Helicobacter pylori and hypergastrinemia in children with recurrent abdominal pain

Abstract  Recurrent abdominal pain (RAP) is a significant problem in the pediatric population, and there has been much recent interest in the role that Helicobacter pylori (Hp) might play in this disorder. In this case control study, the authors aimed to determine whether Hp is an agent responsible for RAP, and to assess fasting gastrin concentrations in children with and without RAP in the Hp-positive and -negative groups. The study was conducted in 42 patients with RAP and 50 healthy children attending routine day-case surgery as a control group, aged 3 to 15 years, over a 12-month period. Of the 42 children with RAP, 30 were seropositive (71.4%) for Hp IgG, and of 50 children in the control group, 32 were seropositive (64%) for Hp IgG ($P > 0.05$). We found that Hp infection was as high in healthy children as in children with RAP. The mean fasting gastrin levels in 62 Hp-seropositive children (60.4 ng/l) were not different from those in 30 Hp-seronegative children (57.3 ng/l) and those in 42 children with RAP (58.2 ng/l) were also not significantly different from those in 50 healthy children (62.9 ng/l). Thus, no association between childhood Hp infection, hypergastrinemia, and RAP was found in our Turkish population.

Key words  Helicobacter pylori · Gastritis · Recurrent abdominal pain · Gastrin · Children

Introduction

Recurrent abdominal pain (RAP) is one of the most common presentations to pediatric surgeons; yet, an organic etiology can be found in only 10% of cases [12]. The relationship between Helicobacter pylori (Hp) and primary gastritis in children was first reported by Drumm et al. [9] in 1987. Microbiologic, serologic, and epidemiologic studies suggest that Hp may have an important role in children with abdominal pain. Hp is found in the gastric mucosa of children with histologically proven gastritis or peptic ulcer disease [13]. Although prospective studies in children with RAP show that the finding of antral gastritis with Hp is more common than in asymptomatic children, the association between Hp and RAP is still controversial [9, 11, 14].

In adults, the association between Hp gastritis and hypergastrinemia has been well documented, but in children this association has yet to be established [16]. It has been reported that children with hypergastrinemia may present with nonspecific abdominal symptoms [2, 19]. The aims of this study were to determine whether Hp is an agent responsible for RAP in children, and to assess fasting gastrin concentrations in children with and without RAP in the Hp-positive and -negative groups.

Patients and methods

In this case control study, 42 children with RAP aged 3 to 15 years (mean 9.40 ± 3.20 years) were the case group, and 50 healthy children (mean age 9.65 ± 3.15 years) attending routine day-case surgery were also studied as a control group over a 12-month period. IgG antibodies to Hp were determined with an enzyme-linked immunosorbent assay (ELISA) of serum samples. A history of RAP was sought in all 42 children. RAP syndrome was defined as a minimum of three episodes of abdominal pain over a period of 3 months, with an intensity that affects the behavior of the child. This definition was similar to that used by Apley and Naish [3].

The initial evaluation included a thorough history and physical examination and routine blood examinations. In case of persistent symptoms, further laboratory tests, radiologic examinations, and sometimes endoscopy were undertaken to search for evidence of entities such as peptic disease, inflammatory bowel disease, and enzyme deficiencies. Patients who had these diseases were excluded from the study. Written informed consent was obtained from the children’s parents in all cases.
Blood samples (2 ml) from 92 symptomatic and asymptomatic patients were stored at −20°C; the ELISA IgG kits (Sentinel CH, Milano) were used according to the manufacturer's instructions. Cooled serum samples were tested at a dilution of 1/101. Each of the incubations was carried out at 37°C. Plates were read at 450 nm with a Ceres 900 microplate reader. By using the calibrator 2 (pediatric calibrator) included with the kit, the seropositivity for IgG was determined according to the cutoff value stated by the manufacturer. Samples were then analyzed for fasting plasma gastrin by a radioimmunoassay using commercially available kits (ICN, USA, no. 06B255017).

The χ² test was used to compare Hp infection in children with and without RAP and the control group, and a Mann-Whitney U test was used to compare fasting gastrin concentrations in four groups: Hp-seronegative children with RAP; Hp-seropositive children with RAP; and Hp-seropositive control children. Values were expressed as mean ± SD. A P value of less than 0.05 was considered significant.

### Results

Of the 92 children studied, 42 were patients with RAP and 50 were controls. Of the 42 children with RAP, 30 were seropositive and 12 were seronegative for Hp (71.4%). In the control group, 32 children were seropositive and 18 were seronegative for Hp (64%) (P > 0.05). The mean fasting plasma gastrin concentrations for the four groups studied are summarized in Table 1. The values in the 62 Hp-seropositive children (60.4 ± 25.9 ng/l) were not significantly different from those in the 30 Hp-seronegative children (57.3 ± 21.5 ng/l) and those in the 42 children with RAP (58.2 ± 24.5 ng/l) were also not significantly different from those in the 50 healthy children (62.9 ± 25.2 ng/l). The mean gastrin concentrations between children with RAP and the control group did not reach statistical significance in either the Hp-positive or -negative groups.

### Discussion

Recurrent abdominal pain is a frequent diagnostic problem in school children and adolescents [8, 13]. However, an organic cause for the symptoms is found in less than 10% of cases [3, 12, 23]. RAP has been related to the presence of Hp in both adults and children [14]; the possible role of Hp in children with RAP has been stressed by a number of authors [9, 11, 13]. Reported prevalence rates of Hp infection range from 0% to 81% in the literature. On the other hand, the relationship between Hp infection and gastrointestinal complaints is still controversial. There is only weak and inconsistent evidence of an association between Hp infection and classic RAP in children, and the prevalence of anti-Hp antibodies in children with RAP was similar to that in asymptomatic children [10, 15–17, 22].

An association between Hp gastritis and hypergastrinemia has not been clearly established in children. Recent work indicates that Hp infection might induce hypergastrinemia via selective gastrin-cell hyperplasia [16, 19, 21]. However, another study found that gastrin levels in infected children did not differ significantly from those in whom there was no evidence of Hp infection [18].

The combination of cultures and histologic examination of gastric biopsy specimens is considered the gold standard for the diagnosis of Hp; however, endoscopic examination of children presents some difficulties, and often must be performed during general anesthesia. IgG antibody determination is a useful and noninvasive screening method for detection of Hp infection in untreated individuals; therefore, we measured IgG antibodies for identification of the presence of Hp infection using ELISA, which is both sensitive (94%) and specific (87%) in children [4–7].

In this study, the Hp infection rate as determined by serology was not significantly different in children with and without RAP. These findings suggest that Hp does not play a causative role in RAP in our setting. However, Hp prevalence was found to be much higher compared to reports from more developed countries [16, 22]. A similarly high percentage of infection (78.8%) in RAP children was also noted in another study from Turkey [1]. Other investigators found a 79% prevalence in asymptomatic Turkish children [20]. This high rate of Hp infection in patients without a history of peptic ulcer disease as well as asymptomatic individuals apparently reflects Turkey’s socioeconomic situation and is typical of a developing country. In our study, no significant elevation of mean fasting gastrin levels was found in Hp-positive individuals as compared to Hp-negative ones, irrespective of the presence of RAP. These findings do not support the hypothesis that Hp infection induces gastrinemia. Furthermore, gastrointestinal symptoms do not appear to be mediated by hypergastrinemia in children with RAP.

In conclusion, there was no association between childhood Hp infection, hypergastrinemia, and RAP in this Turkish population. It is, however, an open question whether this conclusion can be generalized with regard to more developed countries.

### Table 1 Gastrin concentrations and Helicobacter pylori (Hp) status in children with and without recurrent abdominal pain (RAP)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age (n years)</th>
<th>Mean fasting gastrin (ng/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP(+) and Hp(+)</td>
<td>30 9.4</td>
<td>58.33 ± 24.69</td>
</tr>
<tr>
<td>RAP(+) and Hp(−)</td>
<td>12 9.0</td>
<td>58.00 ± 24.94</td>
</tr>
<tr>
<td>RAP(−) and Hp(+)</td>
<td>32 9.2</td>
<td>65.54 ± 26.51</td>
</tr>
<tr>
<td>RAP(−) and Hp(−)</td>
<td>18 9.5</td>
<td>56.60 ± 16.45</td>
</tr>
</tbody>
</table>

### References