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 abdominal 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 IB 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 H₂O₂. 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 to December 2007. The study enrolled (220) cases divided into 2 groups; Patient (120 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 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 10 minutes) 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 14C-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].

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 ± 1 cm) 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.

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

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

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
Moreover, H. pylori have been recently associated with anemia in the absence of active bleeding from the background such as; Takahashi, et al. [18] in Japan, Mahmoud et al. [19] 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 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].

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

| 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 | 133.8 ± 2   | 15(15%) P value =<0.05 OR = 2.9 P value = <0.01 |

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].

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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