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Helicobacter pylori Infections in Children of a Rural Community

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Abstract

Objective: To recognize the various clinical presentations of *Helicobacter pylori (H. pylori)* infections among children of Gizan Community, Saudi Arabia.

Design: Case control study.

Setting: Local tertiary centre in Gizan District, Saudi Arabia.

Participants: In this case control study the number of patients (*H. pylori* positive) were 120 (52.5% Boys) and the control group patients (*H. pylori* negative) were 100 cases, aged 7-12 years old (mean 9.9 ± 3 years). The patient and control groups were matched for age, race and sex. All cases were clinically examined for weight, height, iron deficiency (sideropenic) anemia and gastrointestinal (GIT) symptoms.

Main Exposures: *H. pylori* infections were defined by positive *H. pylori* stool antigen test and Serum IgG or Urea Breath Tests.

Main Outcome Measures: All cases were assessed for weight, height, iron deficiency (sideropenic) anemia and GIT symptoms.

Results: Recurrent abdominal pain, anorexia and recurrent vomiting were 81(67.5%), 24 (20%) and 15(12.5) % respectively in *H. pylori* infected patients, compared to 28 (28%), 8 (8%) and 4 (4%) in control group. Weight and height were (20.4 ± 1 kg and 128.1 ± 1 cm) in patients compared to (25.6 ± 1.7 kg and 133.8 ± 2 cm) in control cases. Sideropenic anemia was 36.7 % in patients compared to 15% in control.

Conclusion: Our findings suggest that Pediatric *H. pylori* infection not only present with recurrent abdominal pain, anorexia and recurrent vomiting, but also negatively affects the growth of children in various modalities; in particular weight, height and the progressive incidence of iron deficiency anemia.

Keywords: *Helicobacter pylori* infections; Urea breath test; *H. pylori* stool antigen test; Recurrent abdomial pain; Sideropenic anemia

Background

Helicobacter pylori infection is common, even in pediatric patients [1]. The organism is the most prevalent gastric microbial pathogen. However, the major route of transmission remains poorly understood. It is currently estimated that about half of the world's human population is infected with *H. pylori.* However, 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 vigorous innate and adaptive immune responses to *H. pylori* infection. Nevertheless, unless specific eradication therapy is provided, the gastric infection persists for lifetime. *H. pylori* organisms are spiral-shaped gram negative bacteria that are highly motile inhabiting the mucus adjacent to the gastric mucosa to induce inflammatory cytokines. The production of the cytokine interleukin lB has been linked to an increased risk of hypochlorhydria and gastric cancer in infected subjects. Numerous studies confirmed the crucial role of H pylori in the pathogenesis of gastritis and peptic ulcers. Recent studies support the conclusion that the association of *H. pylori* with gastric cancer is causal. Moreover, extra gastric MALT lymphoma has been linked to *H. pylori* infection based on the observation that early eradication of this infection in low grade tumors leads to complete remission.

H. pylori produce suspected disease - indicating factors, including urease (base of urea breath test), vacuolating cytotoxin, catalase and lipopolysacchoride (LPS). Urease is a potent antigen that induces increased IgG and IgA production [2]. Catalase helps *H. pylori* survival in the host by preventing the formation of reactive oxygen metabolites from H_2O_2. The LPS outer membrane of *H. pylori* enhances the ability of organism to colonize the stomach [2]. Serological detection of *H. pylori* IgG antibodies is valuable in the assessment of children presenting with recurrent abdominal pain and other gastrointestinal symptoms [3].

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) [1]. Also the natural history of diseases related to *H. pylori* is conditioned by the early acquiring of the bacterium [4].

Methods

Approval of this study was received from the administration of Alemeis National Hospital, Saudi Arabia and the routine consent for laboratory test (according to hospital regulations) from each case. The study was conducted in Gizan District (Saudi Arabia) from August toDecember2007. The study enrolled (220) cases divided into 2 groups; Patient (120cases) 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 7-12 years old and matched with control for age, sex and sociodemographic factors.

One Step *H. pylori* Test Device

Individuals infected with *H. pylori* develop antibodies that correlate strongly with histologically confirmed *H. pylori* infection [5]. 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 [6].

Moreover, there was a rather good correlation between the ELISA antibody test and the rapid urease test, which did not provide further information to the diagnosis of *H. pylori* [7]. 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 [8].

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 [7]. 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 [9]. Breath Tek UBT for *H. pylori* has Excellent Sensitivity (95.5%) and Specificity (96.0%) for Confirming Eradication [10]. Table 1 shows the Tests between Sensitivity and specificity for *H. pylori* infection [11,12].

	Sensitivity	Specificity
UBT	95%	96%
STOOL(antigen test)	93%	93%
Serology (ELISA)†	N/A	N/A
Endoscopic biopsy (Routine histology)	93%	90%

Table 1: Sensitivity and Specificity of Tests for *H. pylori* Infection

*Data are weighted mean values. Compilation of data is not the result of a comparative study.

ELISA=enzyme-linked immunosorbent assay

Active and passive infection

N/A=non-applicable

The UBT and the *H. pylori* stool antigen test were highly sensitive and specific noninvasive tests for the diagnosis of *H. pylori* in Egyptian children [13]. Both tests were easy to perform and are readily available. The specificity of the UBT was slightly lower in the younger children but still provided important clinical information [13].

T-test and Chi-square were used for data analysis. Odd ratios and confidence interval with 95% were calculated. Data were analyzed with SPSS (SPSS Inc)

Results

Of the total 120 Patients infected with *H. pylori*, 81 (67.5%), 24 (20%) and 15 (12.5%) cases presented with recurrent abdominal pain, anorexia and recurrent vomiting respectively compared to 28 (28%), 8 (8%) and 4 (4%) in control group (not infected with *H. pylori*). As shown in Table 2 *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 .

Regarding the complications related to *H. pylori* infection, patient group demonstrated significant reduction in weight (20.4 ± 1 kg) and height (128.1 ± 1c m) compared to control weight (25.6 ± 1.7 kg) and height (133.8 ± 2 cm). In sideropenic (or refractory iron deficiency anemia) the number of anemic children was 44(36.7%) whereas, the number was 15(15%) in control group Table 3.

Group	Recurrent Abdominal Pain	Recurrent Vomiting	Anorexia
-Patient (*H. pylori* +ve)	81(67.5%)	24(20%)	15(12.5%)
-Control (*H. pylori* –ve)	28(28%) OR=5.3 P value=<0.01	8(8%) OR=2.7 P value=<0.05	4(4%) OR=3 P value=<0.03

Table 2: Distribution of patients and control based on clinical presentation and Laboratory investigations

Recurrent abdominal pain, anorexia and recurrent vomiting are more significantly increased in patients infected with H. pylori, compared to non-infected cases "P<0.01, <0.03and <0.05 respectively".

OR=Odds Ratio

Group	Weight (kg)	Height (cm)	Sideropenic Anemia
Patient (no.=120) *H. pylori* +ve	20.4 ± 1	128.1 ± 1	44 (36.7%)
Control (no=100) *H. pylori* –ve)	25.6 ± 1.7 P value =<0.05	133.8 ± 2 P value = <0.01	15(15%) OR = 2.9 P value = <0.03

Table 3: Distribution of patient and control groups according to malnutrition

Differences between patients and controls are significant regarding weight, height and sideropenic anemia.

Discussion

The World Health Organization has classified the *H. pylori* organism as a carcinogen for gastric cancer [14]. Hence early detection and accurate treatment are of great importance.

A positive correlation between *H. pylori* antibodies and food allergy presenting with gastrointestinal symptoms has been reported [16]. In our study there is significant positive correlation between *H. pylori* antibodies in one side and gastrointestinal symptoms (recurrent vomiting and chronic anorexia) on the other side. This is in accordance with Crabtree et al. [3] and Gunther et al. [7]. But an Indian study conducted by Patwari [16], reported that *H. pylori* infection does not seem to be commonly associated with recurrent abdominal pain. However the small sample size of that Indian study limits drawing any firm conclusions.

As shown in the results, *H. pylori* infection has an adverse effect on growth parameters (i.e.) weight and height. These findings were also explored in other studies carried out at different socio-demographic background such as; Takahashi, et al. [18] in Japan, Mahmoud et al. [17] in Egypt and Thomas, et al. [18] in Gambia, although the result of the last study of Gambia suggested that the effect on growth faltering was in early infancy and did not persist into later childhood. As expected, the cumulative impacts of *H. pylori* on growth and stomach could justify the increase development of sideropenic anemia in patient group.

Many studies support the role of *H. pylori* in the development of refractory iron – deficiency (sideropenic) anemia [19,20]. 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 [21].

In short, *H. pylori* infection may be associated with growth retardation in children, although there are some results both with and against this association [22]. A potential biologic possibility for this association could relate to the effect of *H. pylori* inflammation on the gastric derived hormones (e.g. leptin, ghrelin) involved in controlling appetite [23]. Moreover, *H. pylori* have been recently associated with iron deficiency anemia. The main two hypotheses that potentially explain this relation are [1] sequestration of iron due to natural *H. pylori* infection i.e altered iron bioavailability induced by the chronic infection and inflammatory cytokines of the *H. pylori* organism, and (II) decreased non-heme iron absorption caused by hypochlorhydria [2].

Conclusion

Our study demonstrates 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. This must stimulate the medical awareness of pediatricians about the seriousness of the problem in order to remind the potential prevalence of *H. pylori* infection in the event of assessment of chronic gastrointestinal complaints, refractory iron deficiency anemia or growth retardation.

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