Electronic Journal of General Medicine
2023, 20(1), em424
e-ISSN: 2516-3507
https://www.ejgm.co.uk/

MODESTUM

Original Article

OPEN ACCESS

Detection of *Helicobacter pylori* in faeces of children of rural human settlements: An exploratory study in Peru

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Citation: Moya-Salazar J, Manrique FdM, Loayza C, Laopa KV, Moya-Salazar B, Rojas-Zumaran V. Detection of *Helicobacter pylori* in faeces of children of rural human settlements: An exploratory study in Peru. Electron J Gen Med. 2023;20(1):em424. https://doi.org/10.29333/ejgm/12577

ARTICLE INFO

Received: 17 May 2022

Accepted: 03 Sep. 2022

ABSTRACT

Introduction: *Helicobacter pylori* is one of the major infectious agents in low-income countries, and its clinical characteristics are unknown in many populations. Children are a susceptible population and can contract these pathogens through contaminated food and water.

Objectives: To determine the presence of *Helicobacter pylori* in children under eight years of age of rural human settlements in Peru.

Methods: This exploratory study was conducted with 25 child volunteers authorized by the parents for their evaluation, without precedent of any apparent clinical manifestation. Antigen detection of *H. pylori* in faeces by a rapid assay onsite *H. pylori* Ag. Rapid test according to the manufacturer's requirements. Has been evaluated the social determinants related to possible infection.

Results: The average age (2±1.8 years) of 14 girls was different from the average age (2.7±2.2 years) of 11 boys included in the study (p=0.010). Of the total we determinate nine (36%) positive tests, which mainly affected boys (five patients 20%) under two years of age (six patients, 24%). In general, ~90% wash their hands with soap and water and ~70% wash fruits and vegetables with water before eating. In addition, >50% ate foods outside of home and ~24% was asymptomatic and did not have a specific meal schedule.

Conclusions: Among rural children, *Helicobacter pylori* antibody was detected in 36% of the participants, unaffected by gender, and presenting specific dietary patterns.

Keywords: *helicobacter pylori*, faeces, rural population, child, food, Peru

INTRODUCTION

Helicobacter pylori is a gram-negative bacterium, not sporulated, microaerophilic, mobile, gastrocolonizer whose etiological role is related to the development of gastritis, ulcers, and adenocarcinoma since ~58 mil years (first human infection in East Africa) [1]. Since then, it is estimated that the distribution of *H. pylori* is cosmopolitan and currently 50% of the world's population is the carrier of this bacterium, which causes gastritis in all humans affected [2, 3]. The aetiology of *H. pylori* in the development of gastric neoplasm depends on many physiological components such as immunological [4], nutritional [5], and microbiome [6], and also depends on social and economic determinants.

Although the prevalence of *H. pylori* infection is heterogeneous throughout the world, its high rates of mortality could be attributed to socioeconomic components such as the low education and lack of hygiene facilities, especially water and sanitation whose avoid the eradication of infection through antimicrobial therapies and insufficient hygiene measures [7, 8].

Peru is a Latin American country with middle-incomes per family, with ~31 million inhabitants, presents a high migratory flow (>900 mil Venezuelans in 2021), geographically divided in 25 regions, and rooted social and cultural stratification despite the higher economic growth of the last decade. It has been shown that the mountain population (Andean region) of the country has had higher mortality rates than the Amazonian and Coast population, despite the 16% reduction in the mortality rate of stomach cancer between 2008 and 2015 [9]. The risk factors are different in those groups, being necessary to know the prevalence behaviour of *H. pylori*, related to low socioeconomic status, poor nutritional aspects, and low government support for sanitary purpose.

Similarly, to Peru, there are many groups with a high prevalence of *H. pylori* in Latin America [10]. This prevalence is variable and comparison with other countries could result in

contradictory outcomes (2.5%, 34.6%, and 57.6% in Japan, Latin America, Ethiopia, respectively) if we compare with the decreasing trend of prevalence in children [11]. Unfortunately, there are some countries like Peru, China, Polonia, and Ethiopia that continue presenting a high prevalence of *H. pylori* in this age group currently related to the low socioeconomic level and poor sanitation conditions.

This study aimed to determine the presence of *H. pylori* in faecal samples in children under eight years of age during 2019. Likewise, the main social determinants related to the potential infection of *H. pylori* have been shown in this population.

MATERIALS AND METHODS

Design, Study Site, and Inclusion Criteria

This exploratory cross-sectional study was conducted in children of rural human settlements in September of 2019. These children live in the Ica region, in the south of Peru, in the town of Pongo Chico (Pueblo Nuevo) at 410 meters above sea level (14°04′00″S 75°44′00″O). The inclusion criteria for patients were volunteer children (<eight-year-old), authorized by the parents for its evaluation, and without precedent of any clinical manifestation (according to the previous report of parents in the hospital paediatric doctor's office).

Microbiological Assessment

H. pylori antigen were detected in faeces by a rapid on-site *H. pylori* Ag-rapid test (CTK Biotech, CA, USA) at the Universidad Privada San Juan Bautista (UPSJB) in Ica, Peru. All procedures followed the manufacturer's guidelines. The faeces jars were collected at the beginning of the morning, those were labelled with a standard code which was repeated on the rapid test cassettes. Ten minutes post sampling, the reactions (T) or the device control (C) were observed.

Hygiene and Eating Habits

Social determinants associated with the underlying infection by *H. pylori* were monitored by a survey of parents on social determinants (hygiene and dietary habits) associated with the underlying infection. We used a questionnaire for the evaluation of food consumption habits and hygiene characteristics that was adapted from a previous report [12]. This questionnaire was reviewed and approved by the research experts board of UPSJB (internal reliability, α-Cronbach=0.811). The questionnaire has eight-items that include type of food consumed, time of food consumption, hand washing, access to basic services and parents' place of origin. The survey completion time was an average of 12 minutes.

Data Gathering and Analysis

We assessed the collection of data in direct interviews. All the questionnaires were analysed to know their quality of completion and were coded to an Excel database. Each child had a code that was assigned to the questionnaire filled out by each parent. All data were performed using the IBM Statistical Package for the Social Sciences (Armonk, USA) v21.0 for Linux. The data was analysed with descriptive statistics and a non-parametric test of Kendal Tau-b for recollecting sociosanitary data and immunologic results of *H. pylori*. Differences were demonstrated using the non-paired t-test considering an α=0.05 (5%) as significant.

Table 1. Demographic characteristics of rural children according *helicobacter pillory* antigen detection(n=50)

Characteristics		*H. pylori*	
		Positive	Negative
Age group (years)	<2	12 (24)	26 (52)
	3-5	4 (8)	2 (4)
	≥6	2 (4)	4 (8)
Sex	Male	10 (20)	12 (24)
	Female	8 (16)	20 (40)

Ethical Aspects

The ethical advice for this study follows the Declaration of Helsinki and the data is kept confidential [13]. This study used informed consent from parents and informed agreement from participating children and has the approbation of the Institutional Review Board of UPSJB (UPSJB-VRI-Nº 15145-19).

RESULTS

We included 50 children of both sexes. The mean age (2±1.8 years) of 28 girls was different from the average age (2.7±2.2 years) of 22 boys included in this study (p=0.010). The age range was one to seven years old and according to the sex of children in Pongo Chico, 10 (20%) were males. Of the total of samples analysed, we determined 18 (36%) *H. pilory* positive tests, that affected mainly boys (10 patients, 20%) and minors of two years (12 patients, 24%) (**Table 1**).

The main findings in terms of social health assessed in Pongo Chico children are shown in **Table 2**. We found that 84% of the population had water and sewerage services, while 16% had only water services. Therefore, we determined that 76% boil water before consuming it, 16% buy bottled water (distributed to public organizations and private companies), and 8% use bleach (hydrochloric acid) for water consumption. We found an association between symptoms and hand washing in Ica's Pongo Chico children and positive for *H. pylori* (p<0.05). Furthermore, 92% were used to washing their hands with soap and water (with the help of their parents), and 4% were used to washing their hands with water and a gel-alcohol-based soap (of any brand and alcohol concentration). Twenty percent disinfect vegetables and fruits with bleach and water before eating, and 76% use only water to clean vegetables and fruits to consume them.

Of the total, 76% had a fixed feeding schedule and 24% did not. In addition, 52% of the children eat breakfast and lunch at the local nursery and another 48% eat at home. Of these, 76% experienced symptoms such as loss of appetite, bloated stomach, and nausea, and 24% did not experience symptoms of stomach upset (**Figure 1**). Finally, 80%, 16%, and 4% of parents from Ica, Lima, and Ucayali (Peruvian amazon), respectively.

DISCUSSION

In the present study, we identify the *H. pylori* antibody in a third of children <five-years-old even though the ~90% washes their hands with water and soap, and 70% rinsed the vegetables and fruits with water before eating. In that line,

Table 2. Baseline characteristics of hygiene and alimentation of rural children evaluated for H. pylori [Data in n (%)]

Socio-sanitary characteristics	*H. pylori* results		Total	p-value
	Positive	Negative		
Symptomatology				
Stomach swelling	8 (16)	6 (12)	14 (28)	0.034
Sickness	0 (0)	2 (4)	2 (4)	
Lack of appetite	6 (12)	16 (32)	22 (44)	
No stomach upset	4 (8)	8 (16)	12 (24)	
Handwashing*				
Just water	2 (4)	0 (0)	2 (4)	0.022
Water and soap	16 (32)	30 (60)	46 (92)	
Water, soap, and alcohol	0 (0)	2 (4)	2 (4)	
Breakfast and lunch				
At home	8 (16)	16 (32)	24 (48)	0.154
Nest or nursery	10 (20)	16 (32)	26 (52)	
Have a fixed schedule for eating your food				
Yes	6 (16)	32 (64)	38 (76)	0.078
No	10 (20)	2 (4)	12 (24)	
Fruit and vegetables consumption				
Disinfect with bleach	2 (4)	8 (16)	10 (20)	0.051
Rinse only with water	14 (28)	24 (48)	38 (76)	
Not precise	2 (4)	0 (0)	2 (4)	
Water consumption				
Boil	10 (20)	28 (56)	38 (76)	0.113
Bleach	2 (4)	2 (4)	4 (8)	
Buy bottled water	6 (12)	2 (4)	8 (16)	
Basic services				
Water	6 (12)	2 (4)	8 (16)	0.057
Drain	0 (0)	0 (0)	0 (0)	
Both	12 (24)	30 (60)	42 (84)	
Father's place of birth				
Ica	14 (28)	26 (52)	40 (80)	0.705
Lima	2 (4)	6 (12)	8 (16)	
Ucayali	2 (4)	0 (0)	2 (4)	

Note. *Handwashing in children evaluated according to the parent's knowledge

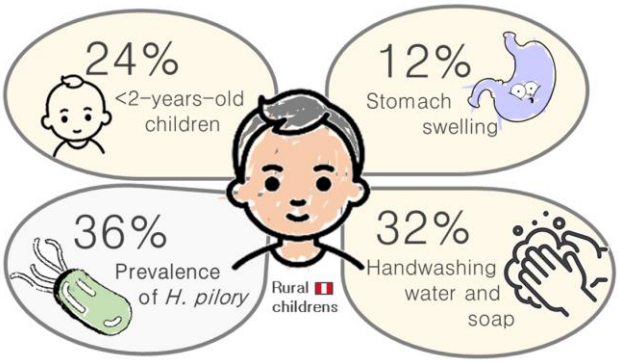

Figure 1. Main findings of children with Helicobacter pylori infection

>50% consumes food outside of home and 24% are asymptomatic and did not have a fixed consumption schedule.

To understand the context of the development of *H. pylori,* it is necessary to understand the phenomena between families and communities, as well as the economic and social aspects in which this cancer-associated infection emerges. *H. pylori* infection occurs during childhood in vulnerable populations around the world. These populations exhibit factors such as persistent diarrhoeal disease, iron efficiency, and loss of immune tolerance that contribute to the persistence of infection and the progression to gastric cancer [14, 15]. Activities to promote health prevention and understanding the environment conducive to infection are important aspects of limiting the eventual increase in cancer. Prioritization must be addressed within the sustainable development goals by 2030 [16].

Screening for *H. pylori*, which is more common in the paediatric population, can be performed by invasive and non-invasive methods [17]. The first includes biopsy and histopathological study (haematoxylin and eosin staining, Giemsa, Warthin-Starry, and immunohistochemical), bacteriological farm, the urease test, and molecular test (such as polymerase chain reaction, in situ hybridization, etc.). The latter include breath tests, direct and indirect immunoassays for the detection of monoclonal or polyclonal immunoglobulins in serum, urine, saliva, and faeces [18]. In children, the stool antigen test is a profitable and useful test for the initial diagnosis of *H. pylori* compared to other techniques, despite its limitations [19]. Most methods require the use of esophagogastroduodenoscopy to obtain gastric mucosal samples, which show that *H. pylori* infection is necessary to initiate treatment [20]. However, the use of the rapid test for the qualitative detection of *H. pylori* antigens in faeces samples could help diagnose an infection due to the cost, ease of performance, time of results, and the few resources involves. Again, this can be used to monitor treatment or as an initial screening test followed by ad-hoc invasive assessments.

In this study, 36% (nine patients) were positive for the *H. pylori* Ag-rapid test, some of them had stomach swelling, caused by the fact of eating outside of home, which is an advantage to catch the bacterium because we ignore the safety standards of how food is prepared. There is a lot of research on

H. pylori infection associated with many different factors in children, and they should be considered a priority because this bacterium is an important one for the World Health Organization due to its high rate of antibiotic resistance [21].

It is important to make three final considerations. First, 18.1% of apparently healthy Chilean schoolchildren were infected with *H. pylori*, while in Cuba, 46% of children <16 years of age were infected [22, 23]. In Peru, the prevalence of *H. pylori* infection was 45% in the three-year cohort of children and 17.2% in the rural population (Cajamarca) [12, 24]. Our results are within the range of infection previously reported and may vary depending on the included population (peri-urban population of Ica), the diagnostic method (faeces antigen test face to histopathological and molecular studies), the evaluation stage (post-treatment or related to other pathologies), among others.

Second, no disease can be understood without considering the context in which the event occurred. *H. pylori* infection is known to be transmitted orally through contaminated water and food, as well as from person to person through saliva, usually acquired in childhood, and persists throughout life. In Peru, the presence of *H. pylori* in water sources was confirmed more than 20 years ago [25]. On the other hand, this resource plays an important role in infection, since people in unsanitary conditions and limited socio-economic resources health workers have more opportunities to catch the infection from the orofecal transmission.

However, social determinants play a role in the verticality of infectious diseases. Sanitation and resource constraints mean that *H. pylori* infection rates are high among low-income populations, and even among these populations, rates are higher in peri-urban or rural communities. According to the report of the Fondo de Cooperacion para el Desarrollo Social (FONCODES), the Municipality of Ica has 14% of the population without access to water and sewers, 20% without electricity, and a malnutrition rate of 10%, which places a Human Development Indicator of 0.648 [26]. These should be evaluated in groups of children with other medical conditions, such as anaemia, other parasites, and the recent increase in non-communicable diseases. Third, the aspects circumscribed by *H. pylori* infection must be regarded in the context of the current molecular topics. The chronic inflammation induced by this bacterium is a critical factor for the development of peptic ulcers and gastric cancer. These should be evaluated in groups of children with other medical conditions, such as anaemia, other parasites, and the recent increase in non-communicable diseases.

Third, the limiting aspects of *H. pylori* infection must be evaluated within the current molecular topic. Chronic inflammation caused by this bacterium is a key factor in the development of peptide ulcers and gastric cancer [27]. During this persistence, the *H. pylori* causes a modulation of the immune response, modulating adaptive immunity principally and achieving a tolerance that facilitates its progression [28]. This progression is followed by an alteration of the gastric microbiota, reducing the immune response in the mucous membranes, and favouring colonization and tissue ulceration [29]. These disease conditions should be evaluated in the paediatric population seeking to promote the use of immunomodulatory and microbiome therapies, but nutrigenomics and nutrigenetics should also be considered as two other co-participant components of the disease.

In our previous discussion about the vast and cosmopolitan Peruvian culinary diversity and its potential impact on gastric cancer [6], children are exposed to adults governed diets that give them a particular response compared to populations with dietary uniformities. To know the importance of nutrition, intrinsic and extrinsic, we consider aspects that are interrelated with the two mentioned, and according to the biological tripartite approach to the development of gastric cancer caused by *H. pylori* infection. Given the association of *H. pylori* with other diseases such as irritable colon, further molecular research directions for *H. pylori* should incorporate this idea, where there is evidence of an interaction between these three components [30].

This exploratory study suggests a 36% of positivity for *H. pylori* antigen in rural children of Peru. Certain dietary characteristics were associated with *H. pylori* positive cases in rural children without distinctive differences between the sex and age groups.

Author contributions: JMS: provided the study concept and design, statistical analysis, data management, and wrote the manuscript; **FdMM:** provided the design, data acquisition, formal analysis, and performed data management; **CL:** provided the design, data acquisition, formal analysis, and performed data management; **KVL:** provided the design, data acquisition, and wrote the manuscript; **BMS:** provided the design, formal analysis, and wrote the manuscript; & **VRZ:** provided the design and data acquisition. All authors have agreed with the results and conclusions.

Funding: No funding source is reported for this study.

Acknowledgements: The authors would like to thank Daniel Cárdenas for facilitating the experimental development of this study during the university campaign of H. pylori discard in children. Also, the authors would like to thank to the Nesh Hubbs team for their logistics support and the field research of this study.

Ethical statement: Authors stated that the study was prepared in compliance with international guidelines for scientific research and all authors have taken into account the ethical responsibilities included in these standards. The study was approved by the Institutional Review Board of UPSJB (UPSJB-VRI-N° 15145-19-). Informed consents from parents and informed agreement from participating children were obtained. The ethical advice for this study follows the Declaration of Helsinki and all data is kept confidential.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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