Niger J Paed 2013; 40 (1):45 – 49

ORIGINAL

Ikpeme EE
Etukudo OM
Ekanem EE

Clinical correlates of *helicobacter pylori* infection in children seen at a Tertiary Hospital in Uyo, Southern Nigeria

DOI:http://dx.doi.org/10.4314/njp.v40i1.8
Accepted: 30th April 2012

Ikpeme EE (✉)
Etukudo OM
Department of Paediatrics,
University of Uyo Teaching Hospital,
PMB1136
Uyo, Nigeria.
Tel: +2348033123336
Email: enpeks@yahoo.com

Ekanem EE
Department of Paediatrics,
University of Calabar Teaching
Hospital, Calabar, Nigeria.

Abstract *Background: Helicobacter pylori (H pylori)* infection is the commonest global chronic human bacterial infection. Data from developed countries show that acquisition occurs in childhood but manifestation of chronic gastroduodenal diseases occur more commonly in adulthood. *H. pylori* infection has however been associated with paediatric primary peptic ulcer disease, though data is rather scanty. There is virtually no data on the clinical correlates of the seropositive Nigerian paediatric subjects though the little data available shows higher prevalence rates compared to that of children from developed countries.
Objectives: A prospective observational survey was carried out to determine the clinical correlates of *H. pylori* infection in ill children admitted in the emergency unit of our department.
Methods: H. pylori Immunoglobulin G antibody was determined from serum samples stored at -20^{0}C using a commercial enzyme-linked immunosorbent assay kit, VicTorch. Data was analysed with using SPSS and correlates determined as appropriate.
Results: The subjects were 132 (57.4%) males and 98(42.6%) females (male: female ratio= 1.3:1.0) with an age range of 0.5-15 years and a mean age of 5.0 (SD±4.0) years. The overall seroprevalence rate was 30.9%. Clinical features including abdominal pains, (p=0.001), fetor oris, (p=0.0001), diarrhoea (0.041) and family history of dyspepsia (p=0.002), showed significant association with seropositivity.
Conclusion: Seroprevalence of *H. pylori* infection in Nigerian children is high and is associated with common gastroduodenal symptoms.

Keywords: *Helicobacter pylori*, children, Nigeria, clinical correlates.

Introduction

Helicobacter pylori (H pylori) infection is the commonest chronic human bacterial infection and about 50% of adults the world over are said to be colonised with the pathogen.[1] The aetiologic agent is a flagellated spiral-shaped Gram negative bacterium with its natural ecological niche being the antral portion of the human stomach.[2,3] Its colonisation of the human gastric antrum has been associated with chronic gastroduodenal diseases worldwide. Manifestations of *H. pylori* associated gastroduodenal diseases have been reported principally in adulthood although the acquisition occurs in childhood.[1] Primary peptic ulcer disease has been shown to be associated with *H. pylori* infection in children.[4] There is a dearth of information on *H. pylori* associated clinical manifestations in children even though higher incidence rates are recorded in the socioeconomically-challenged developing countries where over 50% of children are infected by five years of age.[5-9]

The clinical course of *H. pylori* infection is highly variable. This is influenced by the microbial, host and environmental factors. The dynamics of this global infection are different for different regions but in virtually all infected individuals, *H. pylori* infection causes a chronic inflammation of the gastric mucosa. Gastritis develops rapidly after acquisition of *H. pylori* infection and remains with the persistence of the infection.[10] This gastritis is suggested to be a precursor of gastric cancer with obvious grave consequencies.[11]

In the adult population, acute *H. pylori* infection is accompanied by mild to moderate dyspeptic symptoms and occasional vomiting occurring within a few days of the challenge. These symptoms peak during the second week of illness and then resolve.[12] In children, the symptomatology of acute *H. pylori* infection is not well characterised. Occasionally, acute infection may cause gastric ulcers and haematemesis.[13] There is virtually no data on clinical manifestations of *H. pylori* infection in

Nigerian children though the scanty available data show that the prevalence of this infection is very high.[5,6] In Maiduguri, Holcombe *et al* reported age specific prevalence rates of 82% and 92% in children aged 5-10years and 11-19 years respectively.[5]

This study was therefore undertaken to see whether or not the high seropositivity of *H. pylori* infection as reported in Nigerian children has any clinical correlates in children admitted for treatment of various ailments at a tertiary health centre in southern Nigeria.

Subjects and methods

The study was conducted at the University of Uyo Teaching Hospital, Uyo, in Akwa Ibom State. Akwa Ibom State has a population of 3.9 million people.[14] Uyo is the capital city of Akwa Ibom State. It is predominantly a civil service town. The Teaching Hospital is a 300 bed capacity hospital and the only tertiary health institution in the state.

The study population consisted of 230 children, admitted in the children emergency unit of our hospital, aged between six months and 15 years who required venepuncture, and for whom an informed written consent was obtained. The sample size was calculated using the formula

$$n = \frac{Z^2P(1-P)}{d^2}$$

Where n = Minimum sample size
Z = Standardized normal deviation (1.96)
P = Best estimate of population prevalence rate (82%)[5]
d = Tolerable error margin (5%)

The best estimate of population prevalence rate for *H. pylori* in Nigerian children = 82%.[5]

Therefore, minimum sample size was

$$n = \frac{(1.96)^2 \times 0.82 \times 0.18}{(0.05)^2} = 227$$

A clinical history was obtained from each subject, including the family and social history and the child's socioeconomic status was determined using the parents/ guardians social class according to the social classification scheme proposed by Oyedeji.[15] A quick clinical examination, including oral and dental assessments, was also done. Standard anthropometric measurements were taken. These were recorded on the study proforma.

About 2.0mls of blood was collected from each subject into a plain specimen bottle and taken to the laboratory within 30 minutes and centrifuged to separate the serum, which was stored frozen at -20^{0}C till sufficient samples were pooled for analysis.

The VicTorch *H pylori* IgG test kit, with high sensitivity and specificity of 90-93% and 95-96% respectively, was used for the analysis as described by the manufacturer.[16] The reagents were stored unopened at 4^{0}C. Repeated freezing and thawing of the samples or microbial contamination were avoided and icteric or turbid samples were not used (manufacturer's precautionary advice). The cut off value for positive antibody activity (AA) was taken at greater than 20IU.[16] A definite infection, as determined by the antibody activity of this test kit, was not less than 10% of the cut off value with accuracy level of 85.2%.[16] The test principle is based on appreciation of antibody titre with time and the 20IU is the level at which antibody build up determined a definite infection in comparison with urea breath test of gastric biopsy specimens.

Ethical approval was given by the Ethical Committee of the University Of Uyo Teaching Hospital, Uyo.

Statistical analyses

Statistical analyses were performed using the SPSS software package (Statistical Package for Social Sciences) 15.0 Software. Data were summarised into tables.
The seropositivity for *H. pylori* was computed according to age. Correlates of *H. pylori* were evaluated by a comparison of proportions of children with and without infection using Chi-square(x^2) test and Fisher's exact test as appropriate.

Controlling variables for evaluation with multiple logistic models were age, gender and symptoms.
The statistical significance of the adjusted seropositive rates among comparison groups was also tested. *p*-value of $\leq$0.05 was the significant level.

Results

Two hundred and thirty children aged 6 months to 15 years with mean age of 5.0 (±4.0) years, median age of 4.0 years, comprising 132 (57.4%) males and 98 (42.6%) females had their serum samples tested for IgG antibody reaction to *H. pylori.*

Using the cut-off value for antibody activity (AA) of 20IU, 71 (30.9%) were serologically positive for *H. pylori* IgG antibodies while 159 (69.1%) were negative. The antibody activity (AA) level of seropositive children was >20.0IU with a mean (±SD) value of 42.0IU (±16.1) as given by the manufacturers.

The age distributions of the study subjects were as shown in Table 1. Children less than five years of age constituted 60.0% of the subjects. *H. pylori* seropositivity was highest in the one to five years age group (36.6%) and the cumulative seropositivity was 56.3% in the under five years age group. The least represented age group was 11- 15 years which constituted 12.2% of the study population with 9.9% seropositivity.

The general characteristics of the subjects namely; the mean age, weight, height and body mass index were similar for both male and female subjects and had no association with *H. pylori* Ig G antibody activity.

Table 1: Distribution of subjects by age

Age (years)	subjects	%	Cumulative	HPAP	%	Cumulative	HPAN	%	Cumulative
<1	30	13.0	13.0	14	19.7	19.7	16	10.1	10.1
1-5	108	47.0	60.0	26	36.6	56.3	82	51.6	61.7
6-10	64	27.8	87.7	24	33.8	90.1	40	25.1	86.8
11-15	28	12.2	100	7	9.9	100	21	13.2	100

HPAP =H. pylori Antibody Positive
HPAN =H. pylori Antibody Negative

Table 2 shows that *H. pylori* seropositivity was significantly associated with abdominal pain (p=0.001, 95% CI=1.42,4.59), *fetor oris* (p=0.001, 95% C=2.08,9.74), and diarrhoea (P=0.041, 95% CI=0.14,1.06) but there was no association with irritability, heart burns, blood in stool and frequent vomiting.

Table 3 shows that *H. pylori* seropositivity was associated with a positive family history of dyspepsia (p=0.002 95% CI=1.46,5.83).

Table 2: Relationship between clinical history, symptoms and *H. pylori* seropositivity

Symptom	All subjects	H.pylori IgG Reaction		p	RR	95% CI
		Positive	Negative			
	n (%)	n (%)	n (%)			
Irritability						
Yes	34	12 (35.3)	22(64.7)	0.545	1.26	0.59,2.73
No	196	59 (30.1)	137 (69.9)			
Frequent vomiting						
Yes	123	39 (31.7)	84 (68.3)	0.768	1.09	0.62,1.91
No	107	84(29.9.)	75 (70.1)			
Bad breath						
Yes	19	13 (68.4)	6 (31.6)	0.001	5.71	2.08,9.74
No	211	58 (27.5)	153 (72.5)			
Blood in stool						
Yes	19	12 (35.3)	22 (64.7)	0.545	1.26	0.59,2.73
No	196	59 (30.1)	137(69.9)			
Diarrhoea						
Yes	31	5 (16.1)	26 (83.9)	0.041	0.39	0.14,1.06
No	199	66 (33.2)	133 (66.8)			
Family history of dyspepsia						
Yes	41	21 (51.2)	20(48.8)	0.002	2.92	1.46,5.83
No	189	50 (26.5)	139 (73.5)			

Table 3: Relationship between some symptoms and *H. pylori* seropositivity according to age group of subjects

Symptom	yes		No		NK		p	95% CI
	AA+	AA-	AA+	AA-	AA+	AA-		
Abdominal pain							0.001	1.42.4.59
≤5years	0	0	0	1	39	98		
6-10 years	17	18	5	14	2	8		
11-15years	2	9	4	5	1	7		
Heart burns							0.24	1.079,1.691
≤5 years	0	0	0	0	40	98		
6-10years	10	21	9	7	5	12		
11-15years	2	8	1	5	1	15		
Infantile colic							0.058	1.432,1.657
<1 years	8	20	2	5	4	15		
1-5years	7	20	8	39	11	23		
6-10years	5	7	7	13	22	20		
11-15years	1	4	1	5	8	9		

AA+ = Antibody activity positive
AA- = Antibody activity negative
NK = Not known

Discussion

The seroprevalence rate of 30.9% obtained in this study is high and suggests that *H. pylori* infection is significant in the paediatric age group of the study locality. This is consistent with high prevalence rates reported among children in other developing countries.[5-9, 15, 17] Symptoms which were associated with *H. pylori* seropositivity included abdominal pains, *fetor oris* and diarrhoea.

The association of abdominal pains with *H. pylori* seropositivity has also been reported by other authors.[19,20] This could be as a result of gastritis which has been reported to develop rapidly after acquisition of the infection and remains with the persistence of the infection.[10] Malaty*et al* [19] reported that the younger children who had recurrent abdominal pains were more likely than older children, to be infected with *H. pylori*. Also, in a forty year review article by Bittencourt*et al*,[20] it was stated that in the under-seven years old school children, abdominal pain was described in virtually all cases of *H. pylori* infection. These reports are comparable with our findings of higher occurrence of abdominal pain in the five -10 year olds.

Data from this study showed a significant association between diarrhoea and *H. pylori* seropositivity. Some other studies had also suggested that infection with *H. pylori* may predispose patients to other gastrointestinal infections. Passaro*et al* [21] reported that newly acquired *H. pylori* infection was followed with increased occurrence of diarrhoea. In contrast, the study by Rothenbacher*et al* [22] reported a significantly less occurrence of acute diarrhoeal illness in *H. pylori* infected children and adults, compared to uninfected subjects. It is difficult to exclude other confounding factors which may explain the conflicting reports of these observational studies.

The significance of *fetor oris* as seen in this study was also reported in the voluntary experimental ingestion of a pure culture of *H. pylori* by Marshall.[23] This symptom among others, was noted to have resolved completely within twenty four hours of the start of therapy with Tinidazole (500mg twice a day), for eradication of *H. pylori*.[20]

The production of ammonia from urea by *H. pylori* which is a urease splitting organism has been documented to be the likely physiological basis of fetor oris in *H. pylori* infection.[24]

There was no association between *H. pylori seropositivity* and the weight, height and body mass index of these subjects. The relationship of growth parameters and *H. pylori* infection in children as reported in previous studies has not showed a consistent pattern. The lack of association as seen in this study was also reported by Oderda*et al.*[25] Their study did not show any risk for short stature in *H. pylori* infected children after controlling for the socioeconomic status of their families. In contrast, Chloe *et al.*[26] reported a significantly lower mean height in *H. pylori* infected school children in comparison to their uninfected counterparts.

Conclusion

The IgG seropositvity rate in our study population is high and shows positive association with clinical features such as *fetor oris*, abdominal pain and diarrhoea, as well as with a positive family history of dyspepsia. We recommend that children presenting with any combination of these features should be screened for *H. pylori* infection as early confirmation of infection in childhood with appropriate eradication therapy will impact positively on the reduction or prevention of long term sequelae of this treatable bacterial infection.

Conflict of interest: None
Funding: None

Acknowledgement

Our appreciation is expressed to the parents of the children that participated in this study for giving us the consent to carry out the study, the statistician, Dr B. E. Orimadegun, the laboratory scientists, Dr Item Ekaidem, Anthony Usoro, Vincent Udoh, also, Edu Isaac and Dr Obasi Okorie for assistance with computer techniques.

References

1. Mégraud F, Brassens-Rabbe MP, Denis F. Seroepidemiology of *Campylobacter pylori* infection in various populations. *J Clin Microbiol 1989; 27:1870-1873.*
2. Warren JR. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet 1983; 1:1273.*
3. Marshall BJ. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet 1983; 1:1273-1275.*
4. Blanchard SS, Czinn SJ. Peptic ulcer Disease in children. Nelson Textbook of Pediatrics, 18th ed 2008 Elsevier Inc. www.mdconsult.com
5. Holcombe C, Omotara BA, Eldridge J, Jones DM. *Helicobacter pylori* the most common bacterial infection in Africa: a random serological study. *Am J Gastroenterol 1992; 87:28-30.*
6. Holcombe C,Tsimiri S, Eldridge J, Jones DM. Prevalence of antibody to *Helicobacter pylori in* children in Northern Nigeria Trans R Soc *Trop Med Hyg 1993; 87:19-21.*
7. Naficy AB, Frenck RW, Abu-Elyazeel R. Seroepidemiology of *Helicobacter pylori* infection in a population of Egyptian children. *Inter J Epid 2000; 29:928-932.*
8. Lindkvist P, EnquselassieF,Asrat D, Nilsson LM, Giesecke J.*Helicobacter pylori* infection in Ethiopian Children: a cohort study. *Scand J Infect Dis 1999; 31:475-480.*

9. Bassily S, Frenck RW, Mohareb EW. Seroprevalence of *Helicobacter pylori* among Egyptian newborns and their mothers: A preliminary report. *Am J Trop Med Hyg 1999; 61:37-40.*
10. Imrie C, Rowland M, Bourke B, Drumm B. Is *Helicobacter pylori* Infection a Risk Factor for Gastric Cancer? *Pediatrics2000; 106:373-380*
11. Forman D, Sitas F, Newell DG. Geographic association of *Helicobacter pylori* antibody prevalence and gastric mortality in rural China. *Int J Cancer 1990; 46:608-611.*
12. Graham DY, Opekun AR, Osata MS. Challenge model for *Helicobacter pylori* infection in human volunteers. *Gut 2004; 53:1235-1243.*
13. Mitchell JD, Mitchell HM, Tobias V. Acute Helicobacter pylori infection in an infant, associated with gastric ulceration and serological evidence of intra-familial transmission. *Am J Gastroenterol. 1992b; 87:382-386.*
14. Ukpong EA. Akwa Ibom State socio-economic study report. Ministry of Economic Development. Uyo, Akwa Ibom State, Nigeria. 2005. pp 257-78, 294-9.
15. Oyedeji GA. Socio-economic and cultural background of hospitalised children in Ilesha . *Niger J Paed 1985; 12:111-117.*
16. Enzyme Linked Immunosorbent Assay for the cut-off determination of IgA, IgG, or IgM antibodies to *Helicobacter pylori* in human serum or plasma. Vic Torch(Product Insert). JAJ International 1997.
17. Langat A, Ogutu E, Kamenwa R, Simiyu DE. Prevalence of *Helicobacter pylori* in children less than 3 years of age in health facilities in Nairobi Province. *E Afr Med J 2006; 9:471-477.*
18. Xu CD, Chen SN, Jiang SH, Xu JY. Seroepidemiology of *Helicobacter pylori* infection among asymptomatic Chinese children. *World J Gastroenterol 2000; 6:759-761.*
19. Malaty HM, Abudayyeh S, Graham DY, Gilger MA, Rubeneck L, O'Malley K. A prospective study for the association of *Helicobacter pylori* infection to a Multidimensional Measure for Recurrent Abdominal Pain in Children. *Helicobacter 2006; 11:250-257.*
20. Bittencourt PFS, Rocha GA, Penna FJ, Queiroz DMM. Gastroduodenal peptic ulcer and *Helicobacter pylori* infection in children and adolescents. *Jornal de Pediatria 2006; 82:325-334.*
21. Passero DJ, Taylor DN, Meza R, Cabrera L, Gilman RH, Parsonnet J. Acute *Helicobacter pylori* infection is follwed by an increase in diarrhoeal disease among Peruvian children. *Pediatrics 2001; 108:E87.*
22. Rothenbacher D, Blaser MJ, Bode G, Brenner H. Inverse relationship between gastric colonization of Helicobacter pylori and diarrhoel illnesses in children: results of a population-based cross-sectional study. *J Infect Dis 2000b; 182:1446-1449.*
23. Marshall B, Armstrong J, McGechie D, Glancy R. Attempt to fulfil Kock's postulates for *pylori campylobacter*. *Med J Aust 1985; 142:436-439.*
24. Marshall BJ, Langton SR. Urea hydrolysis in patients with Campylobacter pylori is infection. *Lancet 1986; 1:965-966.*
25. Oderda G, PalliD, Saieva C, Chiorboli E, Bona G. Short stature and *Helicobacter pylori* infection in Italian Children: prospective multicentre hospital based case-control study. The Italian Study Group on Short Stature and *Helicobacter pylori BMJ 1998; 317:514-515.*
26. Choe YH, Kim SK, Hong YC. *Helicobacter pylori* infection with iron deficiency anaemia and subnormal growth at puberty *Arch Dis Child 2000; 82:136-40.*