Original article

Clinical Presentations of *Helicobacter Pylori (H. Pylori)* Infections among Children of Western Uttar Pradesh Population, India

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Abstract

Introduction: *H. pylori* is mostly acquired in the period of childhood.The prevalence of H. pylori is not homogenous worldwide; it varies depending on the patient's chronologic age, country of origin, ethnicity and socioeconomic background during childhood. This study aimed to determine the current prevalence and clinical outcomes of *H. pylori* infection in children.

Materials and methods: The study enrolled (200) cases divided into 2 groups; Patient (100 cases) and Control (100 cases) groups. The patient group was categorized in the basis of the presence of gastrointestinal symptoms for 3 months "Recurrent abdominal pain, chronic anorexia or recurrent vomiting ", in addition to the documentation of H. pylori infection using H. pylori stool antigen test, ELISA and lastly, the Urea Breath Test (UBT) in cooperative children.

Results: From the total 100 Patients infected with H. pylori , 68 (68%), 22 (22%) and 10 (10%) cases presented with recurrent abdominal pain, anorexia and recurrent vomiting respectively compared to 22 (22%), 6 (6%) and 2 (2%) in control group (not infected with H. pylori). Recurrent abdominal pain, anorexia and recurrent vomiting are more significantly increased in patients infected with H. pylori, compared to non-infected cases "P<0.05, <0.02and <0.05 respectively".

Conclusion: In children theInfection with H. pylori is the initiator of vicious cycle of events that result ultimately in malnutrition and growth impairment with micronutrient deficiency. further studies are needed to give more information about the clinical and therapeutic outcome of this apparent association in diverse pediatric populations with different *H. pylori*prevalences and risk factors.

Key words: Helicobacter pylori infections; ELISA , Urea breath test; H. pyloristool antigen test; anorexia, Recurrent abdomial pain.

Introduction

H. pylori infection is witnessed in nearly 50% of the world's population. *H. pylori* is mostly acquired in the period of childhood, and its prevalence is higher in children from the lower socioeconomicstrata.[1,2] Most children are colonized in early childhood, and in a substantial number of cases the infection will last many years unless the child is treated with appropriate antibiotics. [3]

Three different approaches elucidating the pathophysiology of such a negative effect have been suggested. First, malabsorption developing secondary to the suppression of gastric acid secretion leads to gastrointestinal infection and diarrhoea.[4] Second, a decreased appetite and malabsorption caused by *H.pylori* infection results in failure to thrive.[5,6] Finally, iron deficiency anemia due to *H. pylori* infection is also considered to impair growth.[7,8] Also, studies suggesting an association between *H. pylori*

infection and level of plasma ghrelin have recently been published.[9]

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.[10,11] 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.[12,13]

Viable Hpylon organisms have never been isolated from the environment, hence interpersonal transmission is most likely. H pylori seropositivity is more common in household contacts of infected children,[14]but the family contacts of infected adults do not show an increased risk of infection.[15]It is therefore uncertain whether the infection is mainly acquired from other family members. The prevalence of H. pylori is not homogenous worldwide; it varies depending on the patient's chronologic age, country of origin, ethnicity and socioeconomic background during childhood. There are vigorousinnate and adaptive immune responses to H. pylori infection .Nevertheless, unless specific eradication therapy is provided, thegastric infection persists for lifetime.

H. pylori produce suspected disease - indicating factors, including urease (base of urea breath test), vacuolatingcytotoxin, catalase and lipopolysacchoride (LPS). Urease is a potent antigen that induces increased IgG and IgA production.[16] Catalase helps H. pylori survival in the host by preventing the formation of reactive oxygen metabolites from H2O2. The LPS outer membrane of H. pylori enhances the ability of organism to colonize the stomach.[16] Serological detection of H. pylori IgG antibodies is valuable in the assessment of children presenting with recurrent abdominal pain and other gastrointestinal symptoms. Children present an ideal population for studying the interaction between H. pylori and gastric mucosa because pediatric age is free from common causes of secondary gastrointestinal diseases (drugs, tobacco and alcohol).[17]

H. pylori infection can cause a deficiency of vitamins (such as vitamin C, vitamin A, α-tocopherol, vitamin B12 and folic acid) and essential minerals. The relationship between obesity and *H. pylori* infection is controversial. This study aimed to determine the current prevalence and clinical outcomes of *H. pylori* infection among children in western Uttar Pradesh region.

Materials and methods

This study was conducted prospectively at the general outpatient clinic of the Department of Paediatrics, in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, UP, India. Approval of this study was received from the administration ofTMU Hospital, Moradabad. Daily written consent for laboratory test from each case was taken from the parents of children. The study enrolled (200) cases divided into 2 groups; Patient (100 cases) and Control (100 cases) groups. The patient group was categorized in the basis of the presence of gastrointestinal symptoms for 3 months "Recurrent abdominal pain, chronic anorexia or recurrent vomiting ", in addition to the documentation of H. pylori infection using H. pylori

stool antigen test, ELISA and lastly, the Urea Breath Test (UBT) in cooperative children. Cases of hematologic disorders "e.g. sickle cell anemia", collagen vascular diseases or children on antibiotics two weeks ago as well as patients with past or family history of psychic element were excluded from the research. Urea Breath Test was done for certain selected cases (i.e.) cases with recurrent abdominal pain more than one year with negative serology and practically if cooperating. The control cases were defined by the absence of IgG antibodies to H. pylori. Complete blood count and serum ferritin were investigated to document refractory iron deficiency anemia. All patients had been ranged from 5-12 years old and matched with control for age, sex and sociodemographic factors.

Individuals infected with H. pylori develop antibodies that correlate strongly with histologically confirmed H. pylori infection.[18] The one step H. pylori test device (Serum/Plasma) is simple test that utilizes combination of H. pylori antigen coated particles and anti-human IgG, qualitatively and selectively detect H. pylori antibodies in serum or plasma. It is rapid chromatographic immunoassay without cross reactivity indicating high degree of specificity.[19] Moreover, there was a rather good correlation between the enzyme-linked immunosorbent assay (ELISA) antibody test and the rapid urease test, which did not provide further information to the diagnosis of H. pylori.[20]

The one step H. pylori Antigen Test Device (Feces) is another a rapid chromatographic immunoassay (providing results in 10minutes) for the qualitative detection of H. pylori antigen in human feces specimens to aid in the diagnosis of H. pylori infections.[21]

Urea Breath Test (UBT)-The patient should be fasting for 4 hours prior to the test. The patient swallows capsule containing 14 C-Urea with 50 ml water. Peak time is typically 10-30 minutes. This test has been shown to be an extremely accurate method of detecting H. pylori infection because it has the advantage of evaluating the gastric mucosa as a whole. Multiple studies have shown that (UBT) has both high sensitivity and high specificity for diagnosing active H. pylori infection in children.[20] It is demonstrated that the noninvasive tests 13C-UBT and H. pylori stool antigen are highly concordant and specific for the diagnosis of H. pylori infection in children of all ages.[22] Breath Tek UBT for H. pylori has Excellent Sensitivity (95.5%) and Specificity (96.0%) for Confirming Eradication.[23]

Both tests were easy to perform and are readily available.

Data were analyzed with SPSS. T-test and Chi-square were used for data analysis. Odd ratios and confidence interval with 95% were calculated. *P* value less than 0.05 was considered statistically significant.

Result

Group	**Recurrent Abdominal Pain**	**Recurrent Vomiting**	**Anorexia**
-Patient (*H. pylori* +ve)	**68 (68%)**	**22 (22%)**	**10 (10%)**
-Control (*H. pylori* –ve)	**22 (22%)**	**6 (6%)**	**2 (%)**
P value	P value=<0.05	P value=<0.02	P value=<0.05

Table 1: Distribution of patients and control based on clinical presentation and Laboratory investigations

Group	Weight (kg)	Height (cm)	Sideropenic Anemia
Patient (no.=120) *H. pylori* +ve	19.4 ± 2	126.1 ± 1.6	**38 (38%)**
Control (no=100) *H. pylori* –ve)	**26.6 ± 2.4**	**138 ± 2.9**	**18 (18%)**
P value =<0.05	**P value =<0.02**	**P value =<0.01**	**P value =<0.05**

Table 2: Distribution of patient and control groups according to malnutrition.

From the total 100 Patients infected with H. pylori , 68 (68%), 22 (22%) and 10 (10%) cases presented with recurrent abdominal pain, anorexia and recurrent vomiting respectively compared to 22 (22%), 6 (6%) and 2 (2%) in control group (not infected with H. pylori). As shown in Table 1. H. pylori infections in children commonly present with various phenotypic clinical features that were chronic abdominal pain, vomiting and anorexia (i.e.) persisted three months or more. Recurrent abdominal pain, anorexia and recurrent vomiting are more significantly increased in patients infected with H. pylori, compared to non-infected cases "P<0.05, <0.02and <0.05 respectively". Regarding the complications related to H. pylori infection, patient group demonstrated significant reduction in weight (19.4 ± 2 kg) and height (126.1 ± 1.6 c m) compared to control weight (26.6 ± 2.4 kg) and height (138 ± 2 cm). In sideropenic (or refractory iron deficiency anemia) the number of anemic children was 38(38%) whereas, the number was 18(18%) in control group Table 3. Recurrent abdominal pain, anorexia and recurrent vomiting are more significantly increased in patients infected with H. pylori, compared to non-infected cases "P<0.05, <0.02and <0.05 respectively".

Discussion

Our study on the effect of H. pylori infection in early life has Show that the Differences between patients and controls are significant regarding weight, height and sideropenic anemia. During childhood, *H. pylori*

is associated with predominant antral gastritis, and duodenal ulcers.[24,25] Successful eradication of *H. pylori* markedly reduces the rate of recurrence of duodenal ulcers in affected children.[26,27] Gastric ulcers are much less common in children than they are in adults.[28]

Two years later, Dufour*et al*[29]reported a 7-yearold child who presented with *H. pylori*-associated chronic antral gastritis without evidence of hemorrhage or clinical symptoms other than sideropenic anemia, which was refractory to oral iron administration and subsided after *H. pylori* eradication. These case reports were followed by other studies that have identified an association between *H. pylori* infection and pediatric unexplained or refractory IDA, and have indicated improvement of iron stores and anemia after successful *H. pylori* eradication.[30-36] Yet, some pediatric studies have implicated *H. pylori* as a cause of IDA that is refractory to oral iron treatment.[30,31,36]

Many studies support the role of H. pylori in the development of refractory iron – deficiency (sideropenic) anemia. [37,38]Interestingly, sideropenic anemia is not associated with hematemesis or tarry stools, suggesting that long-standing H. pylori infection itself can cause anemia in the absence of active bleeding from the gastrointestinal tract .[39]

In the prospective, longitudinal study by Bravo et al,[1] lower-middle class children from Colombia, in general good health, aged 1-5 years, who tested negative by urea breath test at baseline, were monitored over the following 2.5 years for anthropometric measurements every 2 mo, and for *H. pylori* by urea breath test every 4 mo. The deceleration of growth velocity took place 1 to 2 mo after the onset of infection, and after adjusting for age the slower growth rate was a fairly constant 0.042 ± 0.014 cm/mo (P = 0.003) less than that of uninfected children. The effect of *H. pylori* infection on growth velocity (0.5 cm/year) led to an accumulated growth deficit, which was not compensated after the infection had been established for more than 6 mo. No interactions between growth velocity, *H. pylori* status and the time of exposure, or other socioeconomic variables were observed. As expected,[40] a limitation of this study was the high intrasubject variability of growth velocity.

In a cohort of urban Colombian preschool children, in good general health, with a median follow-up of about 500 d, Mera et al [41] prospectively investigated whether a newly acquired *H. pylori* infection had transient or permanent effects on growth. Breath tests and anthropometric measurements were performed every 2 to 4 mo. The authors observed that the impact of a new infection on growth velocity was more pronounced during the first 4 mo after infection.

Egorov et al[42] prospectively assessed the potential effects of new *H. pylori* infection (defined as positive fecal antigen test and negative serology) on linear and ponderal growth in low socioeconomic status young children living in poor suburbs of Quito, Ecuador. Normally nourished, mildly and substantially malnourished children (defined using weight-for-age z-scores at recruitment) formed one-third each of the study population. Six height and weight measurements were collected during one year. The main finding of this study was that new *H. pylori* infections were associated with reduced linear growth in young children. Several studies have shown negative associations of *H. pylori* with asthma, allergy, and atopic diseases,[43-51]additional studies are needed to examine the strength of the evidence linking disorders in children to *H. pylori*, and to

better understand mechanisms on how *H. pylori* affects them in childhood.

Conclusion:

Our study showing that gastric H. pylori infection, growth faltering and iron deficiency anemia are essentially interrelated pathogenic factors. Infection with H. pylori in children is the initiator of vicious cycle of events that result ultimately in malnutrition and growth impairment with micronutrient deficiency. Many more studies are needed to provide more information about the clinical and therapeutic outcome of this apparent association in diverse pediatric populations with different *H. pylori*prevalences and risk factors.

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