ORIGINAL ARTICLE

HELICOBACTER PYLORI INFECTION AMONG NON-NATIVE EDUCATORS IN ALASKA

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ABSTRACT

Objectives. To determine seroprevalence of *H. pylori* infection in non-Native educators residing in urban or rural settings in Alaska, and to determine potential risk factors associated with infection in this population.
Study design. A cross-sectional survey of non-Native educators residing in urban or rural settings in Alaska.
Methods. Participants completed a questionnaire detailing aspects of residential life; *H. pylori* antibody status was determined by a commercial assay.
Results. Of the 203 non-Native participants, 49 (24%) had antibody to *H. pylori*. Univariate analysis demonstrated that the mean age of seropositive participants was higher than of seronegatives (48 vs. 42 years, respectively, p=.001). In addition, participants who had experienced childhood crowding were more likely to test seropositive for *H. pylori* (p=.058). On multivariate analysis, only age ≥ 40 was associated with infection. No difference in median hemoglobin or ferritin levels were noted among seropositive and seronegative participants. There was no increased risk of seropositivity among participants who had lived in an Alaska Native village or in a developing country for ≥ 6 months.
Conclusions. Overall, 24% of non-Native educators residing in rural Alaska tested positive by serology for *H. pylori*. Age ≥ 40 years was associated with infection. Median hemoglobin or ferritin levels did not differ significantly among seropositive and seronegative participants.
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Keywords: *Helicobacter pylori*, seroprevalence, non-Native, risk factors, Alaska, educators

INTRODUCTION

Helicobacter pylori (H. pylori) is one of the most common infections in humans affecting 30-40% of persons living in the developed world, and 80-90% of persons living in the developing world (1,2). *H. pylori* is a major cause of duodenal and gastric ulcers (3, 4), and infected persons are at increased risk for mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma (5, 6). In addition, infection is also associated with chronic active gastritis (7). Humans appear to be the major reservoir for *H. pylori*. Acquisition occurs by ingestion of the organism; however, transmission is poorly understood with fecal-oral or oral-oral (saliva, vomit) being the most likely modes of transmission (8).

The prevalence of *H. pylori* is chiefly related to age, socioeconomic status and geographic location. In developing countries, acquisition occurs during childhood with up to 70% of persons infected by 10 years of age. In developed countries located in North America and Western Europe, little infection appears to occur during childhood and prevalence slowly increases to approximately 40-60% percent in adulthood (1,9).

Compared with other groups in the U.S., Alaska Native people have a higher prevalence of infection with *H. pylori*. Among Alaska Native people, overall seroprevalence of IgG antibody to *H. pylori* is 74.8% and ranges from 61.3% in the south-central region (Anchorage and vicinity) to 84.4% in the interior region (Fairbanks and vicinity). Seroprevalence appears to increase with age; Alaska Native children by 5 to 9 years of age have a seroprevalence of 66.9% (10). Despite the high overall seroprevalence of IgG antibody to *H. pylori* in the Alaska Native population, little is known about seroprevalence in the non-Native population living in urban or rural Alaska. The objectives of our study were to determine seroprevalence of *H. pylori* infection in non-Native educators residing in urban or rural settings in Alaska and to determine potential risk factors associated with infection in this population.

MATERIALS AND METHODS

Participants and data collection

We conducted a survey among non-Native Alaska educators attending one of three education conferences held between August 1996 and September 1997 in three different locations: Anchorage, Fairbanks and Unalakleet. Conference participants were informed of the study via an information page summarizing the study which was included in all conference registration materials sent to conference attendees. At the start of each conference, study organizers made an announcement about the study and asked educators who wished to participate to sign the informed consent document, fill out a questionnaire and then proceed to a blood-drawing booth for collection of one venous blood sample. The self-administered questionnaire was pretested and took 15 to 20 minutes to complete. Data collected included residence (historical and current), living conditions, water source, sewage disposal, recreational activities, pet ownership, dietary habits, medical history, history of gastrointestinal (GI) symptoms and previous diagnosis or treatment of *H. pylori* infection. This study was approved by the Institutional Review Board at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. Written informed consent was obtained from all participants.

Laboratory testing

Serum specimens, obtained by venipuncture, were separated and transported on ice to the laboratory at the Centers for Disease Control and Prevention (CDC), Arctic Investigations Program (AIP) in Anchorage, Alaska. Serum samples were tested for antibody to *H. pylori* by using an enzyme-linked immunosorbent assay as previously described (11). Serum ferritin levels were measured by imunoradiometric assay (Quantimune Ferritin IRMA, Biorad Diagnostics, Hercules CA). Hemoglobin levels were measured on-site at the time of venipuncture using a portable hemoglobinometer (HemoQue AB, Angelholm, Sweden). Each participant received a copy of their individual laboratory results, and copies of results were sent to health care providers upon request by the participant.

Definitions

Places of residence of 6 months duration or longer in Alaska were categorized into urban centers (Anchorage, Fairbanks and Juneau), hub towns and villages. For the purpose of this study, hub towns were distinguished from villages by population size (>1,000 persons), accessibility (jet air service compared with small propeller planes) and access to medical care (small local hospitals compared with rural health clinics). Surface water as a source of drinking water was defined as river or lake water, or melted snow or ice. Participation in subsistence activities was defined as fishing, hunting, trapping and picking greens and/or berries during the previous three months. Consumption of traditional foods was defined as consuming one or more meals consisting of marine mammals, caribou, moose or musk ox during the previous 3 months. An estimate of crowding during childhood was made for each participant, defined as sharing a bed more than 5 nights per week or 3 or more children sharing a bedroom. History of gastrointestinal symptoms was based on the previous 30 days, and participants were asked to rank severity from none to severe for stomach pain, vomiting, nausea, heartburn, diarrhea (>= 3 loose stools per day), blood in stool, constipation or nosebleeds.

Statistical Analysis

Univariate odds ratios were calculated using Epi Info software, version 6.04b. P values were two-tailed and values < 0.05 were considered statistically significant. Multivariable logistic regression, performed in STATA version 5, was used to determine independent risk factors for seropositivity. Multivariable models included variables significant at the $p \leq .20$ level on univariate analysis as well as variables found to be significant in previous studies.

RESULTS

Of 800 persons attending the 3 conferences, 224 participants were recruited. Of these, 21 were Alaska Native persons and were excluded from further analysis. The remaining 203 participants represented approximately 25% of conference attendees.

The mean age of the 203 participants was 43.5 years (range 21 to 72); 121 (60%) were female. Overall, 49 participants (24%) were positive for antibody to *H. pylori*. Most participants reported currently living in an Alaska village (60%), compared with urban centers (34%) or Alaska hub towns (3%). In terms of residence history, 108 participants (53%) had lived in an Alaska village for 6 months or more (minimum 6 months, maximum 33.1 years, median 6.1 years). Twenty-five participants (12%) had lived in a hub community for 6 months or more (minimum 6 months, maximum 20.3 years, median 4.0 years). Forty-four participants (22%) had lived 6 months or more in a developing country (minimum 6 months, maximum 9.0 years, median 2.0 years). Characteristics of seropositive participants were compared with those who were seronegative. The proportion of persons who were seropositive increased with age, from 4% in 21 to 30 year-olds, to 38% in 51 to 60 year-olds. This trend was statistically significant ($p < 0.001$) (Table I). Mean age of seropositive and seronegative persons were 48 and 42 years, respectively.

Historical places of residence (6 months duration or longer) in Alaska were also examined as potential risk factors. The relative risk of being seropositive was 1.98 times higher for people who had lived 6 months or longer in an Alaska hub town compared with those who had not lived in a potentially high risk setting (p=0.077, 95% CI 1.04, 3.75). No association was seen between seropositivity and a history of living in an Alaska village or a developing country for 6 months or longer, regardless of age at time of residence (Table II).

Current and past living conditions were also examined as potential risk factors. The relative risk of being seropositive was not significantly increased for people who used surface water as their household water source during the previous year, or for those who lacked running water or flush toilets. The relative risk of being seropositive was somewhat increased for those who had experienced crowding during childhood (RR=1.61, p=0.058, 95% CI 1.05, 2.48).

Participants were asked a series of questions related to clinical symptoms experienced during the previous 30 days and about their lifetime medical history. In addition, participants were asked about use of GI medications (e.g., antacids or acid reducers) and non-steroidal anti-inflammatory and Aspirin use during the previous year. Although none of the clinical symptoms or medical history indicators measured were statistically associated with seropositivity, a higher proportion of seropositive participants reported a history of ulcer disease compared with participants without ulcer disease (39% v. 22%, RR 2.07, 95% CI 0.85-5.04, p = 0.187) (Table III).

Table I. Seroprevalence of *H. pylori* IgG antibodies by age group.

	HP seropositive/total in category (%)	p-value
Age (years)		
21-30	1/27 (4%)	
31-40	4/49 (8%)	**Test for trend < 0.001**
41-50	26/76 (34%)	
51-60	15/40 (38%)	
61+	3/11 (27%)	

Table II. *H. pylori* IgG antibody positivity by gender, residence, living conditions, and risk behaviors.

	HP Seropositive/Total (%)	RR*	95% CI	p-value
Sex				
Male	19/82 (23%)	0.95	(0.64, 1.41)	0.922
Female	30/121 (25%)	1.0		
Residence History				
Rural Alaska Village	25/108 (23%)	1.02	(0.78, 1.33)	0.961
Rural Alaska Hub	11/24 (46%)	1.98	(1.04, 3.75)	0.077
Developing Country	10/43 (23%)	1.01	(0.59, 1.74)	0.863
Residence in any above	35/138 (25%)	1.05	(0.86, 1.30)	0.762
No past residence in above locations	14/63 (22%)	1.0		
Any of above at age < 10 years	3/8 (38%)	1.59	(0.63, 4.03)	0.403
No history of residence in above at < 10 years of age	46/195 (24%)	1.0		
Living conditions				
Surface water use in last year	15/55 (27%)	1.18	(0.72, 1.94)	0.652
No surface water use in last year	34/148 (23%)	1.0		
No flush toilet	3/27 (11%)	0.43	(0.14, 1.27)	0.097
Flush toilet available	46/176 (26%)	1.0		
No running water	13/58 (22%)	0.91	(0.54, 1.54)	0.856
Running water available	36/145 (25%)	1.0		
Childhood crowding	20/59 (33%)	1.61	(1.05, 2.48)	0.058
No crowding in childhood	29/144 (20%)	1.0		
Education level				
Master's degree or higher	29/110 (26%)	1.13	(0.86, 1.48)	0.508
Less than a master's degree	19/90 (21%)	1.0		
Behaviors				
Currently own pet	27/111 (24%)	1.03	(0.77, 1.38)	0.967
Don't currently own pet	21/91 (23%)	1.0		
Ever owned a pet	46/184 (25%)	1.58	(0.54, 4.61)	0.573
Never owned a pet	3/19 (16%)	1.0		
Consume AK Native food	30/131 (23%)	0.93	(0.73, 1.20)	0.702
Did not consume AK Native food	19/72 (26%)	1.0		
Collect greens/berries	24/107 (22%)	0.86	(0.64, 1.15)	0.372
Fish	27/120 (23%)	0.87	(0.67, 1.13)	0.363
Hunt	16/64 (25%)	0.88	(0.59, 1.32)	0.674
Trap	3/11 (27%)	0.89	(0.26, 3.04)	0.860
Do not participate in subsistence activities	18/60 (30%)	1.0		
Work with preschool children	15/79 (19%)	0.94	(0.65, 1.36)	0.896
Work with elementary children	34/137 (25%)	1.05	(0.86, 1.29)	0.753
Do not work with preschool or elementary children	12/56 (21%)	1.0		

* Relative Risk

Hemoglobin and serum ferritin values were measured for each participant. There was no difference in median hemoglobin values among seropositive and seronegative participants. The median ferritin level for seropositive women was 40.7 mcg/L compared with 51.3 mcg/L for seronegative women; however, the difference was not statistically significant (p=0.688). There was no difference among seropositive and seronegative participants in the proportion with ferritin values <15mcg/dl (Table IV). A linear regression of serum ferritin

Table III. *H. pylori* IgG antibody positivity by reported GI symptoms and self-reported medical history.

	HP Seropositive/ Total with symptom (%)	HP Seropositive/ Total without symptom (%)	RR	95% CI	p-value
GI Symptoms in last 30 days					
Nausea	10/49 (20%)	33/143 (23%)	0.89	(0.48, 1.63)	0.851
Stomach pain	15/66 (23%)	31/129 (24%)	0.95	(0.59, 1.53)	0.980
Vomiting	3/12 (25%)	40/180 (22%)	1.13	(0.41, 3.11)	0.733
Vomiting blood	0/1 (0%)	43/190 (23%)	0.0	--	1.0
Heartburn	21/88 (24%)	24/108 (22%)	1.05	(0.73, 1.51)	0.920
Diarrhea	21/86 (24%)	27/112 (24%)	1.01	(0.70, 1.46)	0.907
Blood in stool	3/9 (33%)	40/182 (22%)	1.52	(0.58, 3.98)	0.424
Constipation	10/54 (19%)	32/138 (23%)	0.81	(0.45, 1.47)	0.611
Nosebleeds	8/24 (33%)	34/169 (20%)	1.80	(0.83, 3.91)	0.230
Medical History					
Ever hospitalized for GI symptoms	6/16 (38%)	41/181 (23%)	1.91	(0.73, 4.99)	0.304
Ever diagnosed by health care provider:					
Anemia	14/47 (30%)	30/148 (20%)	1.53	(0.90, 2.61)	0.190
Ulcer	7/18 (39%)	40/182 (22%)	2.07	(0.85, 5.04)	0.187
Gastritis	4/12 (33%)	41/181 (23%)	1.47	(0.63, 3.42)	0.479
Stomach cancer	--	44/193 (23%)	--	--	--
Hepatitis A	1/1 (100%)	44/194 (23%)	4.41	--	0.231
Helicobacter pylori	1/1 (100%)	41/191 (21%)	4.66	--	0.219
GI meds in last 12 months	24/100 (24%)	22/100 (22%)	1.06	(0.77, 1.46)	0.867
NSAIDS in last 12 months	39/174 (22%)	7/25 (28%)	0.96	(0.84, 1.10)	0.715

Table IV. Serum hemoglobin and ferritin levels by *H. pylori* IgG antibody and gender.

	Females n=116 HP +	HP -		Males n=80 HP +	HP -	
Hemoglobin						
< 12 g/dl	1/30 (3%)	2/86 (2%)	OR=1.45, p=1.0 95% CI (0.13, 16.5)			
< 13.5 g/dl				0/19 (0%)	2/61 (3%)	OR=0.0, p=1.0
Median (g/dl)	13.5	14.0	p=.071	16.1	16.0	p=0.870
Serum ferritin						
< 15 mcg//L	3/30 (10%)	11/91 (12%)	OR=0.81, p=1.0 95% CI (0.16, 3.48)	1/19 (5%)	0/63 (0%)	OR=NA, p=0.232
Median (mcg/L)	40.7	51.3	p=.688	196.8	151.6	p=0.680

values (measured on a logarithmic scale) adjusted for age and sex, failed to show a significant decrease in ferritins for HP seropositive persons (p=0.238).

Variables found to be significant at the $p \leq 0.20$ level on initial analysis (age ≥ 40 years, residence in a hub town for ≥ 6 months, childhood crowding, lack of sewer/flush toilets and history of ulcer disease) were included in the multivariate model. In addition, the variable education level was also included based on previous studies. Being 40 years of age and older was the only factor that was significantly associated with *H. pylori* seropositivity.

DISCUSSION

In this study, we found that among a cohort of non-Native educators (mean age 44 years) living in Alaska, 24% were seropositive for *H. pylori*. Seropositivity rose significantly with increasing age and was found to be associated specifically with age > 40 years. This study is unique because, while previous studies have documented a high prevalence of *H. pylori* infection in Alaska Native people (10, 12), no studies to date have examined *H. pylori* seroprevalence among a cohort of non-Native people residing in Alaska.

Our overall finding of 24% *H. pylori* seroprevalence among non-Native adults is similar to a previous study of non-Native persons in the U.S. that documented a steady rise in seroprevalence with age with peak seroprevalence of 40-50% in persons 55 to 60 years of age (9). Despite residence in communities with an increased *H. pylori* prevalence, these non-Native educators were not found to have elevated rates of seropositivity, suggesting that their living conditions may have differed significantly from those of the Alaska Native population. Longer duration of residence in Alaska may increase the risk of acquiring *H. pylori*; however, only information on duration of residence for 6 months or longer was obtained.

We found no association between low hemoglobin or low ferritin values and *H. pylori* seropositivity among our cohort of Alaska non-Native educators. A previous seroprevalence study performed in Alaska in the 1990s documented an association between low ferritin values and *H. pylori* seropositivity in the Alaska Native population (10). More recent treatment studies in Alaska have documented an association between active infection with *H. pylori* and both iron deficiency and iron deficiency anemia in Alaska Native children 7 to 11 years of age; however, no significant improvement in iron deficiency or anemia was documented up to 14 months post cure in this population (13,14).

Among our cohort of non-Native educators in Alaska, we did not find an association between *H. pylori* seropositivity and a variety of well-documented risk factors such as lack of running water, lack of a flush toilet, prior residence in a developing country and low education level. Only a history of age greater than 40 years was associated with *H. pylori* seropositivity on multivariate analysis.

In our study, seropositivity for *H. pylori* was not associated with stomach pain or any other clinical symptoms. Previous studies have documented an association between dyspepsia and infection with *H. pylori*. Olafsson et al. demonstrated an improvement in abdominal pain scores in persons cured of their *H. pylori* infections (15), and Blum et al. in a randomized, placebo-controlled trial demonstrated some benefit in terms of symptom improvement to patients (16). However, two randomized, placebo-controlled trials demonstrated no benefit in symptom reduction post-treatment (17,18).

Previous studies have documented an association between *H. pylori* seropositivity and socioeconomic factors, including housing conditions. We evaluated a variety of living conditions as potential risk factors and determined that while childhood crowding was associated with seropositivity on univariate analysis, this association was not present in the multivariate analysis.

The data in this study are subject to several limitations. This study was based on a cross-sectional, convenience sample of educators. The self-administered questionnaire allowed for incomplete answers, reducing the responses for some categories. Also, it was impossible to validate responses, including self-reported medical history. There were small numbers of participants in several categories, and duration of residence was not assessed and therefore could not be evaluated as a risk factor for seropositivity. We did not collect data on socioeconomic status or ethnicity (beyond Alaska Native verses non-Native). In addition, no tests for active infection with *H. pylori* were performed, and outcomes such as iron deficiency or anemia may be more related to active than past infection.

In conclusion, non-Native educators residing in Alaska had a lower seroprevalence than that found in previous studies involving adult Alaska Native persons. This finding argues against a ubiquitous common environmental exposure such as water in the transmission of *H. pylori* to adults. Additional studies to determine risk factors for the spread of *H. pylori* are needed, and the possibility of multiple routes of exposure should be considered.

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REFERENCES

1. Graham DY, Malaty HM, Evans DG, Evans DJ, Jr., Klein PD, Adam E. Epidemiology of Helicobacter pylori in an asymptomatic population in the United States. Effect of age, race, and socioeconomic status. Gastroenterology 1991;100(6):1495-1501.
2. Bardhan PK. Epidemiological features of Helicobacter pylori infection in developing countries. Clin Infect Dis. 1997;25(5):973-978.
3. Tytgat GN, Rauws EA. Campylobacter pylori and its role in peptic ulcer disease. Gastroenterol Clin North Am. 1990;19(1):183-196.
4. Rauws EA, Tytgat GN. Cure of duodenal ulcer associated with eradication of Helicobacter pylori. Lancet 1990;335(8700):1233-1235.
5. Bayerdorffer E, Neubauer A, Rudolph B, Thiede C, Lehn N, Eidt S, et al. Regression of primary gastric lymphoma of mucosa-associated lymphoid tissuetype after cure of Helicobacter pylori infection MALT Lymphoma Stud Group. Lancet 1995;345 (8965):1591-1594.
6. Nomura A, Stemmermann GN, Chyou PH, Kato I, Perez-Perez GI, Blaser MJ. Helicobacter pylori infection and gastric carcinoma among Japanese Americans in Hawaii. N Engl J Med. 1991;325(16):1132-1136.
7. Dooley CP, Cohen H, Fitzgibbons PL, Bauer M, Appleman MD, Perez-Perez GI, et al. Prevalence of Helicobacter pylori infection and histologic gastritis in asymptomatic persons. N Engl J Med. 1989;321 (23):1562-1566.

8. Blaser MJ. Principles and Practice of Infectious Diseases. 5th ed. New York: Churchill Livingston 2000.
9. Taylor DN, Blaser MJ. The epidemiology of Helicobacter pylori infection. Epidemiol Rev. 1991;13:42-59.
10. Parkinson AJ, Gold BD, Bulkow L, Wainwright RB, Swaminathan B, Khanna B et al. High prevalence of Helicobacter pylori in the Alaska native population and association with low serum ferritin levels in young adults. Clin Diagn Lab Immunol. 2000;(6):885-888.
11. Khanna B, Cutler A, Israel NR, Perry M, Lastovica A, Fields PI et al. Use caution with serologic testing for Helicobacter pylori infection in children. J Infect Dis. 1998;78(2):460-465.
12. Gessner BD, Bruce MG, Parkinson AJ, Gold BD, Muth PT, Dunaway E et al. A randomized trial of triple therapy for pediatric Helicobacter pylori infection and risk factors for treatment failure in a population with a high prevalence of infection. Clin Infect Dis. 2005;41(9):1261-1268.
13. Gessner BD, Baggett HC, Muth PT, Dunaway E, Gold BD, Feng Z et al. A controlled, household-randomized, open-label trial of the effect that treatment of Helicobacter pylori infection has on iron deficiency in children in rural Alaska. J Infect Dis. 2006;193(4):537-546.
14. Baggett HC, Parkinson AJ, Muth PT, Gold BD, Gessner BD. Endemic iron deficiency associated with Helicobacter pylori infection among school-aged children. Alaska. Pediatrics 2006;117(3):396-404.
15. Olafsson S, Hatlebakk JG, Berstad A. Patients with endoscopic gastritis and/or duodenitis improve markedly following eradication of Helicobacter pylori, although less so than patients with ulcers. Scand J Gastroenterol. 2002;37(12):1386-1394.
16. Blum AL, Talley NJ, O'Morain C, van Zanten SV, Labenz J, Stolte M et al. Lack of effect of treating Helicobacter pylori infection in patients with non-ulcer dyspepsia. Omeprazole plus Clarithromycin and Amoxicillin Effect One Year after Ttreatment (OCAY) Study Group. N Engl J Med. 1998;339(26):1875-1881.
17. McNamara D, Buckley M, Gilvarry J, O'Morain C. Does Helicobacter pylori eradication affect symptoms in non-ulcer dyspepsia: a 5-year follow-up study. Helicobacter. 2002;7(5):317-321.
18. Talley NJ, Vakil N, Ballard ED, 2nd, Fennerty MB. Absence of benefit of eradicating Helicobacter pylori in patients with non-ulcer dyspepsia. N Engl J Med. 1999;341(15):1106-1111.

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