

***Helicobacter pylori* Infection in Children with Recurrent Abdominal Pain**

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ABSTRACT

Recurrent abdominal pain (RAP) is a very common presenting complaint in pediatric population. There is still a debate regarding the role of Helicobacter pylori (H. pylori) infection as an etiology of RAP. Typically, the inflammatory process in the gastric mucosa of infected individuals is chronic gastritis. Serologic and histologic examination are widely used for the diagnosis. This study was aimed to determine the role of H. pylori infection in Indonesian children with RAP. The presence of serum IgG antibody to H. pylori and upper gastrointestinal endoscopy were performed on the 101 children with RAP. Mucosal biopsies were obtained for histologic analysis. The prevalence of H. pylori infection indicated by serology was 32.7% and by histology was 27.7%. Histologic evidence of gastritis was present in 94.1% children and 45% of them had chronic atrophic and active gastritis. Seventy percent children with H. pylori positive were found abnormal through endoscopy and all of the infected children were revealed abnormal through histological examination. Forty eight percent of seropositive children were found H. pylori positive and 80% of seronegative's children were found to be H. pylori negative through histologic examination. Conclusion: H. pylori infection can be a cause of RAP in children. Work up for H. pylori infection should be performed when symptoms are suggestive of organic disease. Larger prospective studies are needed to be performed for a longer time of period to clarify this issue.

Key words: *H. pylori infection, IgG antibody to H. pylori, Upper GI endoscopy, RAP, Recurrent abdominal pain.*

INTRODUCTION

H. pylori infection is contracted primarily during childhood and will present with peptic disease. Recurrent abdominal pain is one of a very common presenting complaint in pediatric population (10-15% of school age children). There is still debated regarding the role of *H. pylori* infection in etiology of RAP.

Few prospective studies on the association of RAP with *H. pylori* infection have been performed in children. The studies suggested that *H. pylori* gastritis is a possible cause of RAP.^{1,2} Other investigators found that *H. pylori* associated gastritis in the absence of ulcer is not a significant cause of RAP in children.³ Typically, the inflammatory process in the gastric mucosa of infected individuals is chronic gastritis.⁴

A number of non-invasive and invasive methods have

been used to diagnose *H. pylori* infection in children. Serologic and histologic examination is widely used for the diagnosis. The development of methods for the detection of antibodies against *H. pylori* has enabled clinicians to identify infected individuals. The detection of IgG antibody against *H. pylori* by ELISA has been widely adopted for routine use. The accepted gold standard method for the diagnosis of *H. pylori* infection is the demonstration of bacteria in gastric mucosal biopsies.^{5,6}

Because the knowledge of the incidence of *H. pylori* infection in Indonesian children suffering from RAP is not yet published, we investigated this phenomenon to determine the role of *H. pylori* infection in Indonesian children with RAP and the usefulness of serology and histologic test in screening *H. pylori* infection.

PATIENTS AND METHODS

During a 5 years period (1996-2000), a total of 101 RAP children were recruited in the study. These children were seen in The Pediatric Gastroenterology Out-patient Clinic at Dr. Cipto Mangunkusumo Hospital, Jakarta. In most cases, the pain was located in the epigastrium region. Recurrent abdominal pain was considered if the children have had at least three episodes of abdominal pain severe enough to interfere with normal activities during a 3 month period, as defined by Apley.⁷

We performed the presence of serum IgG antibody to *H. pylori* and upper gastrointestinal endoscopy on the 101 children. The serology test was investigated by an enzyme-linked immunoassay method (Biorad) and mucosal biopsies were obtained for histologic analysis. Biopsies were taken from the antrum and the first part of the duodenum. The specimens were stained by Hematoxylin-Eosin, Giemsa and Whartin starry staining when necessary. Gastritis was defined according to the histologic criteria with the Sydney classification.

RESULT

From 101 children who recruited in the study, 42 (41.6%) were boys and 59 (58.4%) were girls. The details of age and clinical manifestation are summarized in table 1 and 2.

Table 1. Age distribution

Age (years)	Number	%
5 - 10	81	80.2
11- 15	19	18.9
> 15	1	0.9
Total	101	100

Table 2. Clinical manifestation

Clinical manifestation	Number	%
Recurrent abdominal pain (RAP)	82	81.2
RAP with vomiting	16	15.9
RAP with hematemesis	3	2.9
Total	101	100

The prevalence of *H. pylori* infection which was indicated by serology was 32.7% and by histology was 27.7% (table 3).

Table 3. Prevalence of *H. pylori* infection

Method of detection	Number	%
Serology	33	32.7
Histology	28	27.7

Of the 101 children with RAP, 58.4% were determined to be abnormal through endoscopy examination (table 4). Histologic evidence of gastritis was present in 95 children (94.1%) and 45% (43/52) of them had chronic atrophic active gastritis (table 5). Peptic ulcer, nodularity, and metaplasia did not occur in these children.

Table 4. Endoscopic appearance in RAP children

Endoscopic appearance	Number	%
Normal	42	41.6
Red or inflamed mucosa (gastric/duodenum)	52	51.5
Erosion of the stomach mucosa	7	6.9
Ulcers	0	0
Nodular	0	0

Table 5. Histologic appearance in RAP children

Histologic appearance	Number	%
Normal	6	5.9
Chronic gastritis/duodenitis	52	51.5
Chronic atrophic active gastritis	43	42.6
Ulcers	0	0

Of the 28 children with *H. pylori* positive (histology), 75% were found abnormal through endoscopy (table 6). However, 100% were revealed abnormal through histological examination (table 7).

Table 7. Histologic appearance in RAP children with *H. pylori* positive

<i>H. pylori</i> (Histology)	Histologic appearance			Total
	Normal	Gastritis	Chronic atrophic active gastritis	
<i>H. pylori</i> (+)	(0)	7 (25%)	21 (75%)	28
<i>H. pylori</i> (-)	6 (8.2%)	45 (61.7%)	22 (30.1%)	73
Total	6(5.9%)	52 (51.5%)	43 (42.6%)	101

All children with an abnormal endoscopic had an abnormal histologic appearance too, and only 6 (14.3%) children who had a normal endoscopic also revealed a normal histologic appearance (table 8).

Table 8. Histological finding in RAP children related to the endoscopic appearance

Endoscopic appearance	Histologic findings		Total
	Normal	Abnormal	
Normal	6 (14.3%)	36 (85.7%)	42
Abnormal	0	59 (100%)	59
Total	6 (5.9%)	95 (94.1%)	101

Of the 33 seropositive's children, 48.5% were found *H. pylori* positive through histologic examination and 82.4% of the 68 seronegative's children were found to be *H. pylori* negative (tabel 9). The sensitivity and specificity of the serological test in this study was respectively 57% and 77%. The positive likelihood ratio (LR+) and negative likelihood ratio (LR-) was respectively 2.5 and 0.5. The preprobability and postprobability test was respectively 27.7% and 48%.

Tabel 9. *H. pylori* related to the serologic findings

Serology findings	<i>H. pylori</i> findings (histology)		Total
	<i>H. pylori</i> (+)	<i>H. pylori</i> (-)	
Seropositive	16 (48.5%)	17 (51.5%)	33
Seronegative	12 (17.6%)	56 (82.4%)	68
Total	28 (27.7%)	73 (72.3%)	101

DISCUSSION

The prevalence of *H. pylori* infection in many population and subgroups is currently well documented. The overall prevalence of *H. pylori* in children is 10% in developed countries and up to 80% in developing countries.⁸ In developing countries, *H. pylori* infects virtually the entire population. Lower socio-economic circumstances, living in overcrowded circumstances and sharing in a bed with a parent were described as a independent risk factors for *H. pylori* infection in children. The major model of transmission of *H. pylori* are still unknown, although oral-oral, gastro-oral, and fecal-oral routes have been proposed.⁶

Pediatric age group have no specific clinical picture of *H. pylori* infection. Recurrent abdominal pain is a significant problem in the pediatric population. There is still controversial conclusion about the relationship between *H. pylori* infection and the presence of RAP in children. Some epidemiologic studies have indicated that *H. pylori* infection was not the cause for the RAP in children. They did not find a significant greater seroprevalence of the anti *H. pylori* antibody in children with RAP than in control children. They suggest that the RAP found in children with *H. pylori* infection seem to be caused by secondary gastroduodenal pathology.⁹⁻¹¹ Other studies have suggested that *H. pylori* infection may be more common among children with RAP than in children without RAP. They found 15-25% children in the RAP and 5-10% in the non-RAP group were seropositive.¹²⁻¹⁴ In this study, the prevalence of *H. pylori* infection in RAP children which was indicated by serologic was 32.7%.

Endoscopy and histology are mandatory for adequate diagnosis. The endoscopy and biopsies were performed

in all children, since it is well established that a normal endoscopic appearance of the stomach and duodenum does not exclude *H. pylori* infection.¹⁵ In this study, abnormal histologic was found in 85% children with a normal endoscopic appearance (table 8) and normal endoscopic was also found in 25% children with *H. pylori* positive in their stomach (table 6).

Recent pediatric gastrointestinal literatures suggest that organic etiology may be more common than previously believed in RAP.¹⁶ In this study, abnormal histologic was found in 94.1% children with RAP (table 5). *H. pylori* associated gastritis to symptoms is controversial. Although several studies have attempted to demonstrate an association between *H. pylori*-gastritis, the relationships is unclear. The inflammatory process in the gastric mucosa of infected children causes chronic gastritis and associated with gastric or duodenal ulcer disease.

In this study, the prevalence of *H. pylori* infection in RAP children which was indicated by histologic was 28%, in comparison with 10-50% in previous study.^{3,15,17} In this study, histologic evidence of chronic gastritis was present in all of the infected children, and 75% of this children suffered from chronic atrophic active gastritis (table 7). These observation suggest that *H. pylori* infection is more frequently associated with chronic atrophic active gastritis. This result is a consistent finding in studies of children with *H. pylori* infection. *H. pylori* infection has been reported to cause both gastric and duodenal ulcer disease in children. In previous study, ulcer disease was present in 14-47% infected children.^{1,3,12,18} In contrast, this study did not find any ulcers in the stomach or duodenum of the infected children. This observation suggest that *H. pylori* infection may cause symptoms in the absence of peptic or duodenal ulcer disease.

From various reports, the macroscopics appearance of nodular gastritis is sometimes found in children infected with *H. pylori*. Nodularity of the antral mucosa was present in 10-12% RAP children, and 60-100% of this children were *H. pylori* positive.^{3,12} This observation indicates an association between *H. pylori* infection and the development of antral nodular gastritis in children. In contrast, this study did not find any nodularity in the stomach of the children. Recurrent abdominal pain with vomiting has been described as a common manifestation of *H. pylori* infection in children.^{3,12} In this study, I found 16% children had also complaint of vomiting. *H. pylori* are not created equal, because important virulence factors are not detectable in all strains. However,

the clinical relevance of the virulence factors is unclear.⁶

Because of no specific clinical picture of *H. pylori* infection in pediatric group, indicating that non-invasive test should be used to screen children with dyspeptic symptom. Some of the expert believed that a serological test was sufficient to detect *H. pylori* infection and could probably replace endoscopy as a primary diagnostic procedure in children,¹⁹ but other expert did not fully agree with that opinion. They believed that the serologic testing for IgG antibodies against *H. pylori* requires validation of the assay in children, since antibody levels differ in children and adults, probably because of the duration of infection and the differences in bacterial load.²⁰ The sensitivity and specificity of serology were respectively 80-90% and 60-80%.^{14,15} In contrast, the sensitivity and specificity of the serological test in this study was respectively 57% and 77%. This study showed that serology test was not good enough to detect *H. pylori* infection in children. This conclusion was supported by the result of the Likelihood ratio and the pre and post probability test.

CONCLUSION

H. pylori infection can be a cause of RAP in children. All infected children had an abnormal histologic. Work up for *H. pylori* infection should be performed when symptoms are suggestive of organic disease. The endoscopic examination cannot be replaced by serological test.

Larger prospective studies are needed to be performed for a longer time of period to clarify this issue. Due to specific problems in pediatric population, a consensus should be achieved on the management of *H. pylori* infection in children.

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