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RAPID COMMUNICATION

Factors associated with *H pylori* epidemiology in symptomatic children in Buenos Aires, Argentina

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Abstract

AIM: To determine prevalence of *H pylori* infection in symptomatic children in Buenos Aires, Argentina, and to investigate factors associated with *H pylori* positivity.

METHODS: A total of 395 children with upper gastrointestinal symptoms referred to the Gastroenterology Unit of the Children Hospital "Sor Maria Ludovica" were evaluated for the presence of *H pylori* by the ^{13}C-Urea Breath Test (^{13}C-UBT). A questionnaire was applied to the recruited population.

RESULTS: Prevalence of *H pylori* infection was 40.0% in this population (mean age 9.97 ± 3.1 years). The factors associated with *H pylori* positivity were number of siblings ($P < 0.001$), presence of pet cats ($P = 0.03$) and birds ($P = 0.04$) in the household, and antecedents of gastritis among family members ($P = 0.01$). After multivariate analysis, number of siblings [Odds ratio (OR) = 1.39; 95% CI, 1.20-1.61] and contact with pet cats (OR = 1.76; 95% CI, 1.00-3.09) remained as variables associated with *H pylori* infection.

CONCLUSION: The prevalence of *H pylori* infection in children with upper gastrointestinal symptoms in Argentina was similar to that reported in developed countries. Children from families with a higher crowding index and presence of pet cats have a higher risk of being colonized with *H pylori*.

Key words: *H pylori*; Children; Epidemiology; Urea breath test; Prevalence

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INTRODUCTION

H pylori bacterium is now recognized as a major etiologic factor in the development of chronic superficial gastritis and peptic ulcer disease in adults and children[1]. Because its association with gastric cancer *H pylori* was classified in 1994 as a group 1 carcinogen by the International Agency for Research on Cancer[2]. *H pylori* acquisition occurs predominantly during early childhood, and its incidence and prevalence is higher in developing than in developed countries[3-5]. Several risk factors have been associated with acquisition and transmission of *H pylori* infection, those factors are mainly correlated with poor sanitary conditions and low socioeconomic status[5-7].

Controversial results have been found in establishing the role of *H pylori* as the etiology for the presence of specific symptoms in children such as recurrent abdominal pain (RAP)[8,9]. Specific symptoms suggestive of acute *H pylori* infection are vague, inconsistent, and similar to several other more common childhood disorders, manifesting as recurrent abdominal pain, dyspepsia or epigastric pain[10].

The aims of our study were to determine prevalence of *H pylori* infection in symptomatic children in Buenos Aires, Argentina, and to investigate risk factors associated with *H pylori* positivity.

MATERIALS AND METHODS

Subjects

The study was performed in 395 children with age ranging from 2 to 17 years (mean age 9.97 ± 3.1 years), who were referred to the Gastroenterology Unit of the Children Hospital "Superiora Sor Maria Ludovica" for upper gastrointestinal symptoms evaluation (gastroesophageal reflux, esophagitis symptoms, ulcerous syndrome, abdominal pain, and upper digestive haemorrhage). The Hospital is a tertiary level health care referral institution with the highest clinical complexity for attending children in the Province of Buenos Aires. The Gastroenterology Unit receives a monthly average of 600 patients who are referred from other services within the same hospital and from primary health care units located in the Province of Buenos Aires. Parents or grandparents identified as the responsible adults of the children, were instructed to carefully read the protocol information and to sign a written consent form according to the Helsinki declaration. Children with a signed consent were included in the study. Participation consisted in the diagnosis of *H pylori* infection by means of the ^{13}C-Urea Breath Test (^{13}C-UBT) and the completion of a questionnaire for epidemiological purposes.

^{13}C- urea breath test (^{13}C-UBT)

Children were instructed to fast for at least 6 h before the diagnostic test was performed. ^{13}C-UBT consisted of the following: two samples of exhaled air were taken previous to the ingestion of the labeled solution to determine basal $^{13}C/^{12}C$ ratios. Then, 150 mL of reconstituted powdered non-fatty milk containing 50 mg of ^{13}C-urea (Cambridge Isotope Laboratories Inc., Massachusetts, USA) were taken by each patient. Breath samples were collected at 30 and 45 min after the ingestion of the labeled solution in hermetically sealed containers (Labco limited, United Kingdom). Each sample of exhaled air was measured in a mass spectrometer coupled to a gas chromatographer (FinniganMAT GmbH, ThermoQuest Corp., Bremen, Germany). A change of > 3.5% in the delta over baseline (DOB) values was considered positive. The ^{13}C-UBT is a highly accurate diagnostic test, with values of sensitivity and specificity over 95%[11].

Epidemiological questionnaire

Parents or grandparents of the participant children were instructed to complete a questionnaire for epidemiological purposes. The questionnaire was focused on variables that might affect the risk for *H pylori* positivity. The evaluated variables were demographic data, family crowding (number of siblings, rooms in the house), socioeconomic status and sanitary standards [type of house (masonry, wooden, rustic), type of flooring (wooden, cement, soil), type of toilet (sewer, septic tank, pit latrine), source of water (well-shaft treated, well-shaft not treated, treated system)], presence of pets in the house, food intake [raw food (uncooked meat, chicken or fish) *vs* cooked food], drinking of beverages shared from the same container (with a special focus on the consumption of *"*mate*"*, a traditional argentine green herbs infusion), habit of chewing the nails, and history of digestive diseases among family members (gastritis, gastric and duodenal ulcers, or gastric cancer).

Statistical analysis

The Fisher Exact test was used to analyze dependency between *H pylori* positivity and other categorical variables. The Chi squared test was applied to variables with more than two categories. To analyze if variances of quantitative variables were homogeneous for both *H pylori* positive and negative groups, the Levene test was applied. Student's *t* test was used when it was proven that variances were homogeneous, if not, the non-parametric Mann-Whitney test was applied. A binary logistic regression equation was used to estimate the impact of different characteristics as predictive variables for *H pylori* status, by the Forward Stepwise (Likelihood Ratio) method. The results of logistic regression included odds ratios (OR) as well as 95% confidence intervals (CI) for each of the variables. Significance levels were set at alpha less than 0.05. The SPSS 10.0 statistical program (SPSS, Chicago, IL) was used to perform all the statistical analyses presented in this article.

RESULTS

All the 395 participating children were tested for *H pylori* infection by means of the ^{13}C-UBT. A total of 158 patients were found to be *H pylori* positive. Prevalence of *H pylori* infection in this symptomatic population was 40.0% (95% CI, 35.2-44.8). Among the 395 enrolled children, 332 (84.1%) completed the epidemiological questionnaire. *H pylori* prevalence was similar between the studied population and those excluded from the analysis because of the lack of the questionnaire. Prevalence of *H pylori* infection among different age groups was as follows: 2-5 years (n = 29), 34.5%; 6-7 years (n = 47), 48.9%; 8-9 years (n = 59), 37.3%; 10-11 years (n = 75), 45.3%; 12-13 years (n = 73), 37.0%; 14-17 years (n = 44), 47.7%. Table 1 summarizes the demographics of the population included in the study. No significant differences were found among age (P > 0.70), gender (P > 0.60), ethnic group (P > 0.15), educational level (P > 0.50) and place of residence (inner city *vs* suburban areas) (P > 0.40), between *H pylori* positive and negative patients.

The most relevant factors evaluated to influence the prevalence of *H pylori* infection are shown in Table 2. As

Table 1 Demographical data of the children included in the study

	H pylori (+)	*n* (%)	*H pylori* (-)	*n* (%)	*P*
n	140		192		
Age (yr) (mean ± SD)	9.89 ± 3.16		10.02 ± 2.96		0.708
Gender					
Female	77	(54.9)	110	(57.4)	
Male	63	(45.1)	82	(42.6)	0.660
Ethnic group					
Caucasian	130	(93.1)	170	(88.7)	
Asian	0	(0.0)	4	(2.0)	
American Indian	10	(6.9)	18	(9.3)	0.156
Educational level					
Kindergarten	14	(9.8)	24	(12.4)	
BGE[1]	116	(83.2)	150	(78.4)	
Polimodal[2]	10	(7.0)	18	(9.2)	0.564
Place of residence					
BA city[3]	6	(4.2)	10	(5.2)	
Great BA[4]	9	(6.3)	7	(3.6)	
BA province[5]	125	(89.5)	175	(91.2)	0.491

[1] Basic general education (for children from 6 to 15 years old); [2] For children from 15 to 18 years old; [3]Buenos Aires city (inner city); [4]Great Buenos Aires (suburban areas); [5]Buenos Aires province (inner city).

Table 2 Potential factors associated with *H pylori* positivity

	H pylori (+)	*n* (%)	*H pylori* (-)	*n* (%)	*P*
Domestic crowding					
Siblings					
0	3	(2.1)	10	(5.2)	
1	38	(27.1)	68	(35.4)	
2	23	(16.4)	58	(30.2)	
3	29	(20.7)	18	(9.4)	< 0.001[b]
4	15	(10.8)	16	(8.3)	
5	9	(6.4)	10	(5.2)	
> 5	23	(16.5)	12	(6.3)	
Rooms in the house					
1	10	(7.1)	14	(7.3)	
2	61	(43.6)	83	(43.2)	
3	44	(31.4)	57	(29.7)	> 0.700
4	12	(8.6)	14	(7.3)	
5	13	(9.3)	24	(12.5)	
Contact with pets					
No	21	(14.7)	32	(16.6)	
Yes	119	(85.3)	160	(83.4)	0.407
Dog	101	(91.8)	132	(91.7)	0.577
Cat	46	(41.8)	42	(29.2)	0.025[a]
Hamster	11	(10.0)	9	(6.3)	0.193
Reptile	6	(5.5)	7	(4.9)	0.518
Bird	20	(18.4)	14	(9.7)	0.036[a]
History of digestive diseases among family members					
No	58	(41.4)	93	(48.5)	
Yes	82	(58.6)	99	(51.5)	0.105
GU[1] or DU[2]	24	(16.4)	30	(15.2)	0.429
Gastritis	74	(50.7)	75	(37.9)	0.012[a]
GC[3]	16	(11.2)	31	(15.8)	0.145

[1] Gastric Ulcer; [2] Duodenal Ulcer; [3] Gastric Cancer; [a]Significantly different ($P < 0.05$); [b]Significantly different ($P < 0.001$).

an indicator of domestic crowding, "number of siblings" was significantly associated with *H pylori* positivity ($P < 0.001$). None of the variables depicting socioeconomic status and sanitary standards were correlated to the infection. On the other hand, we found a significant correlation between having contact with cats and birds, and being positive for the infection ($P = 0.02$ and $P = 0.04$ respectively). Neither the ingestion of raw or cooked food nor drinking of "mate" or other shared drinks were significantly linked to *H pylori*. The habit of chewing nails was also not correlated to the infection. We found a significant correlation between history of gastritis in family members and a positive *H pylori* result in the studied child (index case) ($P = 0.01$).

To estimate the impact of different characteristics as predictive variables for *H pylori* status, the binary logistic regression equation was used by the Forward Stepwise (Likelihood Ratio) method. Under this analysis, predictive variables for *H pylori* positivity were "contact with pet cats" (OR = 1.76; 95% CI, 1.00-3.09) and "number of siblings" (OR = 1.39; 95% CI, 1.20-1.61).

DISCUSSION

Prevalence of *H pylori* infection has been reported to be higher both in children and adults from developing countries than from developed ones[10,12,13]. In Argentina, *H pylori* prevalence has been evaluated in the asymptomatic population in two different studies that included both adults and children[14,15]. Mean age of the children in those previous studies was 7.9 ± 4.6 years[14] and 7.8 ± 5.5 years[15]. The prevalence of *H pylori* in asymptomatic children was 15.7% in both studies. In the present study we evaluated slightly older children with gastrointestinal symptoms (mean age 9.97 ± 3.1 years), and we found a 40.0% prevalence of *H pylori* infection. The differences in prevalence rates found in asymptomatic and symptomatic children from our country, are consistent with one multicenter study representing various parts of the United States of America, in which the seropositivity rate was significantly higher in symptomatic (22.3%) than in asymptomatic children (14.1%)[6]. In a study from the Czech Republic[16], it was also reported a higher prevalence of *H pylori* infection in symptomatic children (33%) when compared with asymptomatic controls (7.5%). These findings suggest that the presence of gastrointestinal complaints may be associated with *H pylori*. Moreover, the lack of association between age and *H pylori* prevalence observed in this study could also be explained by the inclusion of symptomatic children only. Nevertheless, a causal relationship between *H pylori* infection and recurrent abdominal pain in children is still not proven[8]. Although Argentina is considered a developing country, results obtained in the present study (40% *H pylori* prevalence in symptomatic children) versus 15% in asymptomatic children reported previously[14,15] are interestingly similar to the ones obtained in developed countries such as the US.

According to the National Institute of Statistics and

Census of Argentina, INDEC, there is a 44.4 % poverty rate among the population living in Great Buenos Aires metropolitan area. A possible explanation that our studied population of children had good socioeconomic status and high sanitary standards is that more than 95% of the studied children were from inner city and they might mainly represent middle class. This phenomenon may be explained by the following reasons: (1) recurrent abdominal pain is not usually a reason for seeking medical attention among people with low socioeconomic status. (2) patients with a lower socioeconomic status who are referred to the Gastroenterology unit, who are rarely assisted due to monetary limitations, and (3) people belonging to the middle class who used to pay for private medical care attention, have turned to public health care centers due to the fact that economic conditions have become impaired in Argentina during the last years.

The factors associated with *H pylori* positivity were the number of siblings, presence of cats and birds in the house, and antecedents of gastritis among family members (Table 2). After binary logistic regression analysis, only the number of siblings and contact with pet cats remained factors for increasing risk of *H pylori* infection.

The observation that the presence of cats in the house may increase the probability of being positive for *H pylori* infection in children with gastrointestinal symptoms require further investigation, especially because controversial results have been reported for the role of cats and other domestic pets in association with *H pylori*[6,15-18]. Cats are commonly infected with gastric *Helicobacter*-like organisms (GHLOs) as "*H. heilmannii*", that might be transmitted to humans[19-21]. Therefore, a positive Urea Breath Test result in a patient could represent a gastric presence of urease positive *Helicobacter* species other than *H pylori*. However, as prevalence of "*H. heilmanii*" -like organisms in humans is relatively low, this topic requires further clarification.

Low socioeconomic status and poor sanitary standards were described as risk factors for the acquisition and transmission of *H pylori*[5-7]. Given that most of the studied population had good socioeconomic conditions, we could not demonstrate an association between *H pylori* status, socioeconomic conditions and sanitary standards. It is important to point out that the correlation coefficients depends strongly on sample sizes and balance between them[22]. Another factor associated with *H pylori* infection in the studied population was the history of gastritis among family members. In contrast, other authors have not found a correlation between family history of gastric disease and *H pylori* infection in the children[6,17]. Major limitations in the association of clinical history with *H pylori* status are, first, the definition used to establish gastric diseases and second, the technique employed to diagnose *H pylori* infection.

In conclusion, we found that prevalence of *H pylori* infection in children with upper gastrointestinal symptoms referred to a Gastroenterology service in the Province of Buenos Aires, Argentina was 40%, similar to the prevalence reported in developed countries. In addition, number of siblings in the household and presence of pet cats are predicting variables for *H pylori* colonization. Our study provides important information regarding the prevalence of *H pylori* infection in symptomatic children in Buenos Aires, Argentina, and factors associated with increasing risk for *H pylori* positivity in a developing country.

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