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ORIGINAL ARTICLE

Prevalence of and factors associated with *Helicobacter pylori* infection in preschoolers in Havana, Cuba: A population-based study[☆]

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KEYWORDS
Helicobacter pylori;
Prevalence;
Risk factors;
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Abstract
Introduction: *Helicobacter pylori (H. pylori)* infection is usually acquired in childhood. It has not been widely studied in individuals within the pediatric age range in Cuba.
Aim: To identify the prevalence of the infection and its associated risk factors in 3-year-old children in Havana.
Materials and methods: An analytic, cross-sectional, epidemiologic analysis was conducted on 1,274 children belonging to the cohort of participants in the Natural History of Wheezing in Cuba study (*HINASIC* for its Spanish acronym) that were 3 years of age and provided a stool sample. *H. pylori* infection was identified by determining the *H. pylori* antigen (Ag) in stool, utilizing the commercial Spinreact kit, from Spain. The data were collected through a questionnaire applied by the researchers that included sociodemographic, environmental, and lifestyle variables, as well as infection from other parasites. Prevalence and the prevalence ratio with a 95% confidence interval were calculated and the dichotomous logistic regression analysis was employed.
Results: The prevalence of positive *H. pylori* Ag was 5%. Sleeping together was the risk factor found (PR: 1.27; 95% CI: 1.03-1.50). Protective factors were drinking water from water delivery trucks (PR: 0.16; 95% CI: 0.04-0.72) and living in a nuclear family unit (PR: 0.94; 95% CI: 0.85-0.99).

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Conclusions: The prevalence of *H. pylori* infection in early childhood places Havana in an intermediate position at the international level. To control the infection, causal studies should be conducted and opportune interventions implemented.

PALABRAS CLAVE
Helicobacter pylori;
Prevalencia;
Factores de riesgo;
Cuba

Prevalencia y factores asociados a infección por *Helicobacter pylori* en preescolares de La Habana, Cuba. Estudio de base poblacional

Resumen
Introducción y objetivo: La infección por *Helicobacter pylori (H. pylori)* es usualmente adquirida en la infancia. En Cuba su estudio en las edades pediátricas es un campo poco explorado.
Objetivo: Identificar la prevalencia de la infección y los factores asociados en niños de 3 años de edad de La Habana.
Material y métodos: Se realizó un estudio epidemiológico transversal analítico con 1274 niños de 3 años de edad, que aportaron muestra de heces, provenientes de la cohorte de nacimientos de La Habana (HINASIC). Se identificó la infección por *H. pylori*, utilizando el paquete para determinación de antígeno (Ag) de *H. pylori* en heces de la casa comercial Spinreact, España. La recolección de datos fue a través de un cuestionario administrado por los investigadores que incluyen variables sociodemográficas, ambientales, estilo de vida e infección por otros parásitos. Se calcularon prevalencias, razón de prevalencia con intervalos de confianza de 95% y regresión logística dicotómica.
Resultados: La prevalencia de Ag de *H. Pylori* positivo fue de 5%. Dormir acompañado fue el factor de riesgo encontrado RP 1.27 (IC 95%: 1.03-1.50). Consumo de agua de pipa RP 0.16 (IC 95%: 0.04-0.72) y vivir en un núcleo familiar con ambos padres RP 0.94 (IC 95%: 0.85-0.99) fueron factores protectores.
Conclusiones: La prevalencia de infección de *H. pylori* en la infancia temprana ubica a La Habana internacionalmente en una posición intermedia. Estudios de causalidad e intervenciones futuras deberán ser tenidos en cuenta para el control de la infección.

Introduction and aims

Helicobacter pylori (*H. pylori*) colonization of the stomach is the most common of the chronic bacterial infections in humans.[1] It is considered one of the main findings in gastroenterology and is one of the microorganisms of greatest interest in human pathology.[2,3] Its origin dates back some 58,000 years.[4] Between 1985-89, Warren and Marshall[5] associated the presence of the bacterium with chronic gastritis and ulcer, and since then, much work has been carried out in that field. The genesis of chronic gastritis, duodenal and gastric ulcer in children and adults, and both gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphoma have been attributed to it. Once acquired, the infection persists, and the majority of infected individuals remain asymptomatic.

Calculations suggest that approximately half of the world's population is colonized by *H. pylori*, with wide variability between different populations, possibly related to different factors, such as the virulence of the microorganism, host susceptibility, antibiotic use, and environmental conditions that include socioeconomic level. Genetic, racial, and cultural factors are less clearly involved.[6,7] Transmission via the digestive route is well-accepted.[6] Prevalence ranges from 1-2% in studies conducted on asymptomatic children in the Netherlands, to over 90% in Bangladesh.[6] In developing countries, children are infected mainly before 10 years of age, and the highest prevalence peak in adults (80%) is before 50 years of age. In developed countries, studies show that infection is rarely produced before 10 years of age. It increases to 10% between 18 and 30 years of age and to 50% above 60 years of age.[8]

The prevalence of *H. pylori* infection in Cuba has not been widely analyzed. The majority of studies have been conducted on pediatric and adult populations with gastrointestinal symptoms. A high rate of *H. pylori* infection has been identified in adult patients with gastric ulcer (91%), duodenal ulcer (99%), and chronic gastritis (94%), with an elevated expression of the cagA$^+$ gene.[9–12] There are fewer studies on children, but a relation to anemia in school children (79%)[13] and to diagnoses of antral chronic gastritis (67.7%) has been observed.[14] Opportune preventive measures for stopping *H. pylori* transmission will reduce the incidence of those diseases and will depend on knowledge of the history of *H. pylori* infection. Therefore, the aim of the present study was to identify the prevalence of *H. pylori* infection and the associated socioeconomic, environmental, and lifestyle factors in the pediatric population of 3-year-old children in the province of Havana.

Materials and methods

Study population

The participants of the present analysis belong to the third year of the Natural History of Wheezing in Cuba (*HINASIC* for its Spanish acronym) study, a prospective, longitudinal, population study on children, whose aim was to identify risk factors for the development of asthma. Detailed information on the methodological design of the study, including sample selection, and the inclusion and exclusion criteria were previously described.[15] A total of 1,543 three-year-old children who attended any of the 17 polyclinics of the 4 municipalities of Havana (*Arroyo Naranjo*, *Cerro*, *Habana del Este*, *La Lisa*) were interviewed within the time frame of March 2012 to March 2013. Of those children, 1,274 (83%) were eligible to participate in the present study by providing a stool sample.

Data collection

The data were obtained through the application of a questionnaire administered by an interviewer (pediatricians or family physicians) to parents or guardians, after they had given their informed consent for their children to participate in the study. Information on demographics, lifestyle, and home environment, as well as specific questions on anthropometric measurements (weight and height) at the time of the interview, were collected. *H. pylori* infection was diagnosed from the stool sample provided by the participants, utilizing the commercial Spinreact kit (http://www.spinreact.com). As stated in the technical label, it is a qualitative immunochromatographic test that has 94% sensitivity and 95% specificity, compared with a reference standard. Test results were ''positive'' (presence of *H. pylori* IgG) or ''negative'' (absence of *H. pylori* IgG).[16] Another portion of the stool sample was analyzed for parasitic infection, utilizing the direct smear method with Lugol's solution and eosin staining, and the Kato-Katz concentration technique for identifying and quantifying helminth eggs.[17]

Data analysis

The information was collected in a database and obvious errors and non-plausible data were cleaned. The statistical analysis was performed using Stata v12 (StataCorp, Texas, USA) software and survey commands to allow the use of a planned sample design. Descriptive statistics were calculated (absolute frequencies, percentages) and a bivariate analysis was done using 2×2 contingency tables. The prevalence of infection and its 95% confidence interval were calculated in those tables for each exposure category of the variables, interpreting the statistical association when the interval did not contain the unit. The significant variables, and other scientifically plausible ones, were included in the modeling through dichotomous logistic regression. The result of the *H. pylori* test was the dependent variable, *the probability that it was positive was modeled*, and prevalence ratios and their 95% confidence intervals adjusted for each exposure variable were obtained, calculating robust standard errors adjusted by municipality. Sex and anti-parasitic treatment were considered a priori confounders but were not introduced into the final model because they did not modify the association by 10% or more.

Table 1 Description of the study sample.

Variables	Categories	n	%
Sex	Male	668	52
	Female	606	48
Skin tone	Light	570	45
	Medium	539	42
	Dark	165	13
Municipality	Habana del Este	435	34
	Cerro	176	14
	La Lisa	153	12
	Arroyo Naranjo	510	40
Helicobacter pylori test	Positive	70	5
	Negative	1204	95

Ethical considerations

Written statements of informed consent were obtained from the parents or guardians of the underage patients for their participation in the study and the study protocol was approved by the scientific committees of the *Instituto Nacional de Higiene, Epidemiología y Microbiología de La Habana* and the University of Nottingham Medical School in the United Kingdom. The authors declare that no personal information that could identify patients is contained herein.

Results

Of the 1,274 three-year-old children enrolled in the study, 100% of their parents or guardians correctly completed the questionnaire applied by the family physicians. The characteristics of the study participants are shown in Table 1. The prevalence of *H. pylori* infection was 5%.

Table 2 shows the bivariate associations with *H. pylori* and Table 3 shows the factors associated with *H. pylori* infection, after the confounding factor adjustment. The risk factor found for *H. pylori* infection was sleeping together (PR 1.27; 95% CI: 1.03-1.50), and the protective factors were married/living with a partner (PR 0.94; 95% CI: 0.85-0.99) and drinking water delivered by a water truck (PR 0.16; 95% CI: 0.04-0.72).

Discussion and conclusions

To the best of our knowledge, the present analysis is the first population-based study investigating the prevalence of and factors associated with *H. pylori* infection in a population of healthy 3-year-old children in the capital city of Havana, Cuba. The prevalence of bacterial infection in the study population was the result of environmental and

Table 2 Bivariate analysis of exposure to and risk for positive *H. pylori* Ag.

Variables	Categories	Positive *Hp* test (n = 70) n (%**)	Negative *Hp* test (n = 1204) n (%**)	PR (95% CI)	p
Paid working mother	No	32 (7)	458 (93)	1.34 (0.85-2.13)	0.247
	Yes	38 (5)	746 (95)	1	
Mother's educational level	Primary/Secondary	21 (6)	327 (94)	1.46 (0.63-3.36)	0.373
	Pre-university	42 (6)	715 (94)	1.34 (0.61-2.93)	0.461
	University	7 (4)	162 (96)	1	
Mother's civil status	Single	13 (5)	254 (95)	0.53 (0.23-1.20)	0.125
	Married/living with a partner	48 (5)	861 (95)	0.58 (0.29-1.14)	0.122
	Divorced/separated	9 (9)	89 (91)	1	
Family income (NC)	< 225	8 (11)	87 (7)	2.66 (0.90-7.89)	0.067
	225-499	31 (44)	535 (44)	1.73 (0.68-4.38)	0.237
	500-999	26 (37)	429 (36)	1.81 (0.71-4.62)	0.208
	>= 1000	5 (7)	153 (13)	1	
Weight-for- age	< 10 percentile	2 (4)	49 (96)	0.69 (0.17-2.75)	0.845
	10-90 percentile	42 (6)	693 (94)	1	
	> 90 percentile	26 (5)	462 (95)	0.93 (0.58-1.50)	0.773
Height-for-age	< 10 percentile	4 (3)	118 (97)	0.57 (0.21-1.55)	0.529
	10-90 percentile	57 (6)	939 (94)	1	
	> 90 percentile	9 (6)	147 (94)	1.01 (0.51-1.99)	0.262
Weight-for-height	< 10 percentile	3 (3)	104 (97)	0.47 (0.15-1.49)	0.405
	10-90 percentile	38 (6)	595 (94)	1	
	> 90 percentile	29 (5)	505 (95)	0.90 (0.57-1.45)	0.676
Brothers or sisters	No	22 (5)	415 (95)	1	
	Yes	48 (6)	789 (94)	1.13 (0.70-1.86)	0.696
Older brothers or sisters	No	37 (6)	623 (94)	1	
	Yes	33 (5)	581 (95)	0.95 (0.61-1.51)	0.954
Type of family	Functional	57 (5)	1044 (95)	1	
	Dysfunctional	13 (8)	160 (92)	1.45 (0.81-2.59)	0.283
Housing conditions	Good	48 (6)	791 (94)	1	
	Regular	18 (5)	343 (95)	0.87 (0.51-1.48)	0.609
	Poor	4 (5)	70 (95)	0.94 (0.35-2.55)	0.911
Overcrowding	No	45 (5)	794 (95)	1	0.877
	Yes	25 (6)	410 (94)	1.07 (0.67-1.72)	

Table 2 (*Continued*)

Variables	Categories	Positive *Hp* test (n = 70) n (%**)	Negative *Hp* test (n = 1204) n (%**)	PR (95% CI)	p
Children's circle or caretaker's home attendance	No	22 (6)	349 (94)	1	
	Yes	48 (5)	855 (95)	0.90 (0.55-1.46)	0.763
Sleeps accompanied	No	27 (4)	597 (96)	1	0.095
	Yes	43 (7)	607 (93)	1.53 (1.00-2.42)	0.095
Treatment for other parasites	No	60 (5)	1115 (95)	1	
	Yes	10 (10)	89 (90)	1.98 (1.05-3.74)	0.062
Treatment with antibiotics	No	26 (6)	406 (94)	1	
	Yes	44 (5)	798 (95)	0.87 (0.54-1.39)	0.647
Pets	No	43 (6)	723 (94)	1	
	Yes	27 (5)	481 (95)	0.95 (0.59-1.51)	0.918
Dogs	No	51 (6)	811 (94)	1	
	Yes	19 (5)	393 (95)	0.78 (0.47-1.30)	0.410
Cats	No	66 (5)	1144 (95)	1	
	Yes	4 (6)	60 (94)	1.15 (0.43-3.05)	1.000
Other animals	No	59 (5)	1080 (95)	1	
	Yes	11 (8)	124 (92)	1.57 (0.85-2.92)	0.218
Rodents	No	55 (6)	926 (94)	1	
	Yes	15 (5)	278 (95)	0.95 (0.52-1.59)	0.861
Vectors	No	47 (5)	831 (95)	1	
	Yes	23 (6)	373 (94)	1.08 (0.67-1.76)	0.844
Type of water consumed	Bottled	4 (12)	29 (88)	1	
	Aqueduct	55 (6)	910 (94)	0.47 (0.17-1.26)	0.124
	Well	10 (4)	216 (96)	0.37 (0.13-0.97)	0.068
	Tanker	1 (2)	49 (98)	0.17 (0.03-0.69)	0.059
Boils water	No	8 (3)	224 (97)	1.73 (0.84-3.55)	0.176
	Yes	62 (6)	980 (94)	1	

Table 2 (*Continued*)

Variables	Categories	Positive *Hp* test (n = 70) n (%**)	Negative *Hp* test (n = 1204) n (%**)	PR (95% CI)	p
Child's habits					
Plays with soil or sand	No	40 (5)	797 (95)	1	
	Yes	30 (7)	407 (93)	1.43 (0.91-2.27)	0.155
Eats soil or sand	No	67 (5)	1177 (95)	1	
	Yes	3 (10)	27 (90)	1.86 (0.62-5.57)	0.490
Sucks his/her thumb	No	56 (5)	1028 (95)	1	
	Yes	14 (7)	176 (93)	1.43 (0.81-2.51)	0.291
Bites/eats fingernails	No	49 (5)	873 (95)	1	
	Yes	21 (6)	331 (94)	1.12 (0.68-1.84)	0.750
Walks barefoot on the ground	No	48 (5)	890 (95)	1	
	Yes	22 (7)	314 (93)	1.28 (0.76-2.09)	0.400
Scratches his/her anus	No	49 (5)	910 (95)	1	
	Yes	21 (7)	294 (93)	1.30 (0.80-2.14)	0.363
Washes hands after urinating/defecating	No	18 (7)	252 (93)	1	
	Yes	52 (5)	952 (95)	0.78 (0.46-1.31)	0.423
Washes hands before eating	No	7 (5)	130 (95)	1	
	Yes	63 (6)	1074 (94)	1.08 (0.51-2.32)	0.991
Washes hands after playing with soil or sand	No	17 (5)	296 (95)	1	
	Yes	53 (6)	908 (94)	1.02 (0.60-1.73)	1.000
Other parasitic infections					
Parasitic infection	No	5 (14)	1172 (86)	1	
	Yes	65 (5)	32 (95)	2.57 (1.10-6.01)	0.071
Helminthiasis	No	69 (5)	1200 (95)	1	
	Yes	1 (20)	4 (80)	3.68 (0.63-21.6)	0.658
Protozoa	No	4 (13)	1176 (87)	1	
	Yes	66 (5)	28 (95)	2.35 (0.91-6.06)	0.171

95% CI: 95% confidence interval; PR : Prevalence ratio.
%*: Percentage with respect to the total number of children (n = 1274).
%**: Percentage with respect to the total per exposure category.
The p values were obtained from association tests based on the X2 distribution.

Table 3 Multivariate analysis of exposure to and risk for positive *H. pylori* Ag.

Variables	Categories	Positive *Helicobacter pylori* test (n = 70) n (%**)	OR (95% CI) for positive *Helicobacter pylori* test	p
Sleeps accompanied	No	27 (38.6)	1	0.027
	Yes	43 (61.4)	1.27 (1.03-1.50)	
Mother's civil status	Single	13 (18.5)	0.93 (0.80-1.50)	0.061
	Married/living with a partner	48 (68.6)	0.94 (0.85-0.99)	
	Divorced	9 (12.9)	1	
Type of water consumed	Bottled	4 (5.7)	1	0.002
	Aqueduct	55 (78.6)	0.48 (0.16-1.33)	
	Well	10 (14.3)	0.41 (0.12-1.28)	
	Tanker	1 (1.4)	0.16 (0.04-0.72)	

The p values were obtained from Wald significance tests based on X^2 distribution.

$$\boldsymbol{Definitive\,model}:\ \boldsymbol{P}\,(\boldsymbol{Y}=1)=\frac{1}{1+\boldsymbol{e}^{-\begin{pmatrix}-3.1465+0.2342*SleepsAccompanied\\ -0.2492*SingleMother-0.1776*MarriedMother\\ +0.1164*AqueductWater\\ -0.0535*WellWater-0.9912*TankerWater\end{pmatrix}}}$$

lifestyle conditions. The cross-sectional analysis conducted on the 3-year-old children appearing in a database of the longitudinal *HINASIC* cohort provided the knowledge of the magnitude of the infection at that age. Sleeping accompanied was an important risk factor and the civil status of married/living with a partner and drinking water from a water-delivery truck were protective factors.

From the total number of 3-year-old children surveyed, 83% provided the stool samples needed for *H. pylori* testing, which enabled the prevalence of the infection to be calculated. The strengths of our study were the fact that the questionnaires were correctly formulated and applied by qualified medical personnel that had been following the children for several years, the majority of questionnaires were answered by the children's parents (90%), and an internationally validated *H. pylori* test recommended for epidemiologic studies on that age group was employed.[18] In addition, highly qualified technical personnel from the *Instituto Nacional de Higiene, Epidemiología y Microbiología de Cuba* (*INHEM*) carried out the external control of the results of the parasitology tests performed at the parasitology laboratories of the health areas involved, guaranteeing the reliability of the stool test results. The following two limitations of our study were identified: a history of ulcers or gastritis in the parents or guardians of the participating children was not determined and thus could not be analyzed as an associated factor, and the low prevalence of *H. pylori* Ag made it difficult to analyze the possible associated factors. Nevertheless, the results are valuable.

Cuba is a country that has medium and low resource settings. Despite those conditions and the strong economic blockade imposed by the United States for more than 50 years, unlike other countries with the same level of development, its health and education indicators are similar to those of the developed world. That situation, the fact that our study was conducted in an urban zone, and the high rate of antibiotic use in the pediatric population most likely were contributing factors to our study results.[19–22] The prevalence of *H. pylori* in the 3-year-old children analyzed places us in an intermediate prevalence pattern in the international context, but we are close to the pattern of industrialized countries, if we take into account that early childhood prevalence is approximately 1.2% in Western Europe.[6] In the Latin American countries of Ecuador, Chile, Brazil, and Mexico, an important percentage of children are already infected (63%, 25%, 31.1% and 10%, respectively).[21,23–26] On the African continent, studies by Amberbir et al. describe a prevalence of 41% in children 3 years of age in an Ethiopian population, and in Uganda, 28.7% in 1-year-old children, 46% of children between 1 and 2 years of age, and 51.7% of children between 3 and 5 years old are already infected.[27,28] In a recent meta-analysis conducted by Zabala Torres et al., those authors report prevalence of 20% in children under 6 years of age (95% CI: 14%-25%), among other results.[29]

Children sleeping together with other persons was the risk factor identified in the present study. Regardless of not having determined a history of infection in the adults living with the children, a high prevalence of infection detected in the adult Cuban population (75-90%)[8–12,14] and evidence of infection transmission between couples suggest an increased risk for transmission to children living with infected individuals.[24,25,29–32] Family has been found to play a fundamental role in the transmission of the *H. pylori* bacterium, especially within the first years of life, during which the most probable cause is oral-oral transmission from the mother to the child.[24,29,32]

It appears that living in a stable nuclear family unit is a protective factor against bacterial infection. Greater care given to the children is most likely an important factor and a plausible explanation is the presence of better personal and environmental hygiene habits related to a higher educational level of the study population. In addition, the greater antibiotic use detected in the study participants was relevant, which could lend important weight to that result.[24,31]

The consumption of potable water delivered by water truck (tankers) was another factor that contributed to the protection against *H. pylori* infection. The technical condition of the water supply system is not good in all parts of Havana and therefore the distribution of water by tankers is necessary. Despite the inconvenience of that type of public service, it appears that water is safer for drinking, if it does not flow through the water pipeline network, where it can become cross-contaminated due to structural deficiencies. In their 1997 study, Johnson et al. showed that chlorinated water was a factor that inactivated the bacterium, interfering with its transmission by water.[33] A recent review revalidated contaminated water as a source of *H. pylori*, but insists on the need for further detailed study on that route of transmission.[34] Eichelberger et al. presented information on the association between environmental risk factors and *H. pylori* infection in the United States based on data from the National Health and Nutrition Examination Survey (NHANES), indicating that environmental exposure (incorrect water use and occupational contact with soil) play an important role in the transmission of *H. pylori* (adjusted odds ratio [OR] 2.7, 95% CI: 1.3-5.6).[35]

In conclusion, the estimated prevalence of *H. pylori* infection in early childhood places Havana in an intermediate position in the international context. Socioeconomic conditions appear to be important factors in the presence of the infection. Opportune interventions should be implemented to reduce future complications.

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Conflict of interest

The authors declare that there is no conflict of interest.

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