

Helicobacter pylori infection in children from Northeast Argentina: seroprevalence and its relation with nutritional status and socio-sanitary conditions*

Daniel Merino
Miria Galván
Adriana R. Fabre
Silvia E. Balbachán
Olga Miranda
Jorge O. Gorodner
José M. Alonso

Institute of Regional
Medicine
Northeast National
University
Resistencia
Argentina

Resumen

No disponiéndose de datos sobre la infección por *H. pylori* en niños del noreste argentino, se realizó un estudio seroepidemiológico a fin de conocer la prevalencia de este agente entre los menores de 14 años, evaluar si la infección impacta sobre el desarrollo de los niños y analizar la influencia de las variables socio-sanitarias sobre el riesgo de adquirir la infección. Se estudiaron 278 niños de ambos sexos de 4 a 14 años de edad (media = 9 años), 158 de área rural y 120 de área urbana, residentes en 4 localidades del noreste argentino con distintas condiciones sociales y ambientales. Se investigó anticuerpos Ig G anti *H. pylori* y se evaluó el estado nutricional mediante la determinación de peso y talla, clasificándose a los niños en Eutróficos o Distróficos. De los 278 niños, 126 (45,3%) resultaron seropositivos para *H. pylori*, siendo 86 (68,3%) del área rural y 40 (31,7%) del área urbana, lo que señala un riesgo de infección mayor para los primeros. Las prevalencias encontradas en las cuatro localidades estudiadas fueron: Villa Olivari 50%, Albardones 59%, Villa Elisa 42% y el área céntrica de la ciudad de Resistencia 27%. La prevalencia de infección aumentó estadísticamente con la edad, no encontrándose diferencias significativas en relación con el género. Se observó una asociación significativa entre porcentajes de infección y el grado de instrucción de la madre, la carencia de cloacas en los domicilios y la falta de agua potable, no así con el grado de hacinamiento al dormir ni con el nivel de educación del padre. No se encontró asociación significativa entre infección por *H. pylori* y distrofia entre los niños. Los altos índices de infección encontrados aún entre los niños con buenas condiciones sanitarias en sus hogares, inducen a la evaluación de otros factores favorecedores del riesgo de infección.

Palabras claves: *Helicobacter pylori*. Seroprevalencia. Factores de riesgo. Pediatría.

Summary

In order to assess *H. pylori* infection in children from Northeast Argentina and to evaluate its impact on

children's growth and the importance of socio-sanitary conditions as risk factors, a seroepidemiological survey was carried out on 278 children of both sexes, 4-14 years old (158 from two rural locations, 120 from two urban districts). In all of them Ig G antibodies to *H. pylori* were determined and nutritional status was evaluated by weight and height measuring, and thereafter divided into Eutrophics or Distrophics. Results show that 126 out of 278 children (45.3%) were seropositive and that infection is significantly higher in rural areas ($p < 0.05$). The prevalence rates found in the 4 locations studied were: Villa Olivari 50%, Albardones 59%, Villa Elisa 42%, and in the central area of Resistencia city 27%. The infection rates significantly increased with age, but there were no differences with gender. A significant association was found between the infection rates and the lack of sewers, the lack of safe drinking water availability and mothers' educational level, but not with fathers', neither with house overcrowding. There was not a significant association between infection rates and nutritional status of children. Since high rates of *H. pylori* infection were found both in rural children and in urban children, even among those with good sanitary conditions for living, other factors favoring infection should also be evaluated.

Key words: *Helicobacter pylori*. Seroprevalence. Risk factors. Pediatrics.

Introduction

Helicobacter pylori is one of the human infection agents most widely spread world-wide, though it is not completely defined whether its transmission is fecal-oral, oral-oral or both¹. Once acquired the infection remains asymptotically for decades². Although type B gastritis and gastric and duodenal ulcers are the most frequent consequences, there is sufficient evidence in humans for the carcinogenicity of infection with *H. pylori*³.

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Correspondence:
Dr. Daniel Merino
Instituto de Medicina
Regional, Universidad
Nacional del Nordeste
Av. Las Heras 727
3500 Resistencia, Argentina
E mail:
dmerino@bib.unne.edu.ar

The infection rates increase with age but it varies according to the region analyzed⁴. In developing countries the infection is generally high in all age groups as it is acquired during childhood⁵, while in developed countries the prevalence in children is generally low, increasing rapidly with age reaching 50-60 % in people over 50 years of age⁶. Various factors in favor of risk of infection have been pointed out, such as the low socio-economic level, overcrowding at homes, inadequate sanitary conditions, low educational level, etc⁷. It has likewise been signaled that children with nutritional deficiencies would be more exposed to the risk of infection, and chronic diarrhea and malnutrition have also been described as possible secondary consequences of the infection with this agent⁸.

In view of the important pathogenic role assigned to *H. pylori*, the study of infection rates in infantile populations and the evaluation of possible factors favoring infection has been recommended in different types of settlements⁷. Because of this, and since there is no available information about the infection in children from Northeast Argentina, a seroepidemiological study was carried out to assess the prevalence among children younger than 14 years old, to evaluate if the infection has an impact on children's nutritional status and on their growth, and to analyze the influence of some socio-sanitary conditions on the risk of acquiring infection, in order to suggest a course of action for its control.

Material and methods

Study area

The study was performed with a transversal aleatory sample of infantile population in four locations in Northeast Argentina, with different social and sanitary characteristics.

- Villa Olivari and Albardones: two small villages of about 300-500 inhabitants, located in the north of Corrientes Province (27°30'S. Latitude; 57°10'Long. W.). Both of them are so scarcely urbanized that no clear differences could be stated between urban or rural inhabitants; all children were therefore considered rural inhabitants. They both lack of public sewerage system, paved streets and domiciliary garbage collecting service. The first village has a municipal pipeline for potable water though it does not reach all homes, while in the second one people has only well water.

- Villa Elisa: a neighborhood of Resistencia city, in the province of Chaco, (27° 10' S.Lat; 58°58' W.Long.). It has municipal pipeline for potable water and domiciliary garbage collecting service, though it lacks sewerage system and paved streets.
- Downtown area of Resistencia city: The city has 350,000 inhabitants, municipal pipeline for potable water, public sewerage system, daily cleaning of paved roads and domiciliary garbage collecting service.

The children from the first three locations belonged to low socio-economical level, whereas those of the fourth belonged to the middle and middle high class.

Population studied

Two hundred and seventy eight children (140 boys - 138 girls) aged between 4 and 14 (average: 9 years old) were studied; 158 belong to rural areas and 120 to urban areas. Distribution according to age, gender and place of residence is shown in Table 1.

The children's parents were informed about the purposes of the survey previously to perform the sampling and those who accepted their children to be included in the study were present at the time of blood sampling.

Serological procedure

Anti *H. pylori* Ig G antibodies were studied by means of a commercial enzyme immunoassay test (Laboratories Bio 3, Italy). Specificity and sensitivity of this method are 92% and 90%, compared to positive gastric biopsies. Serum anti-HP antibodies were determined qualitatively at 37°C, plates were read by spectrophotometer at 450 nm and the standard curve was drawn with four standards solutions provided in the kit. According to the manufacture's instructions, the OD of the 4 U/ml standard was used as a cut-off to discriminate between negative and positive samples. Measurements within the range of 3.2 and 4.0 U/ml were considered as indeterminate and the test was repeated.

Children evaluation

After measuring weight and height, the nutritional status of children was assessed by means of charts prepared by the National Committee on children growing of the Argentine Pediatrics Society⁹ and performed on the basis of an evaluation of Argentine

Table 1.
Study population in Northeast Argentina according to age, place of residence and gender

Age group (years)	Rural population				Total	Urban population				Total	Total			
	Villa Olivari N = 82		Albardones N = 76			Villa Elisa N = 50		Resistencia N = 70			Total	male	female	total
	Male	Female	Male	Female		Male	Female	Male	Female					
4-7	15	15	9	7	46	10	6	12	11	39	46	39	85	
8-10	12	15	21	16	64	15	10	12	13	50	60	54	114	
11-14	12	13	9	14	48	4	5	9	13	31	34	45	79	
Total	39	43	39	37	158	29	21	33	37	120	140	138	278	

Table 2.
H. pylori serostatus of children in Northeast Argentina, according to age, place of residence and gender

Age group (years)	Rural areas				Total N = 158	Urban areas				Total N = 120	Total			
	Villa Olivari N = 82		Albardones N = 76			Villa Elisa N = 50		Resistencia N = 70			Total	male	female	total
	Male	Female	Male	Female		Male	Female	Male	Female					
4-7	5	6	3	3	17/46= 36.9%	6	2	0	2	10/39= 25.6%	14	13	27/85= 31.7%	
8-10	8	6	14	10	38/64= 59.4%	5	5	5	3	18/50= 36.0%	32	24	56/114= 49.1%	
11-14	7	9	5	10	31/48= 64.6%	2	1	4	5	12/31= 38.7%	18	25	43/79= 54.4%	
TOTAL	20	21	22	23	86/158= 54.4%	13	8	9	10	40/120= 30.0%	64	62	126/278= 45.3%	

children in the age groups: less than 4 years, 4-12 years and 12-19 years. Thereafter children between percentile 10 to 90 were classified as Eutrophics and those above 90 or under 10 as Dystrophics.

A simple questionnaire was also completed asking the parents about the socio-sanitary factors that could influence in acquiring the infection. It included the following criteria: parents' years of education, main characteristics of the house, the number of people living in the house and parent's annual income.

Statistics

To analyze the socio-sanitary variables of the population and their association with the risk of infection, seropositive children were considered as cases and the seronegative ones as controls. Data were analyzed by Epi Info software - version 6.00 employing Chi² Fisher' test and Odds Ratio test and considering $p < 0.05$ as significant.

To evaluate trends between seropositivity and dystrophy, an stratified analyze of eutrophics and dystrophics was carried out considering the socio-sanitary variables and applying Mantel-Haenszel test with a CI of 95%.

Results

Of the 278 children studied, 126 were seropositive for *H. pylori* (45.3%) belonging 86 of them to rural areas (68.3%) and 40 to urban areas (31.7%). The prevalence rates in both areas were 54.4% and 30.0% respectively. These figures indicate a significantly higher risk of infection for children in the rural areas (OR=2.39; $p < 0.05$). The overall prevalence found for the four locations surveyed were: Villa Olivari 50.0% , Albardones 59.2%, Villa Elisa 42.0% and downtown Resistencia 27.1% (Table 2). The infection rates significantly increased with age in both groups but no significant differences were found in relation to gender (OR=1.03; $p = 0.89$). The frequencies of infection found in both areas and its relation with the different epidemiological variables evaluated are shown in Table 3. The analysis of the risk of infection in relation to the educational level of the parents showed a significant association between the degree of mothers' instruction and the infection rate in children, but not with that of the fathers'. In the two urban areas and in one rural area (Villa Olivari), more children whose mothers hadn't completed primary school or were illiterate were found to be infected in comparison with those whose mothers

had reached a higher educational level (Villa Elisa OR=3.86, p=0.02; downtown Resistencia OR=6.53, p=0.04; Villa Olivari OR=5.56, p<0.003). This relationship could not be stated in Albardones, as all mothers were illiterate or had incomplete primary education.

Significant associations were found between the seroprevalence rates and the availability of sanitary facilities for feces disposal. The analysis of settlements in which housing estates had and did not have these conditions showed a prevalence of 34.6% in children corresponding to the former versus 54.7% in the latter (p= 0.001). Similar results were found in relation to safe water availability; the prevalence of infection was 37.7% between children with safe drinking water at home versus 58.3% among those who lack of it (p= 0.001). No significant differences were observed in relation to the degree of overcrowding.

The analysis of the association between infection with *H. pylori* and nutritional status revealed that 43 children out of the 126 seropositives (34%) and 34 among of the 152 seronegatives (22%) were dystrophics (Table 4). Adjustments with socio-sanitary conditions showed that this difference was not statistically significant but confirmed the association between infection rates and deficient socio-sanitary conditions (OR= 2.23, p = 0.00001)

Discussion

Results obtained in this study show a high degree of infection with *H. pylori* in children from Northeast Argentina even from early ages; 36.9% of the children aged between 4 and 7 were found to be infected. This was as expected since various studies previously reported that population with limited sanitation facilities in developing countries are highly exposed to the risk of acquiring the infection^{10,11}.

The percentages of infection found are comparable with those reported from Latin-American countries^{5,7,10,11}, and from poor children population of USA¹², but greater than those reported for children of low socio-economic level living in developed countries^{13,14}.

It is clearly understandable that the deficient sanitary and environmental conditions of the settlements where rural children live may act as risk factors for infection, but in our survey we also found that mothers' educational level would be a significant factor, unlike fathers'. We consider that this last condition may have an implication in favoring the transmission of the infection, as it has already been described in other pathologies in which the transmission of the agent is directly linked to the environmental conditions and to the human behavior, as is the case of geohelminthiasis¹⁵.

Variables	Rural area				Urban area			
	HP positive N = 86		HP negative N = 72		HP positive N = 40		HP negative N = 80	
	N	(%)	N	(%)	N	(%)	N	(%)
Fathers' education (years)								
< 7	44	51	37	51	9	23	11	14
> 7	42	49	35	49	31	78	69	86
Mothers' education (years)								
< 7	62	72	38	53	18	45	12	15
> 7								
Water supply:	24	28	34	47	22	55	68	85
Municipal line	26	30	29	40	40	100	80	100
Well	60	70	43	60	0	0	0	0
Faeces disposal:								
Sewerage	14	16	13	18	31	78	72	90
Latrines	72	84	59	82	9	23	8	10
People per home	Range 1-11 Mean: 3.5		Range 1-9 Mean: 3.5		Range 1-11 Mean: 4		Range 1-12 Mean: 4	
Nº of people/ bedroom	Range 1-4 Mean: 2		Range 1-4 Mean: 2		Range 1-5 Mean: 2.5		Range 1-4 Mean: 2.5	

Table 3. Occurrence of *H. pylori* infection among children from two areas of Northeast Argentina, in relation to socio-sanitary variables

Table 4.
H. pylori infection and nutritional status in children from Northeast Argentina

	Eutrophics		Distrophics		Total
	Urban areas	Rural areas	Urban areas	Rural areas	
Seropositives	19	64	21	22	126
Seronegatives	65	53	15	19	152
Total	84	117	36	41	278

Nevertheless, it is important to signal that the infection rate found among children from urban areas is also high, even amongst those who live in homes provided with good sanitary conditions, such is the case of those living in downtown Resistencia.

Considering the fact that *H. pylori* produces a persistent chronic infection that may be established since early ages, several authors have evaluated the impact it could have on children's growing, finding contradictory results. Patel, *et al.*¹⁴ found a significant decrease in the stature of school age Scottish infected children, particularly amongst girls, and Perri, *et al.*¹⁶ reached to similar conclusions studying Italian children aged 3 to 14. However a multicenter study performed in Italy between 1996 and 1997¹⁷ showed that *H. pylori* could not be considered as responsible for short stature but that the growth delay would be linked to a group of environmental factors within which *H. pylori* is found. Our results are coincident with this last criterion.

As this is the first report published about the infection with *H. pylori* in children from Northeast Argentina and according to the results obtained in the urban population, we understand that other risk factors should also be assessed to explain the high prevalence found. Among them, we think it would be important to evaluate the quality of drinking water and of the ground water layer in relation to this particular agent, the presence and survival of the agent in foods, and the importance of the "mate" in the transmission of the infection. Drinking of mate (an infusion of *Ilex paraguayensis*) is a widely spread and very popular habit in adults as well as in children in Argentina, Paraguay, Uruguay and in South of Brazil. Some characteristics of this habit may link it to the transmission of the infection; mate is always prepared with warm but not boiled water or with iced water, the resulting infusion is sipped through a metallic tube shared by many people at the same moment, and children drink mate since early ages. The presence of *H. pylori* in multiple sites of the oral cavity (tongue and periodontal pockets) has been clearly demonstrated¹⁸, and although this fact has only been accepted so far as an indicator of transient carriage, it may be a route for the transmission of the infection.

According to the results obtained in this survey, we understand that community educational programs should be designed bearing in mind the active involvement of the mothers, in order to raise awareness about the risks of infection with this agent and its consequences on human health.

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