be made based on the state of the entire stomach and is regarded as one of the most reliable methods for the diagnosis of *H. pylori* infection. Our study results, obtained using histopathological diagnosis as the gold standard, demonstrated sensitivity, specificity, and accuracy to be high. Therefore, we are confident that comparisons of the prevalences of *H. pylori* infection at Tama-Nagayama Hospital, Nippon Medical School and Iso Clinic are valid, despite the difference in the diagnostic methods used.

The subjects of this study were patients who visited Iso Clinic with abdominal complaints, including abdominal pain and abdominal fullness. However, also included were patients whose complaints had resolved before the examination due to pharmacotherapy provided before endoscopy and those without abdominal complaints whose clinical course was followed up. There was no association between abdominal complaints and the *H. pylori*-positive rate. These results are in agreement with those of another report<sup>14</sup>. The prevalence of *H. pylori* infection among males did not differ from that among females, which is also consistent with a previous report<sup>15</sup>.

The prevalence of *H. pylori* infection among patients with gastroduodenal disease was high in those with peptic ulcer disease and in those without

localized lesions other than atrophic gastritis. The high prevalence of *H. pylori* infection in patients with peptic ulcers and gastric cancers has been supported by data from Japan and Western countries<sup>16,17</sup>. According to our study, however, the prevalence also appears to be high in patients without localized lesions other than atrophic gastritis. Therefore, we examined 54 patients without localized lesions other than atrophic gastritis and found that 49 (90.7%) had atrophic gastritis. This finding might explain why the prevalence of *H. pylori* was high in patients without localized lesions other than atrophic gastritis. When the gastric mucosa of 193 patients who underwent endoscopy was examined regardless of the diagnosis of disease, atrophy was observed in a large percentage (64.8%) of patients. The *H. pylori*-positive rate was not associated with the degree of atrophy. The *H. pylori* organism has difficulty surviving in the presence of severe atrophy<sup>18,19</sup>. However, we found that the prevalence of *H. pylori* did not tend to decrease. The small number of patients with severe atrophy (only 11 patients) is believed to be one reason for this finding. The sample size was small at Iso Clinic, and no patients had gastric cancer.

Uemura et al. have reported that gastric cancer developed in 5% of *H. pylori*-positive patients during a 10-year period and that the prevalence of cancer was high in *H. pylori*-positive patients with severe atrophy, corpus-predominant gastritis, or intestinal metaplasia<sup>20</sup>. Wong et al. followed up *H. pylori*-positive patients without precancerous lesions, such as atrophic gastritis and intestinal metaplasia, for 7 years in groups with and without *H. pylori* eradication in Changle, Fujian, China, which has a high rate of deaths from gastric cancer. While gastric cancer occurred in 1.19% of patients without eradication, no gastric cancers developed in patients who underwent *H. pylori* eradication, suggesting a beneficial effect of eradication in preventing the incidence of gastric cancer<sup>6</sup>. These results indicate that *H. pylori* eradication in patients without atrophy and intestinal metaplasia, in other words, patients with early cases, is useful for preventing carcinogenesis. Since no biopsies were conducted at

Iso Clinic, the status of intestinal metaplasia is unknown. However, there were many patients with endoscopic atrophic gastritis. Although the reason for the high prevalence of atrophic gastritis is unclear, careful observation is necessary in the future to detect the possible onset of gastric cancer in these patients.

In 1992, Asaka et al. reported the prevalence of anti-HpIgG serum antibody among Japanese people without abdominal complaints<sup>21</sup>. According to this report, a high prevalence of *H. pylori* infection, which is the typical pattern in developing countries, was observed in the population 40 years or older, and a low prevalence, which is characteristic of advanced countries, was observed in the population 29 years or younger<sup>22</sup>. In other words, the prevalence of *H. pylori* infection in Japanese people changed dramatically during the 10-year postwar reconstruction period after 1945. In view of these background factors, we divided the subjects into two groups, i.e., those who were born before the start of period of rapid economic growth (1955 or before) and those born thereafter (1956 or after), and compared the prevalences of *H. pylori* infection in these groups. As a matter of course, the prevalence of *H. pylori* infection was high (71.5%) in the group born before in Iaso or earlier. Considering the timing of the questionnaire, those 46 to 48 years or older were included in this group. From this viewpoint, the prevalence in the group 50 years or older was approximately 70% and was higher than that in the younger group, supporting these results.

The route of infection with *H. pylori* is not completely clear, but the prevalence of infection differs among ethnic groups<sup>8</sup>, races<sup>22</sup>, and economic conditions<sup>15</sup>. One study has suggested a strong correlation with water supplies and sewage systems<sup>23</sup>. According to the data provided by the Water Supply Division, Health Service Bureau of the Ministry of Health, Labor and Welfare, coverage of the water supply system in fiscal year 2003 was 96.9% on average in Japan and 100.0% in Tokyo. In contrast, that in Ibaraki Prefecture was 89.0%, which was ranked 44th among the 47 administrative divisions of Japan, i.e., it was the lowest after Kumamoto, Akita, and Oita. According

to the 2000 version of "Waste Management in Japan" published by the Waste Management Division, Waste Management and Recycling Department, Minister's Secretariat, Ministry of the Environment, flush lavatory coverage was 83.4% on average in Japan and 98.9% in Tokyo. In contrast, that in Ibaraki Prefecture was low (80.4%; 20th place in Japan) indicating that Ibaraki is a prefecture with low flush lavatory coverage.

According to our study, the proportion of those using city water at present in Kasama City was 23.4%, which was much lower than the average for the prefecture (89.0%). On the other hand, 76.7% were using a flush lavatory, which was close to the prefectural average (80.4%). Considering these background factors, we investigated the types of drinking water and lavatories used. Since *H. pylori* infection is often established in early childhood<sup>24</sup>, we investigated status during the preschool period (until the age of 5 years), the period from school age until adulthood (from 6 to 20 years) and at present. Because the prevalence of *H. pylori* infection was examined on the basis of age, years were variable for each subject. According to these data, the prevalence of *H. pylori* infection was significantly higher in people who were drinking well water and using a nonflush lavatory during the preschool and school age periods. Since *H. pylori* infection occurs in early childhood, the high prevalence of *H. pylori* infection in subjects who drank well water and used a nonflush lavatory during the school period is probably explained by the persistence of infections established during the preschool period. In other words, these results indicate that the prevalence of *H. pylori* infection did not increase during the school period, although the living environment did not improve. Ueda et al. conducted a similar study and, like us, found that greatly influence the rate of the type of drinking water and lavatory used during childhood *H. pylori* infection<sup>24</sup>. Our study of the present living environment showed that neither well water nor a nonflush lavatory is a source of *H. pylori* infection for adults.

Most of the subjects examined at Iso Clinic were residents of the western part of Kasama City. A few residents of the eastern and middle parts of Kasama

City also participated. The Inada River, which flows through the western part of Kasama City, joins the Hinuma River, which runs through the eastern and middle parts of the city, into the southern part of Kasama City. In other words, the Inada River is a branch of the Hinuma River and is located upstream from it. The Hinuma River flooded in the past and the Hinuma Basin might have been polluted. However, there was no significant difference in the prevalence of *H. pylori* infection between residents of the Inada and Hinuma basins. In 1982, the Kasumigaura Antieutrophication Ordinance was enacted, and in 1985, Kasumigaura was designated as an area of the Clean Lake Law, and the water quality of the Hinuma River, which flows into Kasumigaura, came under strict regulation. In 1991, Iida Dam, intended to supply the city with water, was completed. At the same time, the Hinuma Water Purification Plant located at the lower reach of the juncture with the Inada River came into operation. As a result, the water supply environment changed dramatically. The initiation of the city water supply appears to be a major turning point from the viewpoint of *H. pylori* infection, though many people continued to use well water, and only a small number of subjects were born after the inauguration of the city water supply project. This probably explains the similar prevalences of *H. pylori* infection.

Neither alcohol consumption nor smoking habit was associated with any significant difference in the prevalence of *H. pylori* infection. The results of a previous study were similar to ours<sup>15</sup>. According to studies of subjects receiving health check-ups, however, the *H. pylori*-positive rate is slightly lower in smokers than in nonsmokers<sup>25,26</sup>. This result was attributed to the by promotion of acid secretion by smoking, and the resultant generation of an environment not conducive to *H. pylori* survival<sup>26</sup>. Another study of subjects who visited a hospital, however, has found that the *H. pylori*-positive rate was higher in smokers<sup>27</sup>. The *H. pylori*-positive rate in drinkers is suggested to be lower than that in nondrinkers because alcohol may kill *H. pylori* in the stomach, but this remains a matter of speculation<sup>26</sup>.

The subjects of our study rarely changed their

places of residence and were still living at the same address as during childhood. This is a phenomenon highly characteristic of rural areas. Since most *H. pylori*-positive patients are infected during early childhood, this phenomenon appears to reflect the status of *H. pylori* infection in Kasama City. The prevalence of *H. pylori* infection differs between those who spent their early childhood in urban areas and those who were brought up in rural areas<sup>28</sup>. Moreover, the prevalence of *H. pylori* infection is known to rise among those spending their early childhood in a large family<sup>29</sup>. We collected data on the number of family members living together, but this factor had to be excluded from our analysis because the subjects' answers contained some ambiguities.

When the prevalence of *H. pylori* infection at our clinic was compared with the data from Tama-Nagayama Hospital, Nippon Medical School, the prevalence of *H. pylori* infection in Kasama City was significantly higher than that in Tokyo, suggesting an obvious geographic difference. This tendency is seen not only in Japan but also worldwide<sup>30,31</sup>. Comparison of *H. pylori* infection in different facilities or areas has been reported, but the method of diagnosis of infection, age composition, and the timing of the examination often differ among populations, and the reliability of the studies is often questionable. In our study, however, the age, sex, and endoscopic diagnosis were matched on the basis of standardized diagnostic criteria, which, we believe, allowed us to obtain accurate findings. Examination of the prevalence of infection by age revealed no differences among young and middle-aged subjects, but geographic differences were seen among the elderly. As mentioned earlier, the peak prevalence of *H. pylori* infection exhibited an age-related rightward shift<sup>7</sup>. Therefore, the living environment in childhood of those who were born before the period of rapid economic growth, in other words, those who are now elderly, appears to have affected the difference in the prevalence of *H. pylori* infection between the two institutions. In the young and middle-aged groups, the prevalence of infection was slightly higher than at Iso Clinic at Tama-Nagayama Hospital, Nippon Medical School, but the

difference was not significant, and the difference in living environments is believed to be small. The annual prevalence of *H. pylori* infection is believed to be 0.44%<sup>32</sup>. The prevalence of *H. pylori* infection in Kasama City is expected to decrease in the future because of the cohort effect. In Kasama City, the number of subjects undergoing mass screenings conducted for regional populations is extremely small. For those consulting Iso Clinic, we intend to provide education about the close association between *H. pylori* infection and peptic ulcer or gastric cancer, and to place emphasis on eradication therapy, particularly for young patients. One study showed the difference in the prevalence of *H. pylori* infection to disappear when the socioeconomic conditions of rural and urban areas are matched<sup>33</sup>. However, it was considered difficult to match such elements as yearly income and commodity prices. We believe our study succeeded in identifying a general trend in *H. pylori* infection among patients who visited a small rural clinic. We wish to apply the results of the present study to future *H. pylori* eradication therapy for preventing such diseases as peptic ulcer.

### Conclusions

We examined the status of *H. pylori* infection in a small number of subjects who visited a clinic in a rural town where there is almost no movement of the population. The prevalence of *H. pylori* infection in Kasama City significantly higher than that in Tama City, Tokyo. The prevalence of *H. pylori* infection was high among those who were born before the period of rapid economic growth, suggesting that the types of drinking water and lavatory used during early childhood have greatly affect on *H. pylori* infection. Our results have shown that the provision of tap water and flush-type lavatories is among the most important steps for decreasing the prevalence of *H. pylori* infection.

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