Seroprevalence and determinants of *Helicobacter pylori* infection among asymptomatic under-five children at a Tertiary Hospital in the South-Western region of Nigeria

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Abstract

Background: The epidemiology of *Helicobacter pylori* (*H. pylori*) infection among under-five children in the South West Nigeria remains largely understudied. There is no data on the subject from the study area.

Objectives: This study was conducted to assess the seroprevalence of *H. pylori* infection among under-five children at a tertiary hospital in the South Western, Nigeria and to determine its associated socio-demographic factors.

Methods: Sera of 360 children were analyzed for anti *H. pylori* Ig G using enzyme linked immunosorbent assay test kit (BQ ELISA Ig G KIT) and *H. pylori* infection risk factors were determined. Determinants of H. pylori infection was determined using binary logistic regression analysis and p-values < 0.05 were taken as statistically significant.

Results: *H. pylori* infection seroprevalence rate was 32.8% and increased with age. Living in one room accommodation, large families, playing with soil, family history of dyspepsia, practice of premastication, sharing of plates and cutlery, and water closet toilet were associated with *H. pylori* Ig G seropositivity ($p<0.05$) on binary regression analysis.

Conclusion: The seroprevalence of *H. pylori* infection in under -five children is high, increasing as the age of the children increased. This may suggest that instituting preventive measures at young age, targeting identified factors may be effective in reducing the burden of *H. pylori* infection.

Keywords: *Helicobacter pylori*, South-Western Nigeria.

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Introduction

Helicobacter pylori (*H. pylori*) infection is one of the most common human bacterial infection worldwide with about 50% of the global population infected[1]. The prevalence of infection varies both between and within countries in relation to race, ethnicity and geographical area[2] such that developed countries have significantly

lower rates of *H. pylori* infection than developing countries. This difference has been attributed to differing rates of acquisition of the organism in childhood as well as sanitation, socio economic and hygiene status of the population3. Most of the infected people develop no clinical symptoms and live their lives with superficial chronic gastritis. However, about 17% of infected subjects will develop peptic ulcers and about 1% will progress to gastric cancer which is the third leading cause of cancer-related deaths in the world, especially in the adult population.[4]

The childhood period may be critical for the acquisition of *H. pylori* infection[2]. It is believed that once the organism is acquired, it persists for life unless there is an intervention[1,5]. However, some authors have reported loss of infection either spontaneously in some rare cases, or as a result of inadvertent exposure to antibiotics[6,7].

Documented risk factors for *H. pylori* infection include poverty,[8] poor sanitation, overcrowding[9,10] and unsafe water source[11], which are prevalent in most communities in Nigeria.

Since the epidemiology of this bacterial infection differs from one geographical area to another and even within countries, it is therefore pertinent that more studies are conducted on people from different backgrounds in order to have better understanding of the burden of *H. pylori* infection. Hence, this study assessed the burden of *H. pylori* infection as well as the socio-economic and demographic factors that may increase the risk of childhood acquisition of infection in a semi-urban community in South Western Nigeria.

Methods

Study location

The study was conducted in two units of the Obafemi Awolowo Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria, These were the Wesley Guild Hospital unit (WGH) Ilesa and the Urban Comprehensive Health Centre unit (UCHC) Ile-ife. Ile –Ife town lies on longitude 40 69'E and latitude 700 50'N.[12] According to the 2006 population census, Ile-Ife has a population of 355,281 and an area of 283 sq.km. Ilesa town is located between latitude 70 37' N and longitude 40 40' E.[13] with a population of about 277,904.[14] The services rendered at these units include Infant Welfare, Nutrition Rehabilitation, School Health, Immunization, Dental, and Physical Rehabilitation. On average, about 1,000 children aged 0-59 months are seen at the various clinics at the WGH and 2,800 children at the UCHC monthly.

Study design

We conducted a cross-sectional study between July 2014 and March 2015.

Study population

The study population comprised of children aged 6-59 months attending the child welfare clinics.

Sampling methods

On average, about 1,000 children aged 0-59 months are seen at the various clinics at the WGH and 2,800 children at the UCHC monthly. Based on this, proportionate sampling was employed in recruiting study participants. A total of 360 children between the ages of 6 months and 59 months were recruited, 265(73.6%) from UCHC and 95(26.4%) from WGH. Recruitment was done based on the average population of children that attend each facility. All consecutive children who met eligibility criteria were recruited and questionnaires were administered to their parents or caregivers.

Data collection

Parental social class was determined using Oyedeji[15] classification method. Children who had taken antibiotics one month before presentation, those on proton pump inhibitors and those on H2 receptor blockers were excluded from the study.

Anthropometric measurements

Weight, length and height were measured by standard techniques as described in the supplementary materials.

H .pylori detection

Two milliliters of whole blood was collected aseptically through venepuncture from each participant into plain bottles. The sample was then left to clot and serum separated after spinning for 10 minutes at 4,000 revolutions per minute. The separated serum was then frozen at -20^0C till the time of analysis. The sample analysis was done in the laboratory of the Department of Biochem-

istry, Obafemi Awolowo University, Ile-Ife, Nigeria. The frozen samples were thawed at room temperature. The "BQ Helicobacter pylori Ig G ELISA" kit (BQ Kits Inc. San Diego USA).was used. Each of the samples was run twice and the mean H. pylori Ig G recorded. According to the manufacturer's manual, the antibody index was interpreted as: < 0.9 – no detectable antibody to H. pylori Ig G by ELISA, 0.9-1.1- Borderline positive > 1.1-detectable antibody to H. pylori Ig G by ELISA

Data analysis

Data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 20.0. Frequencies and proportions were used to summarize socio-demographic variables and this was presented as tables and charts. The sero-prevalence of *H. pylori* infection was determined using percentages. Chi square test of statistic was then used to determine any association between sero-prevalence and the socio demographic factors. Binary Logistic regression with odds ratio at 95% confidence intervals was used to assess the determinants of *H. pylori* seropositivity. Significance level was set at p-value < 0.05 for all tests.

Ethical approval

Ethical approval was obtained from the OAUTHC Ethics and Research Committee. Also, written informed consent was obtained from the parent or guardian of each study participant before the questionnaire was administered.

Results

Sero-prevalence of H. pylori infection: Of the 360 study participants, 118 (32.8%) were serologically positive for *H. pylori* Ig G antibodies while 242 (67.2%) were negative.

Socio-demographic characteristics of the study participants: As shown in Table 1, there was slight male preponderance. Most of the mothers were aged between 20-39 years and virtually all the mothers (98.1%) had formal education.

Table I: Socio demographic characteristics of participants (children aged 6 months-59 months)

Characteristics	Frequency	Percent (%)
Sex of participants		
Males	204	56.7
Females	156	43.3
Mother's age in years		
20-29	143	39.7
30-39	200	55.6
40-49	17	4.7
≥50	0	0.0
Mothers level of formal education		
None	7	1.9
Primary	33	9.2
Secondary	162	45.0
Tertiary	158	43.9
Social class of parents		
Social class 1	38	10.6
Social class 2	99	27.5
Social class 3	186	51.8
Social class 4	37	10.3
Social class 5	0	0.0
Number of children in household		
1 child	102	28.4
2 children	126	35.0
3 children	70	19.4
4 children	43	11.9
≥ 5 children	19	5.3

Majority of parents (52%) were in social class 3. No family was in social class 5 and most households had between one or two children.

Socio-demographic factors associated with H. pylori infection:

As shown in Table 2, the sero-prevalence of *H. pylori* infection increases with advancing age of the children. Also, its prevalence increases with increasing number of children in the households ($p<0.001$). However, there was no difference in the prevalence of *H. pylori* infection with respect to mothers` age, level of formal education and social class of the parents ($p>0.05$).

Table II: Relationship between Socio-demographic characteristics of the study participants and H. *pylori* seropositivity

Characteristic	*H. Pylori* IgG sero-positive		*H. Pylori* IgG sero-negative		Statistical comparison
	Frequency	%	Frequency	%	
Age in months					
6-11	15	12.5	105	87.5	$\chi^2 = 49.49$
12-35	37	30.8	83	69.2	df=2
36-59	66	55.0	54	45.0	**p<0.001**
Sex					$\chi^2 = 1.93$
Male	73	35.8	131	64.2	df=1
Female	45	28.8	111	71.2	P= 0.165
Mother's age in years					
20-29	37	25.9	106	74.1	$\chi^2 = 5.66$
30-39	76	38.0	124	62.0	df=2
≥40	5	29.4	12	70.6	p= 0.059
Mothers level of formal education					
None	3	42.9	4	57.1	$\chi^2 = 3.39$
Primary	15	45.5	18	54.5	df=3
Secondary	53	32.7	109	67.3	p= 0.336
Tertiary	47	29.7	111	70.3	
Number of children in household					
1 child	16	15.7	86	84.3	
2 children	46	36.5	80	65.5	$\chi^2 = 20.52$
3 children	29	41.4	41	58.6	df=4
4 children	20	46.5	23	53.5	**p<0.001**
≥ 5 children	7	36.8	12	63.2	
Social class of parents					
Social class 1	13	34.2	25	65.8	$\chi^2 = 0.78$
Social class 2	29	29.3	70	70.7	df=3
Social class 3	63	33.9	123	66.1	p= 0.855
Social class 4	13	35.1	24	64.9	
Social class 5	0	0	0	0	

p values in bold are statistically significant
χ^2 –chi square, Df- degree of freedom

Relationships between child care practices, environmental characteristics and *H. pylori* sero-positivity: The significant factors associated with *H. pylori* sero-positivity were: practice of premastication, sharing of plates and cutlery, and accommodation type ($p<0.05$) Table III.

Table III: Relationship between feeding history, child care practices, household characteristics of study participants and H. *pylori* seropositivity

Characteristic	H. *pylori* Ig G seropositive		H. *pylori* Ig G seronegative		Statistical comparison
	Frequency	%	Frequency	%	
Mode of feeding - Bottle feeding					$\chi^2 = 1.15$
Yes	49	29.9	115	70.1	df=1
No	69	35.2	127	64.8	p= 0.284
Breast feeding					LR = 0.80
Yes	118	32.9	241	67.1	df=1
No	0	0	1	100	p= 0.372
Child ever attended day-care					$\chi^2 = 1.48$
Yes	39	37.5	65	62.5	df=1
No	79	30.9	177	69.1	p= 0.224
Feeds with cup and spoon					$\chi^2 = 0.156$
Yes	115	33.0	234	67.0	df=1
No	3	27.3	8	72.7	p= 0.693
Practice premastication					$\chi^2 = 4.53$
Yes	50	40	75	60	df=1
No	68	28.9	167	71.1	**p= 0.033**
Accommodation type					
1-room apartment	26	59.1	18	40.9	$\chi^2 = 18.53$
2-room apartment	40	25.0	120	75	df=3
3-room apartment	45	32.6	93	67.4	**p<0.001**
4-room apartment	7	38.9	11	61.1	
Share plates and cutlery					$\chi^2 = 13.99$
Yes	75	42.1	103	57.9	df=1
No	43	23.6	139	76.4	**p<0.001**
Rear domestic animals at home					$\chi^2 = 2.33$
Yes	43	38.4	69	61.6	df=1
No	75	30.2	173	69.8	p= 0.127
Family source of water					
Well water	68	38.0	111	62.0	$\chi^2 = 5.05$
Stream	3	37.5	5	62.5	df=3
Pipe borne water	19	25.0	57	75.0	p= 0.168
Sachet water	28	28.9	69	71.1	

P values in bold are statistically significant
X^2 –chi square, df- degree of freedom

Logistic regression model for factors associated with *H. pylori* infection: Binary logistic regression model for factors associated with *H. pylori* infection shows that Under-fives who reside in houses with water closet type of toilet facility were about two times more likely to have *H. pylori* infection as compared with their counterparts who live in houses with pit latrine toilets [OR 2.40, (95% C.I, 1.20-4.78) p=0.013]. Also, under-fives who shared plates with other family members were almost twice more likely to have *H. pylori* infection as compared with those who did not [OR 1.79, (95% C.I, 1.05-3.04) p=0.032]. Under-fives from homes with 1-room apartment were more likely to be seropositive for *H. pylori* when compared with their counterparts from homes with 4-room apartments

[OR 7.51, (95% C.I, 2.03- 27.82) p=0.003]. Children who play with soil were three times more likely to have *H. pylori* infection as compared with those who do not [OR 3.32, (95% C.I, 1.76-6.29) p<0.001]. Furthermore, under-fives whose caregivers practice premastication were twice more likely to be infected with *H. pylori* than those who did not. [OR 2.09, (95% C.I, 1.23-3.56) p=0.007]. Participants with positive family history of dyspepsia were more likely to have *H. pylori* infection when compared with those with no family history of dyspepsia [OR 2.13, (95% C.I, 1.08-4.21) p=0.029]. Lastly, under-fives from households with two, three and four children were more likely to be seropositive to *H. pylori* than those under-fives from households with only one child.

Discussion

Helicobacter pylori infection can occur early in the life of an individual and if left untreated, could lead to chronic health problems such as peptic ulcer disease and gastric cancer in later life[1]. Despite, these observations, there is scanty data on the subject among Nigerian children and none from the study area. Hence, this study is an important addition to the scanty data on *Helicobacter pylori* infection among children in Nigeria. This is more apt giving the fact that determining the burden of this infection in childhood might aid early diagnosis and enable early therapy for identified children who meet criteria for treatment. In this study we established that *Helicobacter pylori* infection is common among children in our locality.

The *Helicobacter pylori* infection sero-prevalence rate of 32.8% found in this study compares with the 30.9% obtained by Etukudo and colleagues among children aged 6months to 15 years[16] in Uyo, Nigeria but lower than 69% and 65.7% found by Holcombe et al.[17] in Northern Nigeria and Senbanjo et al.18 in Lagos respectively. The studies by both Senbanjo et al[18] and Holcombe et al[17] used participants whose average ages were older than the participants in the present study and this could account for the differences in the *H. pylori* seroprevalences as observed. Nevertheless, the sero-prevalence rate of 32.8% found in this study, is comparable to findings from other developing countries[9,19-22]. For example, Kate et al.[23] reported an overall sero-prevalence of 45% among children up to 15 years old in India. Also, Hestvik et al.[22] reported a prevalence rate of 46.0% among less than 3 years children in Kampala, Uganda.

However, the sero-prevalence rate of H. pylori infection in this study is higher than those reported in developed countries[24-26]. Naito and colleagues reported 4.0-6.7% among Japanese children using urine *H. pylori* antibody based test.[24] Dore et al.[25] obtained 13.3% amongst children aged 6-15 years in Italy. Similarly, Tam and coworkers[26] using 13C-urea breath test reported 13.1% among Chinese children in Hong Kong. These lower prevalence rates in developed countries could be due to the better living conditions and improved hygiene status over there.

In this study it was found that the sero-prevalence of *H. pylori* infection increases with age. This has been corroborated by many authors[19-21, 27,28]. The reason for this, is probably
the increased opportunities for acquisition of the microorganism as a result of increased exposure to the various sources of the infection especially in children as they grow. Children are usually more mobile with increasing age and particularly in under-fives, they have less regard for hygienic practices which may facilitate acquisition of infection especially through faeco-oral mode of transmission. Some authors, however, did not observe any relationship with age[9,16,26]. They opined that this may be due to spontaneous elimination of infection and loss of infection as indirect benefits from use of antibiotics for some other purposes[29].

In this study, the factors found to be associated with the high prevalence of *H. pylori* infection among children included premastication of food by parents, sharing of plates and cutlery with family members, communal residing in one room apartment by families, family history of dyspepsia and having many children in the household. These findings are mixed regarding literature. Sheikhian et al.[27] in Iran reported association between premastication of food by mothers and *H. pylori* infection but found no association with sharing of plates. Nabwera et al.[31] reported sharing of plates as an independent risk factor for *H. pylori* infection. In contrast, Langat et al.[9] reported no association between premastication of food by mother and H. pylori infection.

Ikpeme et al.[32] in Uyo, Nigeria reported an association between H. pylori seropositivity and a family history of dyspepsia. This association probably corroborates the causative role of H. pylori in dyspepsia and possible intra-family spread of the organism which was also observed by Osaki et al.[33] and Nahar et al.[34] in Japan and in Bangladesh respectively.

This study revealed that children who reside with parents in one room apartments were found to be seven times more likely to be infected with *H. pylori* than those who reside in houses with two or more rooms thus highlighting impacts of overcrowding in *H pylori* infection as earlier observed[9,20,30,35].

Surprisingly, the use of water closet as means of sewage disposal was found to be a risk factor for *H. pylori* infection in this study. This might be related to improper and unhygienic use of the water closet toilet facilities especially in developing countries such as Nigeria with poor access to water supply. Similar to this study, Senbanjo et al.[18] in Lagos also found that people who used water closet toilet facilities had higher *H. pylori* seropositivity rate than those who did not. This is in contrast with the findings of Etukudo and coworkers[16] in Uyo, who found that use of pit latrine was more likely to be associated with *H. pylori* infection in children than water closet.
There was no association between *H. pylori* seropositivity and mother's level of education. This is in agreement with findings by Oleastro et al in Lisbon[36].
Our finding of no association may be because most of the mothers of the study participants were literate. However, previous authors have established link between low mother education and increased H. pylori infection[9,26].
This study also revealed no association between types of feeding practice (bottle feeding, breastfeeding and use of cup and spoon) and H. pylori seropositivity rates. Sial et al.[30] in Tunisia reported no association between H. pylori and breastfeeding but found prolonged bottle feeding as a risk factor, thus suggesting that the feeding bottle may be a vehicle of infection.
Langat et al.[9] also found no association between H. pylori infection and breast feeding.

Conclusion

Sero-prevalence of *H. pylori* infection was found to be high in this study and logistic regression model indicated that water closet toilet facilities, sharing of plates and cutlery, one room accommodation, playing with soil outside the house, number of children in the households, practice of premastication of food and family history of dyspepsia were associated with *H. pylori* infection. Therefore, health education targeted at parents and guardians with regards to preventing these factors will be helpful in reducing the prevalence of *H. pylori* infection in children in the study area.

In addition, since vaccination against the infection has been proposed by some researchers in developed countries as a way to combat the scourge of *H. pylori* infection,[37] the findings from this study, raises the need for more longitudinal studies focusing on the evolution of dyspeptic symptoms during childhood and possibly identification of serotypes commonly responsible for *H. pylori* infection in Nigeria for targets for vaccination. Also, such studies may help to identify other determinants of *H. pylori* infection. Hence, this may help government in formulating policies such as inclusion of vaccination against *H. pylori* infection in the routine childhood immunization schedule and improving the general housing conditions of the populace. Finally, there is a need for guidelines that could assist the clinicians in developing countries in identifying which category of children to screen and treat for the *H. pylori* infection.

Limitation of the study

This study was hospital based and has the possibility of being skewed towards severe cases of the health targeted conditions. However, the primary health care units where the study was conducted mainly care for children who are not sick but merely came for well child visitation, for growth and nutritional monitoring and immunization services. Hence, are presumed to closely reflect the community prevalence of *H. pylori* infections.

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