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A seroepidemiologic study of *Helicobacter pylori* and hepatitis A virus infection in primary school students in Taipei

Hsiang-Yu Lin[1], Chih-Kuang Chuang[2], Hung-Chang Lee[1,3], Nan-Chang Chiu[1,4], Shuan-Pei Lin[1,2,5], Chun-Yan Yeung[1]

Departments of [1]Pediatrics and [2]Medical Research, Mackay Memorial Hospital, Taipei; [3]Department of Pediatrics, College of Medicine, Taipei Medical University, Taipei; [4]Mackay Medicine, Nursing and Management College, Taipei; and [5]Department of Infant and Child Care, National Taipei College of Nursing, Taipei, Taiwan

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Helicobacter pylori and hepatitis A virus (HAV) share a common fecal-oral transmission route. The aim of this study was to investigate the prevalence of and risk factors for *H. pylori* and HAV infection in primary school students in Taiwan. We studied 289 Grade 1 to 6 students from a single primary school in Taipei County in 2003. The students volunteered for blood tests for *H. pylori* immunoglobulin G (IgG) antibody and anti-hepatitis A antibody after consent from their parents. Questionnaires were administered to the parents to investigate possible risk factors. The seroprevalence rates of *H. pylori* IgG antibody and anti-hepatitis A antibody were 21.5% (62/289) and 1.4% (4/289), respectively. No statistically significant relationship was found between seropositivity for *H. pylori* and for HAV. If parents had knowledge of *H. pylori* and HAV, their children were significantly more likely to be seronegative for *H. pylori* (p=0.020, odds ratio [OR] 2.1, 95% confidence interval [CI] 1.2-3.7) and HAV (p=0.012, OR 11.2, 95% CI 1.5-83.4). Students whose family members had no history of HAV infection were significantly less likely to be seropositive for HAV (p=0.001, OR 0.04, 95% CI 0.004-0.5). No other factors were found to be significantly associated with seropositivity, including blood type; age; gender; family members' history of *H. pylori* infection; travel to China; parents' educational level; sources of water supply; family members' use of tobacco, alcohol, or betel nut; family members' history of peptic ulcer or gastritis; and students' history of recurrent abdominal pain. Lack of public health knowledge appears to be related to seroprevalence of *H. pylori* in primary school students. The low seroprevalence of anti-HAV antibodies demonstrates the lack of protection against this infection in school-age children in Taiwan and suggests that universal administration of HAV vaccine would be wise.

Key words: *Helicobacter pylori*, hepatitis A virus, prevalence, risk factors

Helicobacter pylori infection is a major cause of chronic antral gastritis, which is associated with duodenal or gastric ulcer and probably gastric adenocarcinoma [1,2]. Although the precise mechanism of transmission is not yet known, there is strong evidence for person-to-person transmission of *H. pylori* via the oro-oral, gastro-oral or fecal-oral route [3-6]. Overcrowding and poor sanitary conditions are risk factors for acquisition of *H. pylori* [7,8].

Hepatitis A virus (HAV) is known to be spread by fecal-oral contact. Its prevalence is related to sanitation status. Seropositivity for HAV in Taiwan declined following increased community awareness of the importance of hygiene and sanitary conditions [9]. Almost all patients with HAV infection recover completely. Fulminant hepatitis leading to death is uncommon in children [10].

The emerging epidemiologic pattern of *H. pylori* infection seems very similar to that of HAV, but there has been little research into risk factors associated with the 2 infections. The aim of this study was to investigate the prevalence of and risk factors for *H. pylori* and HAV infection in primary school students in Taiwan.

Materials and Methods

Study population

We studied Grade 1 to 6 students from a single primary school in Danshuei Township (a suburb near Taipei City with a population of 125,000) in 2003. The students volunteered for blood tests for *H. pylori* immunoglobulin G (IgG) antibody and anti-hepatitis A antibody after

Corresponding author: Chun-Yan Yeung, Department of Pediatrics, Mackay Memorial Hospital., No.92, Sec. 2, Chung-Shun North Road, Taipei, Taiwan.
E-mail: cyyeung@ms2.mmh.org.tw

consent from their parents. The study was approved by the ethics committee of Mackay Memorial Hospital, Taipei, Taiwan. About 50 students were randomly selected from each grade and across classes (rather than a single class), for a total study population of 289 (148 males and 141 females). None of the randomly selected subjects had received HAV vaccination. A blood sample was collected from each student, and serum specimens were kept at –70°C until laboratory examination.

Questionnaire

The questionnaire was designed to obtain demographic characteristics, personal and family history, and to assess the level of knowledge about *H. pylori* or HAV (Tables 1 and 2). Information collected included gender; blood type; age; source of water supply; education of the parents; whether family members were aware of *H. pylori* or HAV; family history of *H. pylori*, HAV, peptic ulcer, or gastritis; whether family members knew about HAV vaccine; family members' recognition of the relationship of *H. pylori* and gastritis; family members' habits of smoking, drinking, and chewing betel nut; history of travel to China; and whether students had complained of recurrent abdominal pain. Questionnaires were answered by the parents of the enrolled students.

Laboratory examination

Serum antibodies against *H. pylori* were analyzed by means of enzyme-linked immunosorbent assay (ELISA). The ELISA procedure for the Pyloriset EIA-G III assay (Orion Corporation, Orion Diagnostica, Espoo, Finland) was performed according to the manufacturer's instructions. Serum samples were also screened for antibodies against HAV by microparticle enzyme immunoassay (Hepavase A-96; General Biologicals Corporation, Taiwan) on a Hepavase A-96 analyzer.

Statistical analysis

Univariate analysis was performed with the Pearson chi-squared test and Fisher's exact test for categorical data. A *p* value of less than 0.05 was considered to be statistically significant. Odds ratios (OR) with 95% confidence intervals (CIs) were calculated to indicate the magnitude of associations. Multiple logistic regression analysis was performed to examine the weight of factors affecting seropositivity for *H. pylori* and for HAV.

Results

H. pylori

The seroprevalence of *H. pylori* IgG antibody was 21.5% (62/289). The association of various factors with *H. pylori* infection is shown in Table 1. We found that students whose parents did not know about *H. pylori* were significantly more likely to be seropositive (p=0.020, OR = 2.1, 95% CI = 1.2-3.7). Other factors including blood type, age, and gender of students; sources of water supply; parents' educational level; status of family members' *H. pylori* seropositivity; family members' recognition of the relationship of *H. pylori*

Table 1. Association between demographic factors, personal/family history and *Helicobacter pylori* infection

	Overall		*p*	OR (95% CI)
	n[a]	Infected (%)		
Study subjects	289	62 (21.5)		
Gender			0.174	0.6 (0.4-1.1)
Male	148	37 (25.0)		
Female	141	25 (17.7)		
Blood type			0.339	Undefined
A	69	13 (18.8)		
B	77	14 (18.2)		
O	116	31 (26.7)		
AB	27	4 (14.8)		
Age (years)			0.059	Undefined
7	55	8 (14.5)		
8	61	10 (16.4)		
9	46	14 (30.4)		
10	54	8 (14.8)		
11	40	14 (35.0)		
12	33	8 (24.2)		

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	Overall		*p*	OR (95% CI)
	n[a]	Infected (%)		
Source of water supply			0.326	Undefined
Tap water	245	52 (21.2)		
Well water	8	1 (12.5)		
Bottled water	9	4 (44.4)		
Others	1	0 (0.0)		
Father's educational status			0.935	Undefined
Primary	13	4 (30.8)		
Junior high	76	17 (22.4)		
Senior high	20	3 (15.0)		
College	113	23 (20.4)		
University or higher	45	10 (22.2)		
Mother's educational status			0.382	Undefined
Primary	12	2 (16.7)		
Junior high	65	17 (26.2)		
Senior high	30	3 (10.0)		
College	128	27 (21.1)		
University or higher	29	5 (17.2)		
Family members' knowledge of *H. pylori*			0.020	2.1 (1.2-3.7)
Yes	182	31 (17.0)		
No	103	31 (30.1)		
Family history of *H. pylori* infection			0.144	0.6 (0.2-1.6)
Yes	23	7 (30.4)		
No	255	55 (21.6)		
Family members' knowledge of relationship between *H. pylori* and gastritis			0.073	1.7 (0.9-3.2)
Yes	103	17 (16.5)		
No	178	45 (25.3)		
Family history of peptic ulcer or gastritis			0.852	1.2 (0.6-2.1)
Yes	105	21 (20.0)		
No	178	40 (22.5)		
Family members' smoking			0.065	Undefined
Yes	132	36 (27.3)		
Occasional	34	7 (20.6)		
No	105	14 (13.3)		
Family members' use of alcohol			0.326	Undefined
Yes	50	11 (22.0)		
Occasional	95	25 (26.3)		
No	126	21 (16.7)		
Family members' betel nut habit			0.753	Undefined
Yes	17	5 (29.4)		
Occasional	39	7 (17.9)		
No	214	45 (21.0)		
Family members' travel to China			0.566	1.1 (0.6-1.9)
Yes	95	20 (21.1)		
No	190	42 (22.1)		
Student's travel to China			0.324	0.7 (0.3-1.8)
Yes	21	6 (28.6)		
No	262	56 (21.4)		
Students' complaint of recurrent abdominal pain			0.909	1.1 (0.6-2.1)
Yes	85	17 (20.0)		
No	196	43 (21.9)		

Abbreviations: OR = odds ratio; CI = confidence interval

[a]An n value of less than 289 in these categories indicates that some items in the questionnaires were left blank.

and gastritis; family members' and student's history of travel to China; and family members' habits of smoking, drinking, or chewing betel nut were all found to be insignificant ($p>0.05$). Interestingly, no significant relationship was found between a history of peptic ulcer or gastritis in family members and seropositivity for *H. pylori* in students ($p=0.852$, OR = 1.6, 95% CI = 0.6-2.1), nor between a student's complaints of recurrent abdominal pain and seropositivity ($p=0.909$, OR = 1.1, 95% CI = 0.6-2.1).

Hepatitis A

The seroprevalence of anti-hepatitis A antibody was 1.4%. The association of various factors with HAV infection is shown in Table 2. We found that students were significantly more likely to be seropositive for HAV if their parent did not know about HAV ($p=0.012$, OR = 11.2, 95% CI = 1.5-83.4). Students were less likely to be seropositive if there was a negative family history for HAV ($p=0.001$, OR = 0.04, 95% CI = 0.004-0.5). None of the other factors were significantly associated with HAV positivity ($p>0.05$).

Association between *H. pylori* and hepatitis A

Cross-tabulation showed that none of the 289 subjects were seropositive for both *H. pylori* and hepatitis A antibodies, and 223 (77.2%) were negative for both. There was thus no statistically significant relationship between seropositivity for the 2 organisms ($p=0.294$).

Discussion

In our study, the seroprevalence of *H. pylori* in primary school students was 21.5%, which is higher than in previous reports [11-13]. However, the seroprevalence of HAV (1.4%) was low compared with figures published in Taiwan over the past decade or so [9, 14-17]. Some seroepidemiologic studies have provided evidence that the 2 pathogens share a similar mode of transmission, including the fecal-oral route [18-21]. However, we found no significant relationship between seropositivity for *H. pylori* and HAV. Others, including Chen et al [22], Furuta et al [23], Webb et al [24] and Luzza et al [25], have had similar results, casting doubt on the contention that *H. pylori* and HAV share a common mode of transmission. When parents did not know about *H. pylori* and HAV, their children were significantly more likely to be seropositive. Our findings are in agreement with those of Angelillo et al [26] and emphasize the need for public health education about proper sanitation, food handling, etc.

Table 2. Association between demographic factors, personal/family history and hepatitis A virus (HAV) infection

	Overall		*p*	OR (95% CI)
	n[a]	Infected (%)		
Study subjects	289	4 (1.4)		
Gender			0.961	3.2 (0.3-31.1)
Male	148	1 (0.7)		
Female	141	3 (2.1)		
Blood type			0.699	Undefined
A	69	1 (1.4)		
B	77	2 (2.6)		
O	116	1 (0.9)		
AB	27	0 (0.0)		
Age (years)			0.430	Undefined
7	55	1 (1.8)		
8	61	0 (0.0)		
9	46	0 (0.0)		
10	54	2 (3.7)		
11	40	0 (0.0)		
12	33	1 (3.0)		
Source of water supply			0.949	Undefined
Tap water	245	4 (1.6)		
Well water	8	0 (0.0)		
Bottled water	9	0 (0.0)		
Others	1	0 (0.0)		

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	Overall		*p*	OR (95% CI)
	n[a]	Infected (%)		
Father's educational status			0.599	Undefined
Primary	13	0 (0.0)		
Junior high	76	2 (2.6)		
Senior high	20	0 (0.0)		
College	113	1 (0.9)		
University or higher	45	0 (0.0)		
Mother's educational status			0.821	Undefined
Primary	12	0 (0.0)		
Junior high	65	1 (1.5)		
Senior high	30	0 (0.0)		
College	128	3 (2.3)		
University or higher	29	0 (0.0)		
Family members' knowledge of HAV			0.012	11.2 (1.5-83.4)
Yes	260	2 (0.8)		
No	25	2 (8.0)		
Family history of HAV			0.001	0.04 (0.004-0.5)
Yes	5	1 (20.0)		
No	275	3 (1.1)		
Family members' knowledge about HAV vaccination			0.601	2.9 (0.3-28.0)
Yes	137	1 (0.7)		
No	145	3 (2.1)		
Family members' smoking			0.698	Undefined
Yes	132	1 (0.8)		
Occasional	34	1 (2.9)		
No	105	2 (1.9)		
Family members' use of alcohol			0.587	Undefined
Yes	50	0 (0.0)		
Occasional	95	1 (1.1)		
No	126	3 (2.4)		
Family members' betel nut habit			0.827	Undefined
Yes	17	0 (0.0)		
Occasional	39	1 (2.6)		
No	214	3 (1.4)		
Family members' travel to China			0.912	1.5 (0.2-14.7)
Yes	95	1 (1.1)		
No	190	3 (1.6)		
Student's travel to China			0.813	Undefined
Yes	21	0 (0.0)		
No	262	4 (1.5)		

Abbreviations: OR = odds ratio; CI = confidence interval

[a]An n value of less than 289 in these categories indicates that some items in the questionnaires were left blank.

Our study also revealed a significant relationship between a history of HAV in the family and HAV seropositivity of the student. This suggests possible transmission of the disease within the family. No significant relationship was found between students' blood type and seropositivity for *H. pylori* or HAV, consistent with the findings of Wu et al [13], Niv et al [27], and Loffeld and Stobberingh [28]. This contrasts with the study of Boren et al [29], who suggested that the availability of *H. pylori* receptors might be reduced in individuals of blood group A and B phenotypes, as compared with individuals with blood group O.

According to the literature, the prevalence of both *H. pylori* and HAV seropositivity increases with age [9, 11-17,19,21,25]. However, this was not the case in our study. Perhaps the sample size and the age range in our study were too small to show a difference. But our

findings may simply reflect the rarity of HAV infection in Taiwanese school-age children in the present day. Because of improved sanitation, HAV seropositivity among children in Taiwan has been declining over the past 20 years [9,14-17].

We investigated several factors that might be expected to influence seropositivity but which were not associated with it in our study. There was no significant relationship between a history of *H. pylori* infection in family members and seropositivity for *H. pylori* in the student. Whether the parents knew about HAV vaccine to prevent HAV infection also did not influence seropositivity. Travel to China (an area endemic for HAV [30]) by either the student or family members was not associated with seropositivity for HAV or *H. pylori* in the student. Parents' lack of knowledge about the relationship between *H. pylori* infection and peptic disease was also not associated with students' seropositivity for *H. pylori*.

There was no significant association between the students' gender; source of water supply; and family members' habits of smoking, drinking, or chewing betel nut and seropositivity for *H. pylori* and HAV. These findings are consistent with previous studies [12,21,31]. Interestingly, no significant relationship was found between a history of peptic ulcer or gastritis in family members and students' seropositivity for *H. pylori*, a finding consistent with that of Cheng et al [11].

There have been conflicting results of studies looking for an association between infection with *H. pylori* and recurrent abdominal pain in children [11,32,33]. We did not find such an association. A low educational level has been reported to be positively associated with the prevalence of *H. pylori* infection [7,11,34]. A study from South Africa did not find such an association [21]; however, nor did we.

The low seroprevalence of anti-HAV IgG antibody among school children in our study points to the lack of protection against hepatitis A in this population. Hepatitis A vaccine is available in Taiwan for anyone over the age of 1 year. However, it is not covered under the National Health Insurance program and has still not been widely taken up by the general public in Taiwan [9,14-17]. Given the low level of protection, it would be worth considering a mass HAV vaccination program for the prevention and control of HAV outbreaks in the community. We believe that public health education is needed to decrease the prevalence of *H. pylori* and that universal HAV vaccination would be of benefit to our population.

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