Original Article

Helicobacter pylori Infection in Malnourished Children in Lagos

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Abstract

Background/Aim: *Helicobacter pylori* infection is acquired in childhood, but there are conflicting reports on malnutrition and the infection. This study aimed to determine the prevalence of *H. pylori* infection among malnourished children and highlight the socioeconomic (SE) and clinical factors associated with the infection. **Methodology:** This was a descriptive cross-sectional study of 122 malnourished children and 120 healthy controls. Anthropometry was done for all the study participants, and the *H. pylori* status was determined with the use of monoclonal stool antigen test in all the participants. Logistic regression analysis was used to determine the factors that could predict the occurrence of the infection in the children. **Results:** Seventy percent (70.8%) of the malnourished children had moderate malnutrition, whereas 29.2% were severely malnourished. The prevalence of *H. pylori* in the malnourished children was 22.8% compared to 32.5% in the controls ($P = 0.09$). The infection was most prevalent in toddlers (60.7%). The SE class was significantly related to the infection ($P = 0.01$) and about a fifth (21.3%) of the malnourished children who belonged to the low SE class were *H. pylori* positive compared to 9.2% of the controls. About 64.3% of the malnourished children with *H. pylori* infection had fever and 25.8% had diarrhea. Multivariate analysis showed that stunting was significantly related to the infection ($P = 0.02$). **Conclusion:** *H. pylori* infection was prevalent among the toddlers and was significantly associated with stunting in this cohort of malnourished children. Screening of children for the infection is still advocated, and infected children should be referred for appropriate treatment and follow-up. The relationship between SE class and the infection still requires further research.

Keywords: Children, *Helicobacter pylori,* Lagos, malnourished, prevalence

Introduction

Helicobacter pylori infection is believed to be acquired in childhood and results in chronic gastric inflammation and gastric atrophy with resultant reduction in gastric acid secretion.[1-3] This hypochlorhydria produces impairment in the gastric barrier which predisposes the infected children to the acquisition of other enteropathogenic bacteria with resultant diarrheal illness and iron deficiency anemia.[4,5] These latter factors have been linked to malnutrition in children in the developing world.[6-10]

Malnutrition, on the other hand, is characterized by some immunosuppression, thus such malnourished children are susceptible to infections generally and possibly to *H. pylori* infection too.[11,12] In Bangladesh and Iran, a higher prevalence of *H. pylori* infection has been observed in the malnourished children compared to the controls.[10,13] However, other reports have found a lower prevalence in malnourished children.[14-16] Thus, there are conflicting reports on the relationship between nutritional status and *H. pylori* infection.[6-8] In Nigeria, in a cohort of apparently well children, Senbanjo *et al*.,[9] in 2014, documented a prevalence of 63.6% with the use of the ELISA technique and observed that there was no relationship between *H. pylori* infection and stunting or thinness. Many of the studies on *H. pylori* in children have focused on apparently healthy children, and in sub-Saharan Africa, there is a dearth of literature on the prevalence of *H. pylori* in malnourished children.

The aim of this study was to determine the prevalence of *H. pylori* infection in malnourished children and to document the socioeconomic (SE) and clinical factors associated with the infection.

Methodology

Setting

The study was a cross-sectional observational study conducted in the Paediatric Department of Lagos University Teaching

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Hospital (LUTH) and Massey Street Children's Hospital over a 6-month period (October 2016–March 2017). LUTH is a fee-paying, public-funded tertiary health facility which has a 760-bed capacity. It is located in the Mushin local government area and serves as a referral center for different parts of the country. Massey Street Children Hospital, on the other hand, is a secondary health facility which is owned by the Lagos State Government and provides care at no cost to the family. It is located on the Lagos Island area and is a very busy health facility which also receives referrals from different parts of the state and the neighboring states too.

Selection of subjects

All children aged 6 months–12 years diagnosed with malnutrition were consecutively recruited from the outpatient clinics and pediatric wards of these health facilities during the study.

The diagnosis of the malnutrition was made with the use of the WHO charts. The controls who were age, sex, and SE matched with the participants were recruited from the outpatient and immunization clinics. These were apparently healthy children who were on follow-up visits in the general outpatient clinic and children who presented at the routine immunization clinics.

The details of the study and its relevance were explained to the parents and caregivers of the malnourished children, and the study participants were then recruited after informed consent was obtained from the parents or caregivers. Assent was also obtained from children 7 years of age and above. The information obtained from the study participants included demographics, SE status, presenting symptoms, and ongoing treatment. Each family was categorized into a SE class using the Ogunlesi *et al*. classification.[11] Clinical symptoms which included gastrointestinal symptoms, fever, cough, or any other relevant clinical feature were also documented in a standardized pro forma.

Children who had been on proton-pump inhibitors, H2-receptor antagonists, or antibiotics within 2 weeks before the study were excluded from the study. Furthermore, children with HIV infection or other chronic illnesses such as structural heart disease, chronic kidney disease, or chronic liver disease were excluded from the study. All the study participants were clinically examined and their anthropometric parameters, namely weight, length (for <2 years or older that were unable to stand) or height (for those older than 2 years) were documented. The infants were weighed on the infant weighing scale while children >1 year were weighed on a regularly calibrated scale in light clothing. Weight was measured to the nearest kilogram. The length of the infants was determined with an infantometer, whereas the height of the older participants was determined to the nearest cm with the stadiometer. These anthropometric measurements were then plotted on the WHO charts to determine the weight for age, weight-for-height, and height-for-age (Z score) for the study participants. The nutritional status was classified using the following Z scores: >−1 standard deviation (SD) as normal, −2 SD–−3SD as moderate malnutrition, and <−3 SD as severe malnutrition, respectively.[12]

The temperatures of each of the study participant were recorded and fever if the present was noted. Their hydration status was also noted, especially when they had diarrhea.

The stool samples from the participants and controls were tested for *H. pylori* stool antigen, and the results for the malnourished children were compared with those of the control group.

Stool collection and the *Helicobacter pylori* stool antigen test

The stool samples were collected into plain universal bottles and stored in a temperature of 2°C–8°C in at the AIDS Prevention Initiative in Nigeria laboratory in LUTH and the samples were analyzed on the day of collection or the next day. *H. pylori* was detected with the use of the rapid strip *H. pylori* stool antigen kit (HpSA kit). This is a 5 min immunoassay test based on a monoclonal antibody for the qualitative detection of *H. pylori* antigens in human stool. The rapid strip HpSA is based on a lateral flow chromatography technique. This method identifies the *H. pylori* antigens present in the stool by utilizing a monoclonal anti-*H. pylori* antibody. This test has been found to have a sensitivity of 98%, specificity of 99%, and positive and negative predictive values of 98% and 99%, respectively.[13] To detect the antigen a strip is introduced into the tube-containing diluted stool samples of each participant. The appearance of a pink-red line in the reading area indicates a positive result after 5 min of incubation at room temperature. All the stool specimens were tested by a medical microbiology laboratory scientist.

Ethical considerations

Ethical approval was obtained for the study from the Health Research and Ethics committee of the study centers. Participants' privacy and confidentiality of data management were ensured during and after the study. The *H. pylori*-infected participants were referred to the gastrointestinal clinic for treatment and follow-up.

Data analysis and presentation

The data were analyzed using the SPSS version 21, SPSS Statistics for Windows, version 21.0, (IBM Corp., USA). The means and SDs were determined for the continuous variables, whereas proportions were calculated for categorical variables. The means of the continuous variables were compared with the Student's *t*-test, whereas the categorical variables were compared using the Pearson Chi-squared test. Logistic regression analysis was used to evaluate the relationship between the sociodemographic factors and the *H. pylori* infection.

A value of $P < 0.05$ was accepted as statistically significant.

Results

General characteristics

Two hundred and forty-two participants were recruited comprising 122 malnourished children and 120 controls.

Table 1 shows the general characteristics of the study participants. The median age was comparable in the participants and controls (P = 0.73); however, the median weight (P = 0.00) and length (P = 0.00) were significantly lower in the participants compared to the controls. Over half (54.1%) of the study participants belonged to the middle SE class and majority were toddlers.

According to the WHO classification, 70.8% of the malnourished children had moderate malnutrition and about a third (29.2%) were severely malnourished; 61 (50%) of the malnourished children were stunted, while a third (32.1%) were wasted [Table 2].

Helicobacter pylori status

Sixty-seven of the study participants were *H. pylori* positive giving an overall prevalence of 27.7%. Table 3 highlights the *H. pylori* status in the study participants and its relationship to the age, gender, and SE status. The prevalence of the infection was lower (22.9%) in the malnourished children compared to the controls (32.5%), but this was not statistically significant (P = 0.09).

Table 1: Clinical characteristics of the study participants

Parameter	Malnourished	Controls	*P*
Age (months), median (IQR)	12.0 (9-24)	12.0 (9-15)	0.734
Age categories (years)			
0-<1	29 (23.8)	29 (24.2)	
1-3	81 (66.4)	79 (65.8)	0.99
>3	12 (9.8)	12 (10.0)	
Gender, *n* (%)			
Male	62 (50.8)	77 (64.1)	0.04
Female	60 (49.2)	43 (35.8)	
Weight, median (IQR)	7.2 (6.1-8.0)	10.0 ()	0.00
Length	69.0 (64.5-77.0)	73.0 (68.4-80.3)	0.00
WHZ, median (IQR)	−2.0 (−3.4-−2.8)	1.3 (0.3-2.32)	0.00
LFA/HFA (Z), median (IQR)	−3.0 (−3.82-−2.12)	0.4 (−1.6-0.70)	0.00
Mother's Age, median (IQR)	30.0 (25.0-33.0)	30.0 (27.0-33.0)	0.29
Religion, *n* (%)			
Christianity	55 (43.1)	55 (45.8)	0.661
Islam	67 (56.9)	63 (52.5)	
Others	0 (0)	2 (1.7)	
Tribe/ethnicity, *n* (%)			
Yoruba	93 (76.2)	85 (70.8)	0.327
Igbo	15 (12.3)	19 (15.8)	
Hausa	5 (4.1)	2 (1.7)	
Others	9 (7.4)	14 (11.7)	
Socioeconomic status, *n* (%)			
High	30 (24.6)	44 (36.6)	0.01
Middle	66 (54.1)	65 (54.2)	
Low	26 (21.3)	11 (9.2)	

IQR – Interquartile range; WHZ – Weight for height *Z* score; LFA/HFA (Z) – Length for age/height for age *Z* score

The *H. pylori* status was not significantly related to the age and sex of the participants. The infection was more prevalent in males and in the 1–3 years age group and least prevalent in the children >3 years. However, the SE class of the children was significantly associated with the infection (P = 0.01) and 28.6% of the malnourished children who belonged to the low SE class were *H. pylori* positive compared to 7.7% of the controls in the same SE class.

Table 4 illustrates the severity of malnutrition, clinical symptoms, and *H. pylori* status in the malnourished participants. A greater percentage (82.1%) of the moderately malnourished than the severely malnourished children (17.9%) had *H. pylori* detected in their stools. Majority of the participants who were stunted were also *H. pylori* positive (P = 0.00).

Clinical features

The most common presenting symptoms among this cohort of malnourished children were fever, cough, and diarrhea. Fever was seen in 64.5% of the children with *H. pylori* infection, whereas 25.0% of them had diarrhea. None of the clinical features were significantly related to the infection [Table 4].

Multivariate analysis with the binary logistic regression revealed that stunting was the only significant predictor of the infection in the malnourished children (P = 0.026) [Table 5].

Discussion

This study determined the prevalence of *H. pylori* infection among malnourished children and it was observed that the majority of the participants with malnutrition were moderately malnourished.

This agrees with some reports in southwestern Nigeria where moderate forms of malnutrition were seen more commonly compared to severe forms of the disease.[17,18] Stunting remains a prevalent problem[4,10,14,17] and in this study half of the study participants were malnourished.

Almost a third of the study population had *H. pylori* antigen detected in their stools, but a higher prevalence of the infection was observed in the controls compared with the malnourished children. The reason for this is not quite clear, but a similar observation has been reported in previous studies.[13-15]

This finding, however, raises the possibility of unidentified inhibitory factors which may hinder the proliferation of

Table 2: Nutritional status of the malnourished children (*n*=122)

Parameter	Frequency (100%)
Nutritional status (*Z* score)	
Moderate (−2-−3SD)	84 (70.8)
Severe (<−3SD)	38 (29.2)
Categories of malnutrition	
Underweight	29 (23.8)
Stunted	61 (50.0)
Wasted	32 (26.2)

SD – Standard deviation

Table 3: *Helicobacter pylori* prevalence and distribution of *Helicobacter pylori* stool antigen according to age, sex and socioeconomic status in the study participants

Parameters	Cases (*n*=122), *n* (%)	Controls (*n*=120), *n* (%)	*P*
H. pylori status			
Positive	28 (22.9)	39 (32.5)	0.09
Negative	94 (77.1)	81 (67.5)	
Gender			
Male	15 (53.5)	23 (58.9)	0.65
Female	13 (46.5)	16 (41.0)	
Age categories (year)			
<1	5 (17.8)	6 (15.4)	0.79
1-<3	17 (60.7)	25 (64.1)	
3-<5	3 (10.7)	6 (15.4)	
≥5	3 (10.7)	2 (5.1)	
Socioeconomic class			
High	5 (17.8)	16 (41.0)	0.03
Middle	15 (53.6)	20 (51.3)	
Low	8 (28.6)	3 (7.7)	

n – Number of children; *H. pylori – Helicobacter pylori*

Table 4: Severity of malnutrition, clinical presentation, and *Helicobacter pylori* status in the malnourished children

Parameter	*H. pylori* positive, *n* (%), 28 (100)	*H. pylori* negative, *n* (%); 94 (100)	*P*
Nutritional status (*Z* score)			
Moderate (−2-−3SD)	23 (82.1)	61 (64.9)	0.08
Severe (<−3SD)	5 (17.9)	33 (35.1)	
Categories of malnutrition			
Underweight	2 (7.1)	27 (28.7)	0.00
Wasted	2 (7.1)	30 (32.0)	
Stunted	24 (85.7)	37 (39.3)	
Clinical features seen in the malnourished children			
Fever			
Yes	18 (64.3)	56 (59.6)	0.65
No	10 (35.7)	38 (40.4)	
Diarrrhea			
Yes	7 (25.0)	28 (29.8)	0.62
No	21 (75.0)	66 (70.2)	
Cough			
Yes	16 (57.1)	40 (42.6)	0.17
No	12 (42.9)	54 (57.4)	
Poor growth			
Yes	5 (17.8)	32 (34.0)	0.10
No	23 (82.2)	62 (66.0)	
Dermatoses/skin rash			
Yes	1 (3.2)	9 (9.6)	0.31
No	27 (96.8)	85 (90.4)	
Hepatomegaly			
Yes	1 (3.2)	8 (8.5)	0.41
No	27 (96.8)	83 (91.5)	

H. pylori – Helicobacter pylori

the organism in malnourished children. Nevertheless, these previous workers concluded that there was no significant association between malnutrition and *H. pylori* infection.[13-15]

In contrast to the lower prevalence of the infection seen in the malnourished children in the present study, workers from Iran[10] who used a similar method of diagnosis (monoclonal stool antigen) as in the current study documented a higher prevalence (35%) in malnourished children compared to the controls (10%). This latter finding was attributed to the immune suppression, which accompanies malnutrition.[19] Thus, these children are predisposed to infections generally and *H. pylori* infection may not be an exception. Similar observations have also been documented by other workers from South Western Nigeria[18] and Iran.[10]

In the current study, up to half of the malnourished children were stunted, and stunting was significantly related to the *H. pylori* infection in this cohort. This finding is consistent with previously documented reports who have found an association between stunting and the infection.[10,15,20] Growth impairment and malnutrition in *H. pylori* infection have been attributed to hypochlorhydria which occurs with the infection.[4,5,21] This transient loss of the gastric acid barrier predisposes to other enteric infections, diarrheal disease, and iron deficiency anemia which may ultimately affect the growth of children.[4,5,21-24] The cause and effect may, however, be difficult to determine as malnutrition may predispose to *H. pylori* infection due to reduced immunity and *H. pylori* infection may also predispose individuals to malnutrition. On the other hand, other workers have not observed any association between stunting and the *H. pylori*.[9]

The effect of age on *H. pylori* infection appears to have been well studied in apparently well children in Nigeria.[2,25,26] In Northern Nigeria, an increasing prevalence with increasing age was observed by Holcombe *et al*.[26] and age-specific prevalence rates of 50%, 82%, and 92% were documented in children <5 years, 5–10 years, and 11–19 years, respectively. In this present study, majority of the *H. pylori* positive participants were in the age group of 1–3 years. This may be related to the fact that children who belong to this age bracket are vulnerable to infections due to loss of the maternal acquired immunity, the children are more adventurous, and thus, the risk of ingestion of contaminated food and water is high which may predispose them to acquisition of the *H. pylori* organism and other enteropathogenic organisms and subsequent diarrheal illness.[4] There is the possibility that *H. pylori* infection acquired by malnourished children during this time may become persistent throughout childhood and thereafter if left untreated.[13,14] Najim and Habeeb,[10] however, observed that the infection was more prevalent in the infants and this finding was explained by the absence of breastfeeding in the cohort studied; however, the relationship with breastfeeding and the infection was not explored in the current study.

The mode of acquisition of the *H. pylori* infection has been well studied and known risk factors include ingestion of contaminated food and water, poor hygienic practices,

Table 5: Predictors of the Risk of occurrence of *Helicobacter pylori* in the malnourished children: Logistic regression

Parameter	*B*	SE	Wald	Sig	Ex (*B*) (OR)	CI	
						Lower	Upper
Age	−0.088	0.106	0.684	0.408	0.916	0.744	1.128
Sex	−0.072	0.318	0.052	0.820	0.930	0.498	1.736
Socioeconomic status	−0.274	0.648	0.178	0.673	0.760	0.213	2.710
Stunting	1.501	0.673	4.969	0.026	4.485	0.199	16.779
Diarrhea	0.000	0.394	0.000	1.000	1.000	0.462	2.164
Fever	0.076	0.343	0.000	0.992`	0.997	0.515	1.927
Cough	−0.003	0.337	0.240	0.625	0.980	0.904	1.063
Dermatoses	0.388	1.142	0.115	0.734	1.474	0.157	13.180
Hepatomegaly	0.276	0.837	0.000	0.992	0.997	0.515	1.927

Sig – $P<0.05$ is significant. SE – Standard error; CI – Confidence interval; OR – Odds ratio

lack of breastfeeding, poor sanitary facilities among other factors.[1,3-14,26] All these factors have also been linked with the low SE status and it is believed that children who belong to low SE status are exposed to these risk factors which can predispose them to the acquisition of *H. pylori* infection and other enteropathogenic agents.[5,7,8]

In the present study, the mode of acquisition of the infection was not explored in view of the available robust evidence on the subject, but the relationship between the infection and the SE status was explored. Majority of the malnourished subjects and the healthy controls in this study belonged to the middle SE status (SES) class which may be a reflection of the study locations, i.e. in the urban setting. However, compared to the controls a significant proportion of the malnourished children in the lower SES were *H. pylori* positive. Nevertheless, in view of the fact that these numbers are small, the significance of the influence of low SES on the *H. pylori* status may be difficult to extrapolate. Previous workers, however, have reported that low SES may be linked to the occurrence of the *H. pylori* infection.[5,7,8]

The common presenting symptoms in this cohort of malnourished children were fever, diarrhea, and cough. The occurrence of diarrhea in malnourished and *H. pylori*-infected children has also been reported by other workers[10,27] who observed a higher prevalence of the infection in malnourished children with diarrhea. The occurrence of diarrheal illness has also been linked to the hypochlorhydria as outlined earlier. In this study, only about a quarter of the children with *H. pylori* infection had diarrhea. Nevertheless, it must be noted that it may be difficult to attribute the diarrheal illness in malnourished children to *H. pylori i*nfection alone as there is usually underlying villus atrophy and possibly other concurrent enteropathogenic organisms.[10,27]

Conclusion

H. pylori infection was prevalent among the toddlers and was significantly associated with stunting in this cohort of malnourished children. Screening of children for the infection is still advocated and infected children should be referred for appropriate follow-up and treatment. The relationship between SE class and the infection still requires further research.

Limitations

This was a hospital-based study examining the stools of malnourished children at a single point in time. A longitudinal study in the community would have been more desirable, but this was not possible due to logistic difficulties. Other causes of stunting and diarrheal illness seen in the study population were also not explored in the study.

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Conflicts of interest

There are no conflicts of interest.

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