

The administrative project of *Helicobacter pylori* infection screening among junior high school students in an area of Japan with a high incidence of gastric cancer

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Abstract

Objective *Helicobacter pylori* infection is a common chronic infection that is closely associated with gastric cancer, known to be decreasing worldwide. We set up an administrative project of screening examination for *H. pylori* infection in junior high school students in Akita Prefecture to investigate the current prevalence of *H. pylori* infection in childhood in an area where the incidence of gastric cancer is particularly high.

Subjects and methods All students in their second or third year of junior high school (13 to 15 years old) in two cities in Akita Prefecture were recruited. First, a urine-based enzyme-linked immunosorbent assay for detection of *H. pylori* antibody was performed. Then, a ¹³C-urea breath test (¹³C-UBT) was carried out in students who tested positive on the urinary test. Written informed consent was obtained from all participants and their parents.

Results A total of 1813 students were recruited in this study; 1765 (97.3%) students agreed to participate in this project and underwent a screening examination. Among 96 students (5.4%) testing positive for *H. pylori* on the initial

screening examination, 90 (93.7%, 90/96) underwent a subsequent ¹³C-UBT, and 85 (4.8%, 85/1765) were diagnosed as positive for *H. pylori*.

Conclusions The current prevalence of *H. pylori* infection among students was low even in an area of Japan with a high incidence of gastric cancer.

Keywords Children · *Helicobacter pylori* infection · Gastric cancer · Health screening · Junior high school

Introduction

Helicobacter pylori (*H. pylori*) infection is a common chronic infection that has been confirmed to be significantly associated with gastric cancer [1–3]. The high prevalence of *H. pylori* infection and gastrointestinal disease in adults is closely related to *H. pylori* infection during childhood [4]. It also has been proved that eradication of *H. pylori* infection reduces the incidence of gastric cancer in healthy asymptomatic Asian individuals [5] and that early-stage eradication is more effective than late-stage eradication to reduce such incidence in animal experiments [6]. Based on these studies, treatment of *H. pylori* infection in younger individuals is thought to be beneficial.

H. pylori infection occurs mainly during childhood, under the age of 5 years, and new infection in the teen years or later is rare [7, 8]. Although the infection route of this bacteria has not been clarified, its prevalence has dramatically decreased mainly in developed countries over the past decades, possibly because of the improvement of sanitation. Therefore, it is important to determine the current status of *H. pylori* infection in children to predict the future incidence of *H. pylori*-related diseases, including gastric cancer, which could be incorporated into a prevention strategy [9, 10]. However, the

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suitable method and age for screening examinations for *H. pylori* infection in childhood remain unclear.

We started this administrative project of screening examinations for *H. pylori* infection in junior high school students in Akita Prefecture in Japan. The aim was to investigate the current prevalence of *H. pylori* infection in childhood in an area where the incidence of gastric cancer is particularly high. The local government and our research group set up a public project for this cross-sectional study, and we evaluated the feasibility of our screening method.

Subjects and methods

This prospective study was performed in two cities adjacent to each other in Akita Prefecture: Yurihonjo City and Nikaho City. They are located in rural areas and have a population of 100,000 in total. There are 13 junior high schools with a total of approximately 3000 students in three year grades. Those in their second or third year in 2015, aged between 13 and 15 years, were selected for inclusion in this study.

Education through junior high school is compulsory in Japan, and all students undergo annual health checkups including urinalysis. After obtaining informed consent from students and their parents, this urine sample was used for the first screening examination using a urinary test (RAPIRAN; Otsuka Pharmaceuticals, Tokyo, Japan) to detect the anti-*H. pylori* antibody by immune chromatography. The diagnostic sensitivity and specificity of this test have been reported to be 89 and 93%, respectively [11, 12].

Then, students who tested positive for *H. pylori* on the urinary test were requested to visit Yuri Kumiai General Hospital where they underwent a medical interview and a ¹³C-urea breath test (¹³C-UBT). The ¹³C-UBT was conducted on site at the hospital according to a previously validated method. Baseline breath samples were collected 4 h after a meal. Then, ¹³C-urea (100 mg) was administered to each subject, and a repeat breath sample was collected after 30 min. Samples were analyzed by using isotope-ratio mass spectrometry, and a positive result was defined by a cutoff value of 3.5%.

The study protocol was approved by the Institutional Review Board of Yuri-kumiai General Hospital, and written informed consent was obtained from all participants and their parents. This study is registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (No. UMIN000016926).

Statistical analysis

The associations between *H. pylori* infection and potential risk factors were evaluated using the χ^2 test, with *P* values of <0.05 considered significant. Statistical interpretation of

data was performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA).

Results

A total of 1813 students (Yurihonjo City, 1348; Nikaho City, 465) were recruited in this study; 1765 (97.3%) students agreed to participate in this project and underwent the first screening examination. Ninety-six students (5.4%, 96/1765) tested positive for *H. pylori* on the urinary antibody test; 90 (93.7%, 90/96) underwent a subsequent ¹³C-UBT. Eighty-five of them (94.4%, 85/90) also tested positive for *H. pylori* on the ¹³C-UBT. This accounted for 4.8% of 1765 screened students (Fig. 1).

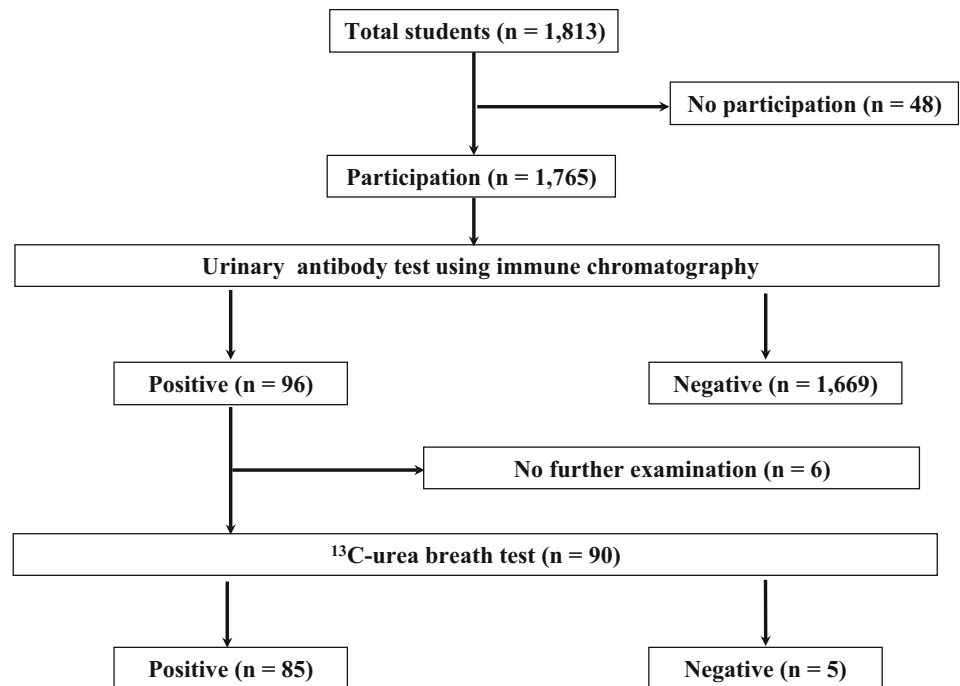
The rate of positive *H. pylori* results on the urinary antibody test was slightly higher in boys (6.3%, 56/894) than in girls (4.6%, 40/871), but the difference was not statistically significant (*P* = 0.074). There was no difference in urinary antibody test results between school grades or cities (Table 1).

Discussion

Incidence and mortality rates of gastric cancer in Japan show some geographical variation, and those in the northeast area including Akita Prefecture are particularly high. The age-adjusted incidence and mortality rates of gastric cancer in Akita Prefecture in 2011 were 117.5 and 36.3 per 100,000 individuals, respectively, [13], which were well above the national average (80.4 and 27.4) and were the highest in Japan.

The prevalence of *H. pylori* infection in adults also shows geographic variation in Japan [14]. There is no report on such prevalence in Akita Prefecture, but in a study comparing seven Japanese regions (Hokkaido, Aomori, Yamagata, Gunma, Aichi, Shiga and Kagawa), Yamagata Prefecture, located just next to Akita Prefecture, showed the highest prevalence (54.5%). Thus, it could be postulated that *H. pylori* positivity in adults in Akita Prefecture is also high. In these situations, it is meaningful to investigate the accurate prevalence of *H. pylori* infection in children in this region.

There are already several reports on the prevalence of *H. pylori* infection in Japanese children ranging from 1.8% in Hyogo to 12% in Aomori (Supplement 1) [15–18]. The prevalence was generally lower in children than in adults [19, 20], reflecting the decreasing trend of infection over the past decades. However, those previous reports may have some selection bias because they did not include all children of a target age and/or area with relatively low participation rates. In our study, on the other hand, all

Fig. 1 Summary of the screening study**Table 1** Associations between the rate of positive *Helicobacter pylori* results on urine-based enzyme-linked immunosorbent assay and sex, grade and location of school

	<i>H. pylori</i> infected, n/total (%)	<i>P</i> value
Sex		
Male	56/894 (6.3)	0.074
Female	40/871 (4.6)	
Grade, year		
Second	46/869 (5.3)	0.436
Third	50/896 (5.6)	
Location of school		
Yurihonjo City	76/1320 (5.8)	0.186
Nikaho City	20/445 (4.5)	

students in their second or third year of junior high schools in two cities (representing all children in their generation in that area) were recruited with a very high participation rate in the two-step screening (urine test 97.3%; ^{13}C -UBT 94.0%). Therefore, our results reflect an accurate infection rate of children with little bias in an area where the mortality rate of gastric cancer is high.

There is no consensus on the methods and age for screening of *H. pylori* infection in childhood. For adults, biopsy with histologic examination, urease test and culture has been widely used to directly detect the bacteria, but they are invasive and may show false-negative results in the cases of patchy colonization of the organism. Among

noninvasive tests, accuracy of the urinary antibody test is reported to be similar to that of the serum-based test. The latter has been found to be less reliable in children than in adults. ^{13}C -UBT has shown high accuracy in several studies in children, e.g., overall sensitivity and specificity of 97.8 and 98.5% with a cutoff value of 3.5% in the study by Kato et al. [21].

We used the urinary test as the first screening because urinary samples were available from all junior high school students because of the Japanese educational system. The sensitivity and specificity of this test (89 and 93%) were slightly lower than those of ^{13}C -UBT, but its simplicity is a definite advantage over ^{13}C -UBT for screening. We then used ^{13}C -UBT in students who tested positive for *H. pylori* on the urinary test to confirm infection. The participation rate was very high in our study; thus, we can regard this 4.8% as the true prevalence of *H. pylori* in children between 13 and 15 years old in this area. This combination of urinary test and ^{13}C -UBT in junior high school students seems to be an adequate method to determine the *H. pylori* infection rate in the young generation and can be used as nationwide screening at least in Japan and other countries having similar educational and health care systems.

In conclusion, the current prevalence of *H. pylori* infection among junior high school students in an area of Japan with a high incidence of gastric cancer was low at only 4.8%. This project showed the possibility of performing the screening of *H. pylori* infection in junior high school, which may lead eradication therapy for young people to prevent gastric cancer.

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Compliance with ethical standards

Conflict of interest None.

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Human rights statement and informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or a substitute for it was obtained from all patients for being included in the study.

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