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Prevalence of *Helicobacter pylori* among Alaskans: Factors Associated with Infection and Comparison of Urea Breath Test and Anti-*Helicobacter pylori* IgG antibodies

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Abstract

Background: *Helicobacter pylori* is one of the most common human infections in the world and studies in Alaska Native people, as well as other Indigenous peoples, have shown a high prevalence of this gastric infection. This study was undertaken to determine the prevalence of *H. pylori* infection by urea breath test (UBT) and anti-*H. pylori* IgG among Alaskans living in four regions of the state and to identify factors associated with infection.

Methods: A convenience sample of persons > 6 months old living in five rural and one urban Alaskan community were recruited from 1996 to 1997. Participants were asked about factors possibly associated with infection. Sera were collected and tested for anti-*H. pylori* IgG antibodies; a UBT was administered to participants > 5 years old.

Results: We recruited 710 people of whom 571 (80%) were Alaska Native and 467 (66%) were from rural communities. Rural residents were more likely to be Alaska Native compared with urban residents ($p < 0.001$). Of the 710 people, 699 (98%) had a serum sample analyzed and 634 (97%) persons > 5 years old had a UBT performed. *H. pylori* prevalence was 69% by UBT and 68% by anti-*H. pylori* IgG. Among those with a result for both tests, there was 94% concordance. Factors associated with *H. pylori* positivity were Alaska Native racial status, age > 20 years, rural region of residence, living in a crowded home, and drinking water that was not piped or delivered.

Conclusions: *H. pylori* prevalence is high in Alaska, especially in Alaska Native persons and rural residents. Concordance between UBT and serology was also high in this group. Two

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socioeconomic factors, crowding and drinking water that was not piped or delivered, were found to be associated with *H. pylori* positivity.

Keywords

Helicobacter pylori; Alaska; UBT; IgG antibody; prevalence

Introduction

Helicobacter pylori is one of the most common human infections with over 50% of persons infected in some countries (1). Numerous studies from around the world have shown that the prevalence of *H. pylori* infection is related to age, gender, ethnicity, and a variety of socioeconomic indicators (2–6); moreover, intrafamilial clustering also occurs (7–10). *H. pylori* colonization of the stomach results in an inflammatory response, gastritis, that can persist for decades (11), and infected persons have a 10 to 20% lifetime risk of developing peptic ulcer disease and a 1 to 2% lifetime risk of developing gastric cancer, particularly in populations with specific host-genetic risk (12–14). Because of this, *H. pylori* is characterized as a group I carcinogen by the International Agency for Research on Cancer (World Health Organization) (15).

Gastric cancer incidence and mortality is decreasing in many parts of the world, but this is not true for Alaska Native people for whom gastric cancer is the third most common cause of cancer-related death (16–18). Additionally, the gastric cancer mortality rate among Alaska Native people is more than three times higher than among U.S. whites (11.3 vs. 3.2 per 100,000 persons) (19). Past studies in Alaska have shown that *H. pylori*-infected persons have a higher risk of gastric cancer compared with non-infected persons and that 75% of Alaska Native people have *H. pylori* IgG antibodies (20, 21). This study was undertaken to determine the prevalence of *H. pylori* infection by both urea breath test (UBT) and anti-*H. pylori* IgG among Alaskans living in four regions of the state and to identify factors associated with infection.

Methods

Study Participants

Persons living in five rural Alaska Native communities and one urban city were invited to participate. The six communities were selected to represent four geographic regions (Figure 1). Study approval was obtained from the regional health corporations and village leadership. The study was approved by Institutional Review Boards of the Centers for Disease Control and Prevention and the Alaska Area Indian Health Service.

Recruitment occurred during 1996 and 1997. A convenience sample of persons living in all six communities were recruited using public advertisements and personal contact with study staff. All residents >6 months old were eligible to enroll. Participants 18 years old provided written, informed consent whereas parents or legal guardians provided consent for participants <18 years old.

Data collection

The head of a household provided information about the number of household members, size of the house, and drinking water source(s) for the home. We obtained age, sex, ethnicity, education level, and water use behaviors for individual household members. We also asked about clinical information and medication use that could be related to an *H. pylori* infection. A chart review was not done to confirm the self-reported clinical information nor did we confirm whether or not the clinical diagnoses (gastritis, ulcer, gastric cancer, *H. pylori* infection) were determined by esophagogastroduodenoscopy.

From each participant, we collected a whole blood specimen in a standard serum separator tube. We centrifuged the specimens in the field, decanted the serum, and transported them on ice packs to Anchorage where they were frozen at -30°C until analysis. After all sera were collected, they were shipped to the CDC's Foodborne and Diarrheal Diseases Laboratory in Atlanta where they were tested for *H. pylori* IgG antibodies with an enzyme-linked immunosorbent assay (ELISA) used previously in this population (21–23). This assay has a sensitivity of 92% and a specificity of 98% compared with upper endoscopy. A value of 0.8 was considered positive.

Each participant >5 years old underwent a urea breath test (UBT) for current *H. pylori* infection using the commercial Meretek UBT® (now called BreathTek UBT, Otsuka Pharmaceuticals) according to the manufacturer's instructions. Discontinuation of medications was not a requirement for UBT testing. Breath samples were kept at room temperature and sent to the Meretek testing laboratory (Houston, TX) where they were assessed for $^{13}\text{CO}_2$ by mass spectrophotometry. The amount of $^{13}\text{CO}_2$ in each person's baseline and 30-minute samples was compared and a ratio of >2.4 was considered positive.

Statistical analysis

Proportions were compared using a chi-squared or Fisher's exact test as appropriate, and logistic regression was used to examine multiple factors simultaneously. All factors were examined in a univariate fashion to assess preliminary significance. In addition, multiple options for grouping categorical and ordinal variables were assessed. A backwards selection procedure was used beginning with a comprehensive model with all factors; the adjusted odds-ratios for all factors are reported. Logistic regression analyses were repeated treating household as a random effect with very similar results (not presented). Water use in a village was classified into two groups, "Piped and delivered water only" and "Other water sources". The former included piped municipal water, well water, water delivered by municipal truck, and bottled water; the latter included water hauled from a municipal spigot and natural water sources such as that from rivers and lakes, or acquired from rain or melted snow and ice. Analyses were performed using Stata V10. P-values are two-sided and those less 0.05 are considered statistically significant.

Results

We recruited 710 people (age range, 2–92 years) of whom 382 (54%) were female and 571 (80%) were Alaska Native (Table 1). Participants from rural regions A-C were more likely to

be Alaska Native than participants from urban region D ($p < 0.001$; Figure 1). As compared with the 2000 census population for these six communities, study participants were more likely to be female and Alaska Native. This remains true when the rural and urban communities are analyzed separately. The most common clinical symptom related to a possible *H. pylori* infection was stomach pain, with 33% of participants reporting it. Diagnoses of gastritis, ulcer, gastric cancer, or a previous *H. pylori* infection were uncommon with 7%, 8%, 0.1%, and 1%, respectively, of persons reporting each (Table 1).

We analyzed UBT samples from 634 (97%) of 655 eligible persons >5 years old. Six persons had indeterminate results and were not included in the final analysis. Characteristics of the remaining 628 persons are in Table 2. We analyzed 699 serum samples for IgG antibodies to *H. pylori* (Table 2). *H. pylori* prevalence was similar by UBT and anti-*H. pylori* IgG (69% and 68%, respectively). For persons with a result for both tests, there was 94% concordance between the two results.

Univariate analysis showed that *H. pylori* positivity as detected by UBT or anti-*H. pylori* IgG was associated with Alaska Native race, rural region of residence, being part of a large family, living in a more crowded house, and, among persons 20 years old, having 12 years of education (Table 2). Gender was not associated with *H. pylori* positivity using either test. In multivariate analysis, factors associated with *H. pylori* positivity were Alaska Native racial status, age 20 years old, and rural region of residence. Household crowding remained associated with seropositivity but not a positive UBT.

In the three rural regions where drinking water sources could vary, active *H. pylori* infection as detected by UBT was associated with drinking water source (Table 3). Persons having access to municipal piped or delivered sources of water had a lower prevalence of infection. Moreover, among persons <20 years old, access to municipal piped or delivered water was also associated with a lower prevalence of anti-*H. pylori* IgG.

Discussion

Despite the high *H. pylori* seroprevalence (21) and high rates of gastric cancer in the Alaska Native people (19), few studies have been published investigating factors in this population that may be associated with infection. In this 1996–1997 study of *H. pylori* infection in four Alaska regions using UBT and serology, we found associations between *H. pylori* positivity and race, rural residence, and age 20 years old. Two socioeconomic factors, living in a crowded home and drinking water source, were also associated with infection. Prevalence was nearly 70% for both UBT and serology and concordance between the two tests was high, at 94%.

H. pylori prevalence varies around the world. Recent reviews by Peleteiro et al. and Eusesbi et al. reported prevalence ranging from 13% in Finland and the United Kingdom to 94% in Nigeria (3, 24). Data collected from the 1999–2000 United States National Health and Nutrition Examination Surveys show an all-ages U.S. seroprevalence of 27% (25). The prevalence in our study, particularly among Alaska Native people, is similar to the prevalence reported in developing countries rather than the general U.S. population (3, 5, 24,

26). It is also high when compared with the prevalence among Aboriginal adults living in Arctic communities. In a review of six relevant studies of *H. pylori* prevalence among Aboriginal populations of Canada, Greenland, and Russia, Goodman et al. identified only two populations with a prevalence higher than the Alaska Natives in our study (27). One was from Arctic Russia in 1990 (prevalence 77%) and the other from Northern Manitoba in 1996 (prevalence 95%) (28, 29).

Similar to other populations, socioeconomic factors are likely the major reason for the high prevalence of *H. pylori* infection in Alaska (1, 30–35). Our finding that *H. pylori* infection is associated with living in a more crowded home is not surprising because crowding leads to close contact between household members and *H. pylori* transmission is mainly intrafamilial (1). Other studies have shown intrafamilial clustering of infections (7–10) and in a previous study conducted in Alaska, household family members' infection status was associated with risk of becoming reinfected with *H. pylori* after successful eradication (36).

Water source has been identified as a possible risk factor for *H. pylori* infection in other epidemiologic studies (32, 37–40) and *H. pylori* organisms have been detected in a variety of water sources (40–43). We did not test water as part of this study; however, ingestion is not the only means of transmission potentially affected by water. Lee et al. showed that infrequent hand washing was associated with increased prevalence of *H. pylori* in Malaysia (44) suggesting that *H. pylori* infection could be related to inadequate hygiene practices. Previously, we have identified lack of in-home water service in Alaska to be a risk factor for reinfection with *H. pylori* (36) as well as for skin and respiratory infections (45–47). It is possible that the availability of clean water was a surrogate for the availability of water in general and that lack of water for hygiene contributed to transmission in the rural communities. More work is needed to better understand improvement in water source as a potential approach to preventing infection.

In this population *H. pylori* is typically acquired in childhood, thus it is not surprising we found increasing prevalence until adulthood. In persons >20 years old, prevalence appeared stable at about 70%. In contrast, other groups have found increasing prevalence past 20 years of age (6, 34, 35, 48–52). It is thought that the increase in prevalence in older age groups is due to a birth cohort effect in which childhood acquisition rates have decreased over time presumably due to improved sanitary, hygiene, and socioeconomic factors in subsequent generations of children. However, overall seroprevalence rates do not appear to be decreasing in rural Alaska. Prevalence in this 1996–1997 study was similar to that found in a serosurvey from 1980–1986 (21). This is an important observation because gastric cancer incidence remains high among Alaska Native people (16). Peleteiro et al. presented an analysis of gastric cancer incidence as it relates to *H. pylori* prevalence around the world, concluding that prevalence of infection was at least two-fold higher in countries with high gastric cancer incidence (24). High *H. pylori* prevalence in Alaska is likely at least partly responsible for the continued high incidence of gastric cancer among the Alaska Native people and, as there is no evidence of improvement, it is becoming increasingly important to develop strategies to address this disparity.

This is one of the few studies that tested for *H. pylori* infection in the same people using both UBT and serology; the 94% concordance is informative. Using serology to diagnose an *H. pylori* infection is not recommended in populations where infection is common (53). This is because antibodies circulate long after eradication, so many people who are no longer infected may have a positive test result, resulting in a low test specificity (54). However, a study by Bruden et al. showed that false positive serology results were associated with previous *H. pylori* treatment (55). In our study group, a previous *H. pylori* diagnosis was uncommon at study entry, so it is unlikely many participants had formerly been treated for the infection. Therefore, data from our study suggests that UBT and serology results are comparable when persons have not been previously treated for infection. We can have confidence comparing results across studies of untreated populations where prevalence of infection was determined using different methods.

This study has four important limitations. A cross-sectional survey that includes primarily adults is not a suitable method for understanding factors associated with an infection usually acquired during childhood, because factors may have changed over time. However, it is likely that many of the factors studied, related to living in rural, primarily Alaska Native communities, did not change for many persons between the time they acquired an *H. pylori* infection and the time of the study. The convenience sampling methodology we used, particularly in the urban region, may have resulted in a non-representative sample. Therefore, generalizations to the entire population should be made with caution. The water source used and reported at the time of the study may have been different from the water source used when the organism was acquired. Finally, the samples were collected and tested over 20 years ago and *H. pylori* prevalence may have changed during that time. However, numerous studies published since these data were collected show that *H. pylori* infection and gastric cancer continue to negatively affect the Alaska Native people (16, 36, 53, 56, 57). Thus, it is important these older data be published as a prevalence baseline as we continue to address this health disparity.

In conclusion, *H. pylori* prevalence is high in Alaska, especially in Alaska Native people. Concordance between UBT and serology was high which gives increased validity to the results and confidence in interpreting data between studies of untreated persons that use different testing methods. Socioeconomic factors associated with infection in Alaskans are living in a crowded home and drinking water from a less protected source. The prevalence in this study conducted in the late 1990s was similar to a seroprevalence study from the 1980s. This, combined with the stable prevalence in persons 20 years old in this study, indicate more recent birth cohorts may not be at decreased risk of *H. pylori* infection as seen in other populations around the world. This has health implications for addressing the high incidence of gastric cancer in the Alaska Native people. Because the socioeconomic conditions in rural Alaska are similar now as compared with 20 years ago, an updated prevalence study in a similar cohort could be considered to investigate whether or not prevalence continues to be stable.

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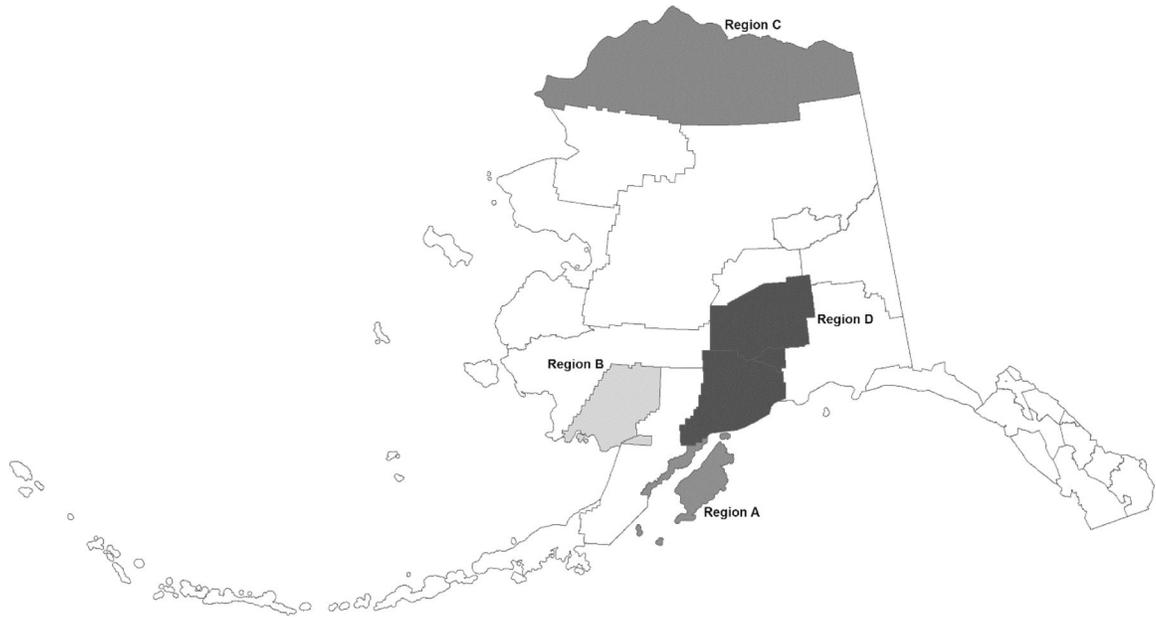


Figure 1.
Map of Alaska with study regions identified; Alaska 1996–1997.

Table 1.

Characteristics of study participants; Alaska 1996–1997.

Region	Region A ^a n (%)	Region B ^a n (%)	Region C ^a n (%)	Region D n (%)	Total n (%)
Participants	122	226	119	243	710
Female	54 (44)	115 (51)	76 (64)	137 (56)	382 (54)
Alaska Native	116 (95)	224 (99)	105 (88)	126 (52)	571 (80)
Age					
<5	4 (3)	17 (8)	7 (6)	12 (5)	40 (6)
5–9	16 (13)	31 (14)	16 (13)	25 (10)	88 (12)
10–19	30 (25)	44 (19)	17 (14)	59 (24)	150 (21)
20–34	13 (11)	59 (26)	20 (17)	38 (16)	130 (18)
35–49	34 (28)	42 (19)	16 (13)	67 (28)	159 (22)
50	25 (20)	33 (15)	43 (36)	42 (17)	143 (20)
Clinical ^{b,c}					
Stomach pain	38/122 (31)	82/226 (36)	42/119 (35)	75/241 (31)	237/708 (33)
Gastritis	8/120 (7)	12/212 (6)	9/113 (8)	21/239 (9)	50/684 (7)
Ulcer	16/121 (13)	8/217 (4)	6/115 (5)	25/242 (10)	55/695 (8)
Gastric cancer	0/122 (0)	0/218 (0)	0/114 (0)	1/243 (0.4)	1/697 (0.1)
<i>H. pylori</i>	0/121 (0)	1/217 (0.5)	2/111 (2)	2/242 (1)	5/691 (1)
Medications ^{b,c,d}					
Antacids	55/122 (45)	30/222 (14)	31/117 (26)	99/242 (41)	215/703 (31)
PPI ^e	0/121 (0)	1/216 (0.5)	1/109 (1)	5/241 (2)	7/687 (1)
H2 blocker	16/120 (13)	5/219 (2)	9/111 (8)	34/241 (14)	64/691 (9)

^a rural region

^b denominator differences are due to each participant's ability and/or willingness to answer each question

^c self-reported; no chart review done

^d any use in the past 12 months

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Table 2.

Prevalence of *Helicobacter pylori* infection as determined by urea breath test and enzyme linked immunosorbent assay; Alaska 1996–1997.

Characteristic	Urea Breath Test positive			<i>H. pylori</i> IgG positive		
	Positive/total (%)	Univariate OR ^a (p value)	aOR ^b (p value)	Positive/total (%)	Univariate OR (p value)	aOR (p value)
Overall	433/628 (69)			478/699 (68)		
Sex						
Female	240/347 (69)	Ref	Ref	265/376 (70)	Ref	Ref
Male	193/281 (69)	0.98 (0.897)	1.18 (0.470)	213/323 (66)	0.81 (0.199)	0.87 (0.466)
Race						
Alaska Native	409/500 (82)	19.5 (<0.001)	11.3 (<0.001)	422/561 (75)	10.5 (<0.001)	7.20 (<0.001)
Non-Native	24/128 (19)	Ref	Ref	36/138 (26)	Ref	Ref
Age						
<5	N/A			14/37 (38)	0.25 (<0.001)	0.09 (<0.001)
5–9	36/54 (67)	0.83 (0.590)	0.37 (0.029)	55/85 (65)	0.74 (0.313)	0.36 (0.005)
10–19	98/147 (67)	0.83 (0.467)	0.43 (0.016)	100/148 (68)	0.85 (0.511)	0.46 (0.017)
20–34	91/126 (72)	1.08 (0.773)	0.66 (0.266)	96/129 (74)	1.18 (0.544)	0.93 (0.828)
35–49	107/158 (68)	0.87 (0.586)	1.09 (0.809)	112/158 (71)	0.99 (0.963)	1.17 (0.623)
50	101/143 (71)	Ref	Ref	101/142 (71)	Ref	Ref
Grouped Age						
<20	134/201 (67)	Ref	Ref	169/270 (63)	Ref	Ref
20	299/427 (70)	1.17 (0.397)		309/429 (72)	1.54 (0.009)	
Region						
Region A ^c	81/114 (71)	3.68 (<0.001)	1.47 (0.185)	94/122 (77)	4.07 (<0.001)	1.91 (0.026)
Region B ^c	186/193 (96)	39.9 (<0.001)	13.4 (<0.001)	187/220 (85)	6.86 (<0.001)	2.56 (0.001)
Region C ^c	78/101 (77)	5.09 (<0.001)	2.49 (0.004)	88/116 (76)	3.81 (<0.001)	1.99 (0.020)
Region D	88/220 (40)	Ref	Ref	109/241 (45)	Ref	Ref
Region type						
Urban	88/220 (40)	Ref	Ref	109/241 (45)	Ref	Ref
Rural	345/408 (85)	8.21 (<0.001)		369/458 (81)	5.02 (<0.001)	
# persons in household						
5 persons	234/306 (76)	2.02 (<0.001)	0.96 (0.877)	263/361 (73)	1.54 (0.008)	1.05 (0.847)
< 5 persons	198/321 (62)	Ref	Ref	214/337 (64)	Ref	Ref
Household crowding						
> 1 person/room	212/247 (86)	4.41 (<0.001)	1.72 (0.064)	235/287 (82)	3.16 (<0.001)	2.00 (0.009)
1 person/room	220/380 (58)	Ref	Ref	242/411 (59)	Ref	Ref
Education (among those 20 years)						
12 years	207/245 (84)	6.31 (<0.001)	1.27 (0.511)	204/248 (82)	3.72 (<0.001)	0.72 (0.362)

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Characteristic	Urea Breath Test positive		<i>H. pylori</i> IgG positive	
	Positive/total (%)	Univariate OR ^a (p value)	aOR ^b (p value)	Positive/total (%)
>12 years	76/164 (46)	Ref	Ref	91/164 (55)
				Univariate OR (p value)
				aOR (p value)
				Ref

^aOR = Odds Ratio

^baOR = adjusted OR

^crural region

Table 3.

Relationship of participant's drinking water source with *Helicobacter pylori* infection status as determined by urea breath test and enzyme-linked immunosorbent assay, rural residents only; Alaska 1996–1997.

	Piped or Delivered Water ^a	Other Water Sources ^b	OR ^c (p value)
Urea Breath Test positive			
All Ages	195/250 (78%)	150/159 (94%)	0.21 (<0.001)
Age <20 years	55/80 (69%)	46/48 (96%)	0.10 (0.002)
Anti- <i>H. pylori</i> IgG positive			
All Ages	218/280 (78%)	151/178 (85%)	0.63 (0.067)
Age <20 years	74/111 (67%)	56/65 (86%)	0.32 (0.006)

^a piped municipal water, well water, water delivered by a municipal truck, bottled water

^b water hauled from a municipal spigot, natural water sources such as from rivers, lakes, rain, melted snow/ice

^c Odds Ratio