Original Article

Helicobacter pylori associated with breastfeeding, nutritional status and recurrent abdominal pain in healthy Nigerian children

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Abstract

Introduction: There is limited knowledge about the associations of *Helicobacter pylori (H. pylori)* infections in developing countries. This study aimed to determine the current prevalence and associations of *H. pylori* infection with breastfeeding practices, nutritional status, and recurrent abdominal pain (RAP) in a group of apparently healthy children and adolescents in Lagos, Nigeria.

Methodology: This was a prospective hospital-based study conducted at the Lagos State University Teaching Hospital that involved 118 children who came to the hospital for routine pediatric care. Seroprevalence status of the children was determined by measuring immunoglobulin G antibodies against *H. pylori* using enzyme-linked immunosorbent assay (ELISA).

Results: Seventy-five (63.6%) children were seropositive for *H. pylori*. The prevalence of *H. pylori* infection increased significantly from 40.4% in children less than five years of age to 85.1% at six to ten years of age ($\chi^2 = 20.9$, $p < 0.001$). *H. pylori* infection was associated with low social class (OR = 3.24; 95% CI = 1.20-8.23, p = 0.016) and with RAP (OR = 3.47; 95% CI = 1.55-7.79, p = 0.002), but no association was observed with exclusive breastfeeding, duration of breastfeeding, and under-nutrition.

Conclusions: The prevalence of *H. pylori* infection is high, particularly among children from low socioeconomic backgrounds in Lagos, Nigeria. It is associated with RAP. The effect of this infection on children's health requires further studies.

Key words: *Helicobacter pylori*; prevalence; breastfeeding practices; malnutrition; recurrent abdominal pain

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Introduction

Helicobacter pylori is a Gram-negative, microaerophilic, spiral-shaped bacterium that was first identified by Barry Marshall and Robin Waren in 1982 [1,2]. This microorganism is ubiquitous and infects over half of the global population [1,2]. The rate of infection is higher in developing than in developed countries [1,2]. The organism was initially isolated from a human gastric biopsy and is considered an etiological factor of active and chronic gastritis, peptic ulcer disease, and gastric adenocarcinoma [1-3]. The list of disease entities with which the organism is causally related has increased to include recurrent abdominal pain, gastric mucosa-associated lymphoid tissue lymphoma, gastro-esophageal reflux disease, obesity, growth retardation, and, more recently, extragastric diseases such as coronary heart disease, normal tension glaucoma, and idiopathic thrombocytopenic purpura [3,4]. In developing countries, there is evidence that *H. pylori* can cause suppression of the gastric acid barrier, allowing enteropathogens ingested from contaminated weaning foods to gain access to the small intestine. This predisposes to childhood diarrhea, malabsorption of essential nutrients such as vitamins C and B12, and growth failure in childhood [5,6].

H. pylori infection is acquired early in life and builds up; once established, persists into adulthood [2]. Despite several epidemiological studies, the route of transmission of the infection is not entirely clear [2,3]. Evidence suggests that human-to-human contact may play a significant role in its transmission [7]. This mode of transmission may be mediated by breastfeeding, overcrowding, and poor hygienic practices. The finding of *H. pylori* in saliva, dental plaque, oral cavity, tonsillar tissue, oesophagus, and treated drinking water supports the possibility of human-to-human transmission occurring either through oral-oral and feco-oral routes [7].

Most studies focusing on *H. pylori* infection in Nigeria focused on adults. Only a few studies on children are available [8,9]. Unfortunately, none of the

pediatric studies examined the relationship between *H. pylori* infection, feeding practices, and child nutritional status. Similarly, there has been no report on the association between *H. pylori* infection and recurrent abdominal pain among healthy children in Nigeria. Therefore, this study aimed to determine the current prevalence and determinants of *H. pylori* infection among healthy children in Lagos, Nigeria. It also aimed to determine if the infection was associated with recurrent abdominal pains, breastfeeding, and the nutritional status of the children.

Methodology

Setting

This study was conducted prospectively at the general outpatient clinic of the Department of Paediatrics and Child Health, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos. The hospital is a tertiary health facility owned by the Lagos State Government. It has about 200 bed spaces for children and is located in the Ikeja Local Government Area. Health care is provided free of charge to children and the elderly. The hospital serves the inhabitants of Lagos State and the neighboring Ogun State.

The general pediatric outpatient clinic is open every weekday and is closed on Saturdays, Sundays, and public holidays. An average of 150 patients are seen daily, about 10 of whom are on routine follow-up visits.

Selection of subjects

The subjects were children who had recovered from acute illnesses such as malaria, upper respiratory tract infection (URTI), vernal conjunctivitis, otitis media, and urinary tract infection (UTI) and were on follow-up visits to the general pediatric outpatient clinic. They were recruited between March 5 and March 28, 2009. Subjects were included in the study if the accompanying parents or guardians gave informed consent; additionally, children older than six years of age gave their assent. Each parent/guardian was interviewed in a private room by one of the researchers in accordance with a proforma specifically designed for the study. Information about demographics, breastfeeding practices, socio-economic and environmental characteristics of the family was obtained. Families were classified into a socio-economic class according to the method of Ogunlesi *et al.* [10].

History of recurrent abdominal pain was specifically sought from the parent/guardian. Clinically significant recurrent abdominal pain was defined according to Ukarapol *et al.* [11] as a minimum of three episodes of upper abdominal pain experienced within the last three consecutive months of the clinic appointment that were severe enough to affect the normal activities of the child and required medical attention. Children who had received proton pump inhibitors, H2-receptor antagonists, amoxicillin, metronidazole, or clarithromycin within two weeks prior to the study were excluded. A complete history that focused on dyspeptic symptoms was done and a physical examination was performed by a pediatric gastroenterologist (IOS). Peptic-like or dysmotility-like dyspepsia was diagnosed according to the criteria of Ukarapol *et al.* [11].

Ethical approval

Ethical clearance was obtained from the hospital's research/ethics committee. The ethical approval file number is LREC/10/06/297.

Serological test for Helicobacter pylori

Approximately 1.5 mL of venous blood was aseptically collected from each patient. The sample was centrifuged at 2000 g for two minutes, and the serum was separated and frozen until assayed. Determination of immunoglobulin G to *H. pylori* was done by enzyme-linked immunosorbent assay. This involved using a test kit produced by Dia.Pro Diagnostic (Bioprobes, Milano, Italy). The kit was over 98% specific and sensitive.

Data analysis and presentation

Data was analyzed by descriptive and inferential statistics using SPSS for Windows software version 11. Means and standard deviations (SD) were calculated for continuous variables while proportions were calculated for categorical variables. Categorical variables were compared using the Pearson chi-squared (χ^2) test. Odds ratios with 95% confidence intervals (95% CI) were calculated to measure the degree of relationship between risk factors for *H. pylori* infection and *H. pylori* seropositivity. Probability (p value) of less than 0.05 or 95% CI not embracing unity was accepted as statistically significant.

Results

The sample population consisted of 118 children. The mean age was 7.01 ± 3.58 years, and 58 (49.2%) were females. The social class distribution showed that 20 (16.9%) and 98 (83.1%) belonged to upper and

lower socio-economic classes, respectively. Seventy-five (63.6 %) children were seropositive for *H. pylori* infection.

Table 1 shows the relationship between *H. pylori* and socio-demographic factors of the study group. Twenty-one (40.4%) children up to five years of age were infected with *H. pylori*, and the prevalence increased significantly ($\chi^2 = 20.9$, $p < 0.001$) with age to 85.1% at 6-10 years. Subsequently, the rate decreased significantly to 73.7% at 11-15 years ($\chi^2 = 6.17$, $p= 0.012$). The only identified risk factor for *H. pylori* infection was low social class (OR = 3.24; 95% CI = 1.20-8.23, p = 0.016). However, *H pylori* infection was not significantly associated with other household factors.

Table 2 shows the associations of *H. pylori* with feeding practices, nutritional status, recurrent abdominal pain. There was no significant association with exclusive breastfeeding for six months ($\chi^2 = 0.683$, $p = 0.409$), duration of breastfeeding ($\chi^2 = 2.699$, $p = 0.100$), formula feeding ($\chi^2 = 1.13$, $p =0.289$), thinness ($\chi^2 = 0.072$, $p = 0.789$), and stunting ($\chi^2 = 0.234$, $p = 0.629$).

There was a threefold higher chance of recurrent abdominal pain in children infected with *H. pylori* (OR = 3.47, 95% CI = 1.55-7.79, p = 0.002). Of the 118 subjects studied, 30 (25.4%) had epigastric tenderness and of those, 22 (40.0%) had a history of RAP. Thus, abdominal tenderness was more often encountered among children with RAP ($\chi^2 = 11.7$, $p = 0.003$).

Discussion

The overall prevalence of *H. pylori* infection in our study of apparently healthy children in Lagos, Nigeria was 63.6%, which is similar to the 69% reported for a pediatric age group from the northern part of Nigeria [8], but higher than the 14% reported from southern Nigeria [9] and the 11% among children who presented with dyspepsia in a tertiary health facility in Abakaliki in southeastern Nigeria [12]. The reason for this difference in prevalence within the Nigerian population is largely unknown, but could be due to the difference in socio-cultural factors, which affect carriage of the organism. For instance, the people from southern and southeastern parts of Nigeria are known to freely consume many vegetables and traditional herbal medicines compared to those from southwestern and northern parts of Nigeria [13]. Many of these plants include *Allium* vegetables, *Morinda lucida* vegetables, *Ocimum gratissimum*, *Carica papaya*, and *Phyllantus amarus*, which are known to have antibiotic properties against *H. pylori.* [14,15]. The inhibitory activities of these plants on *H. pylori* proliferation may have affected the rates of infection in different geographic zones in Nigeria.

Comparing our data with those from other developing countries, the prevalence of *H. pylori* infection in our study was as high as the rates previously reported among pediatric age groups in the Republic of Benin [16], Egypt [17], India [18], and Pakistan [19]. In contrast, a significantly lower prevalence of 7% to 24.8% has been reported among pediatric age group in New Zealand [20], Germany [21], and the United States [22]. Low socio-economic status and poor environmental and living conditions have been named as possible reasons for the differences in the prevalence of *H. pylori* infection among children in the developing and developed countries [16,17]. In the present study, a significantly high risk of *H. pylori* infection was observed in the low socio-economic class, similar to the findings in previous studies [1,8,11]. It is conceivable that the living conditions and sanitary habits of children from families with low incomes may likely be poor, thus increasing their susceptibility to *H. pylori* infection; however, this may not be true in all cases, as an alternative source of *H. pylori* infection that is independent of social class may exist.

One of the advantages of breastfeeding over formula feeding is that breast milk contains biological compounds of anti-infective nature. However, the results of studies on the protective effect of breastfeeding against acquisition of *H. pylori* are conflicting. Ertem *et al.* [23] reported in their study that breastfeeding has protective effects against *H. pylori* infection, which was in contrast to the lack of protective effects reported by Rodriques *et al.* [24]. In a prospective study in Gambia, Thomas *et al.* [25] found a high titre of specific IgA antibodies against *H. pylori* in mothers' breast milk. These anti-*H. pylori* antibodies have been shown *in vitro* to inhibit adherence of the organism to gastric cells. On the contrary, Rothenbacher *et al.* [26] reported an increase in the rate of *H. pylori* infection with breastfeeding, especially in children breastfed longer than six months. In our study, we did not find any significant protective effect of breastfeeding against *H. pylori* infection, but the decrease in the prevalence of *H. pylori* infection with increase in duration of breastfeeding up to 17 months would suggest a dose response protective effect of IgA antibodies in breast milk.

Table 1. Influence of socio-demographic factors on seropositivity for *Helicobacter pylori* infection

	H. pylori-positive	*H. pylori*-negative	OR	95% CI
Age (years)				
≤5	21 (40.4)	31 (59.6)	1	
6-10	40 (85.1)	7 (14.9)	8.44	3.18-22.4*
11-15	14 (73.7)	5 (26.3)	4.13	1.29-13.2**
Gender				
Male	36 (50.0)	24 (40.0)	1	
Female	39 (67.2)	19 (32.8)	1.12	0.85-1.47
Mother's level of education				
Postsecondary	61 (61.0)	39 (39.0)	1	
At least secondary	14 (77.8)	4 (22.2)	1.85	0.95-1.71
Father's level of education				
Postsecondary	69 (62.2)	42 (37.8)	1	
At least secondary	6 (85.7)	1 (14.3)	1.38	0.99-1.93
Social class				
Upper	8 (40.0)	12 (60.0)	1	
Lower	67 (68.4)	31 (31.6)	3.24	1.20-8.73*
Household size				
≤4	66 (65.5)	35 (34.7)	1	
Greater than 4	9 (52.9)	8 (47.1)	1.23	0.77-1.98
Water supply				
Safe	22 (56.4)	17 (43.6)	1	
Unsafe	53 (67.1)	26 (32.9)	1.58	0.72-3.46
Toilet facility				
Water closet	61 (63.5)	35 (36.5)	1	
Pit latrine	14 (63.6)	8 (36.4)	1.00	0.71-1.42

Figures in parenthesis are percentages of the total in the respective row; OR = odds ratio; 95% CI = 95% confidence interval;
*p < 0.001; **p < 0.05

Table 2. Association of *H. Pylori* infection with feeding practices, nutritional status and recurrent abdominal pain

	H. Pylori-positive	*H. Pylori*-negative	OR	95% CI
Exclusively breastfed for 6 months				
No	60 (61.9)	37 (38.1)	1	
Yes	15 (71.4)	6 (28.6)	1.54	0.55-1.54
Duration of breastfeeding				
< 6 months	2 (50.0)	2 (50.0)	1	
6-11 months	8 (36.4)	14 (63.6)	1.75	0.21-14.9
12-17 months	18 (32.7)	37 (67.3)	2.03	0.20-20.8
≥ 18 months	15 (40.5)	22 (59.5)	1.45	0.14-15.3
Infant formula feeding				
No	30 (69.8)	13 (30.2	1	
Yes	45 (60.0)	30 (40.0)	0.65	0.29-1.44
Height-for-age z-score				
Not stunted	72 (63.2)	42 (11.4)	1	
Stunted	3 (75.0)	1 (25.0)	1.02	0.91-1.09
BMI-for-age z-score				
Not thin	65 (63.1)	38 (36.9)	1	
Thin	10 (66.7)	3 (33.3)	1.02	0.89-1.17
Recurrent abdominal pain				
No	32 (50.8)	31 (49.2)	1	
Yes	43 (78.2)	12 (21.8)	3.47	1.55-7.79*

Figures in parenthesis are percentages of the total in the respective row; *p < 0.01; OR = odds ratio; 95% CI = 95% confidence interval

Future community-based studies that involve a larger sample size may be necessary to ascertain this relationship.

Similarly, there have been conflicting results about the association of *H. pylori* infection with growth in children. While many researchers reported an association of *H. pylori* infection with growth delay [5,6,17,27,28], a few did not find such an association [29-31]. Our study did not show a significant relationship with stunting and thinness of the children studied. It is worth noting that, even in those studies that reported a significant relationship between *H. pylori* infection and nutritional status, it may be difficult to ascribe the relationship to a direct effect of *H. pylori* on growth due to the presence of other confounders that may affect both *H. pylori* acquisition and nutritional status of the children.

The association between *H. pylori* infection and RAP continues to generate controversial reports. Studies from India [32], Sweden [33], and Canada [34] have shown no association between *H. pylori* and RAP. Similarly, many meta-analyses and reviews [35,36] have shown that there is no association between *H. pylori* and RAP. However, in this study, we found that the prevalence of *H. pylori* infection among children with RAP was three-and-a-half times greater than those without RAP. Similar findings have been reported in Saudi Arabia [37] and the United States [38]. In sub-Saharan Africa, RAP is common in children and helminthiasis is the proven etiology, particularly in low socio-economic settings [39]. This has been responsible for the common practice of parents administering anthelmintics to their children following complaints of RAP. However, our findings suggest a possible additional role of *H. pylori* in RAP, although this will need to be confirmed by an interventional study in a larger population of children to ascertain the role of *H. pylori* in RAP.

A major limitation of this study is that it was based on subjects recruited from the hospital. Excluding subjects from the general pediatric population made it difficult to generalize our results. As in most other developing countries, it is very difficult in Nigeria to get subjects from the general pediatric population to give their consent or assent for blood sampling for research purposes. This limitation may have contributed to the dearth of community-based studies on *H. pylori* in Africa. Therefore, further research involving the urea breath test or the fecal antigen test, which may be relatively more acceptable to people in the community, may be desirable and useful in developing countries.

We concluded that the prevalence of *H. pylori* infection among apparently healthy children and adolescents in Lagos, Nigeria was high, particularly in the lower socio-economic class. There was no significant association between *H. pylori* infection and breastfeeding or the nutritional status of children. However, the prevalence of *H. pylori* infection was significantly high in children with RAP. Community-based studies, as well as interventional studies, are required to ascertain the causal relationships between *H. pylori* infection and RAP identified in the present study.

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