

# ***Helicobacter pylori* Infection in Children with Recurrent Abdominal Pain and Positive Biopsy Findings**

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## **ABSTRACT**

*Risk factors for Helicobacter pylori (H. pylori) infection include residence in a developing country, poor socio-economic status, overcrowding family, ethnic and genetic predisposition. The diagnosis and management H. pylori have not been satisfied yet; however, there is a problem of increasing H. pylori antibiotic resistance. We reported a case of 8 year-old girl who suffered from H. pylori infection. The diagnosis was made based on history, clinical findings, and laboratory work-up. Suspicion of H. pylori infection was started when she had recurrent abdominal pain. The result of serologic testing for H. pylori immunoglobulin G (IgG) was positive. Endoscopic biopsy revealed the presence of H. pylori. Patient received regimens for first line eradication of H. pylori, i.e. amoxicillin, clarithromycin and omeprazole for two weeks. Afterward, her condition improved markedly without any further complaint.*

**Keywords:** *Helicobacter pylori, children, recurrent abdominal pain*

## **ABSTRAK**

*Faktor risiko terjadinya infeksi Helicobacter pylori (H. pylori) meliputi tinggal di negara berkembang, kondisi sosial ekonomi yang rendah, jumlah anggota keluarga yang banyak, serta kecenderungan etnis dan genetik. Tatalaksana dan diagnosis H. pylori masih belum memadai karena adanya resistensi antibiotik pada pasien H. pylori.*

*Dilaporkan seorang anak perempuan usia 8 tahun 6 bulan yang terinfeksi kuman H. pylori. Diagnosis ditegakkan berdasarkan anamnesis, pemeriksaan fisik, dan hasil laboratorium. Pasien diduga terinfeksi H. pylori karena mengalami nyeri perut berulang. Dari hasil pemeriksaan laboratorium didapatkan serologi IgG H. pylori positif. Pada hasil endoskopi biopsi ditemukan adanya kuman H. pylori. Pasien mendapat terapi eradikasi lini pertama untuk infeksi H. pylori yaitu amoksisilin, klaritromisin dan omeprazol selama dua minggu. Setelah itu kondisi pasien membaik tanpa ada keluhan lebih lanjut.*

**Kata kunci:** *Helicobacter pylori, anak, nyeri perut berulang*

## **INTRODUCTION**

The diagnosis and treatment of upper gastroduodenal disease have changed dramatically. Peptic ulcer approaches is nowadays perceived as an infectious disease, which requires elimination of etiology.<sup>1,2</sup> There are also increasing interests in the pathogenesis of gastroduodenal disease. Greater availability of clinical specimen and isolation of *Helicobacter pylori* (*H. pylori*) via endoscopic biopsy has brought essential progress in current health care.<sup>1</sup>

*H. pylori* infection has spread all over the world and it is estimated that the infection has attacked half of the world's population.<sup>1,3-5</sup> *H. pylori* prevalence worldwide is about 20% in developed countries and it reaches 90% in developing countries.<sup>6,7</sup> In general, children younger than 10 years of age commonly suffered from *H. pylori* infection and the infection increases with age.<sup>8</sup> The virulence factors of *H. pylori* infection are person-to-person transmission, living in slums area, low socio-economic status or poor personal hygiene,

genetics and working area at the endoscopy unit.<sup>7,9</sup>

Many patients still assume the symptoms of dyspepsia as an ulcer and that diet, stress, and lifestyle may be important risk factors. However, it is now obvious that *H. pylori* eradication has played the central role to the management of the disease.<sup>3</sup> The diagnosis and management *H. pylori* have not been satisfying yet; thus there is a problem of increasing *H. pylori* antibiotic resistance.<sup>3,7</sup>

Endoscopy is the gold standard for detection of *H. pylori* infection that offers a lot of advantages. It may detect *H. pylori* infection through direct observation of the size and severity of mucosal damage. However, there are several drawbacks of endoscopy for children as the procedure can be invasive and frightening for children and their parents; moreover, the cost may be prohibitive.<sup>10,11</sup> Diagnosis can be made by finding the bacteria in gastric mucosal biopsies, which are stained with hematoxylin-eosin. We could know the site of infection by evaluating the bacteria mucus attached to the surface of epithelial cells, which commonly found on the intestinal crypt. Therefore, hematoxylin-eosin smears are not reliable for establishing diagnosis when there is only few of microorganism found.<sup>1</sup>

## CASE ILLUSTRATION

A 8-year old girl was admitted to M. Djamil Hospital with main complaint of recurrent abdominal pain 3 days before admission. She had been hospitalized in Sungai Dareh Hospital for 3 days and was referred to M. Djamil Hospital Padang with diagnosis of colic abdomen. At the emergency department, her case was consulted to surgery department, which revealed no medical issues for department of surgery; subsequently, the case was consulted to pediatric department.

The abdominal pain was located especially on epigastrium area and made the patient often woke up at night because of pain. She often had recurrent abdominal pain since 3 months ago and diarrhea 3 days before admission. The diarrhea last for 2 days. The frequency was 3-6 times/day and the amount of 100 mL/each defecation. The stool was soft and without blood or mucus. She had vomiting since 2 days before admission. The frequency of vomiting was only once in a day, which contained 2 glasses of undigested food and drink for each vomiting. It was a non projectile vomiting. There was no fever, cough or breathlessness. She could drink well, but refused to have oral electrolyte solution (*oralit*). There was loss of appetite and she only ate noodle once daily. The

last urination was an hour before hospital admission with normal amount, no color changes and no history of passing stone in the urine.

She was exclusively breastfed until the age of 2 years. She had weaning food of steamed rice at 7 months, smooth textured rice at 9 months and solid meal since 12-month old. At the moment of examination, she had the family meal about 2-3 times daily. The meal usually contained a piece of meat and fish.

The physical examination revealed normal results; however, her body weight was 23 kg and the body height was 130 cm with nutritional status was undernourished. The laboratory work-up demonstrated following results: hemoglobin level of 14.2 g/dL, white blood count of 6,600/mm<sup>3</sup>, and normal differential count. Urine and fecal examination showed normal results.

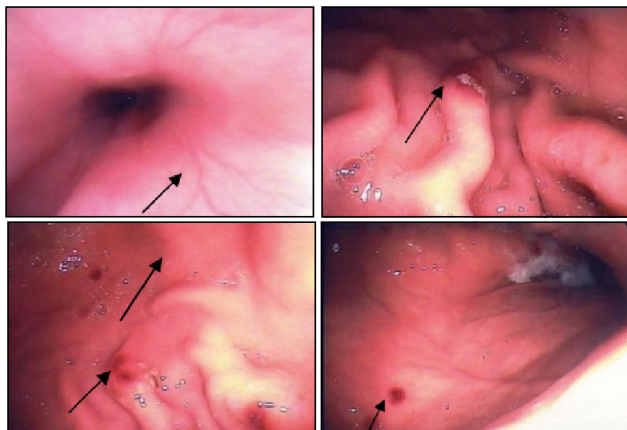
The working diagnose was observation on recurrent abdominal pain due to erosive gastritis. The differential diagnosis was *H. pylori* and duodenal ulcer. The patient's nutritional status was undernourished. The treatment included oral administration of H<sub>2</sub> receptor antagonist in a dose of 25 mg twice daily. Serologic testing of *H. pylori* immunoglobulin G (IgG) and IgM, endoscopic examination and biopsy were ordered.

On the 3<sup>rd</sup> day of hospitalization, the patient's condition was good. The physical examination still revealed normal results. Laboratory findings demonstrated *H. pylori* IgG level of 1.11 (positive) (normal limit < 1.0); therefore, the treatment was modified. She got oral amoxicillin 350 mg three times/day, oral clarithromycin 200 mg twice daily, and oral proton pump inhibitor (PPI) 20 mg once daily for two weeks. Endoscopic examination was ordered after having her family's informed consent.

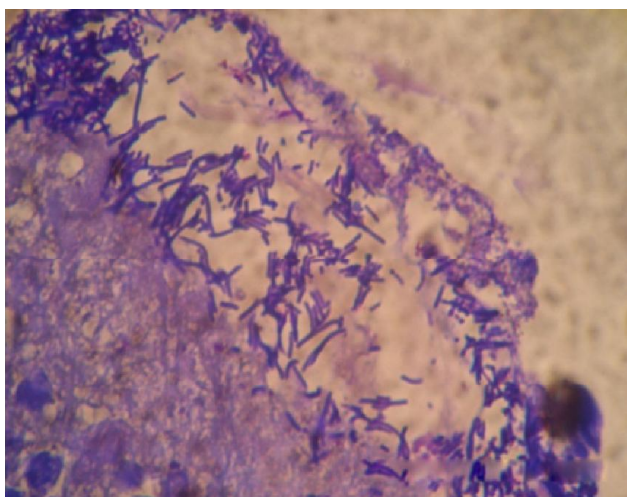
On the 5<sup>th</sup> day of hospitalization, the endoscopy revealed following results: grade A esophagitis or gastroesophageal reflux disease (GERD), corpus ulceratum and moderate antrum gastritis (Figure 1). Biopsy specimen was taken during the endoscopy and revealing gastric mucus with hyperplasia in almost half of ducts, plenty of plasma cells, lymphocytes, eosinophilic infiltrates, and *H. pylori* at several sites (Figure 2).

On the 7<sup>th</sup> day of hospitalization, no complaint was reported and there was increased appetite. On the follow up of nutritional status and anthropometric measurement, her body weight increased to 23.5 kg. The biopsy examination indicated chronic gastritis due to *H. pylori* infection. After two weeks of treatment,

her condition was better and no more complaints or symptoms were reported. On her last visit, the treatment was stopped. She was advised to have another visit in the next 3 month to evaluate her clinical improvement and to observe a decrease of *H. pylori* IgG titer.



**Figure 1. Inflammation, erosion and ulcerative process in gastrointestinal tract due to *Helicobacter pylori* infection**



**Figure 2. Biopsy examination showing hyperplasia, increased plasma cells, lymphocytes, eosinophils and the presence of *Helicobacter pylori***

## DISCUSSION

In general, *H. pylori* infection in children is usually accompanied with gastritis more often than peptic ulcer. Gastritis in children usually has a symptom of stomachache. Therefore, recurrent abdominal pain in children should be assumed as clinical symptom related to *H. pylori* infection.<sup>1</sup>

Recurrent abdominal pain is a common sign which brings patient to search medication. It is similar to non-ulcer dyspepsia in adult. Some scientists suggest that recurrent abdominal pain is related to *H. pylori* infection. About 30% of recurrent abdominal pain cases in children demonstrate positive findings of *H. pylori*

in the antrum; while 10% cases have positive results in the corpus area. Gastrointestinal ulcers are rarely found in children; however, the possibility of *H. pylori* infection should always be considered.<sup>12</sup>

Gastric disturbance consists of two conditions. First, it includes hypersecretion of gastric acid (hyperchlorhidria), which can affect gastritis and part of sequels for duodenal ulcer and gastric ulcer. Second, the condition may also comprise hyposecretion of gastric acid (hypochlorhidria) due to atrophy of gastric mucosa. Vomiting is commonly found in this case as a result of irritation of esophageal mucosa due to hypersecretion of gastric acid.<sup>12</sup>

Acute or chronic diarrhea may occur due to the hyposecretion as there is an increased gastric protection that allows enteric infection. A meta-analysis study showed that diarrhea in of *H. pylori* infection may be caused by antibiotic treatment, which alter the intestinal flora qualitatively and quantitatively.<sup>13</sup>

Recurrent abdominal pain in children is similar to the non-ulcer dyspepsia in adult. Moostriich consensus suggests that all patients with dyspepsia should be screened with non-invasive test such as serologic or urea breath test for *H. pylori* infection. If the result of the test is positive, the patient should be treated immediately without waiting for the results of endoscopy.<sup>2</sup>

This case reported a patient with recurrent abdominal pain, who was assumed to have *H. pylori* infection. Although urea breath test is the most sensitive of non-invasive diagnostic test, but in this case, the serologic examination was the diagnostic test of choice since there was less facility and human resource for urea breath test. The study of Gunel in Turkey, which evaluated patients with recurrent abdominal pain, showed that 60% patients were seropositive for *H. pylori* IgG and 25% were seropositive for IgA.<sup>14</sup> The definitive diagnosis was made based on *H. pylori* examination of gastric biopsy from gastric mucosal specimen of one or more gastric area. The histological examination demonstrated that there were severe gastritis cases including gastric atrophy and duodenal metaplasia. A study conducted by Mahjoub et al, in Turkey indicated that *H. pylori* infection were found in the biopsy of 9.7% male and 8% female subjects. There was a significant association between *H. pylori* infection with gastric activity ( $p = 0.001$ ).<sup>15</sup>

If serologic test result was positive, eradication treatment should be initiated. The selection of regimen should be made by considering the duration of existing symptoms and the level disturbance to daily activity

in normal life. Other causes including bladder stone, constipation, and psychological factors should be excluded, especially when conventional treatment with antacid and H<sub>2</sub> antagonist do not offer any improvement. The treatment of choice in our case was triple therapy regimen (a PPI plus two antibiotics) as suggested by the American and European experts consensus. We did not repeat serologic testing since the symptom of recurrent abdominal pain was relieved. However, we suggested the patient to have another visit to evaluate the *H. pylori* IgG titration. If the antibody titration reduced more than 50%, we could conclude that the eradication treatment was successful.

*H. pylori* bacterial culture may provide definitive diagnosis as well as revealing bacteria sensitivity and antibiotic resistance. Urea breath test was a non-invasive test with high sensitivity and specificity. This test is important to recognize the presence of *H. pylori* infection. Eradication rate, as assessed by 13C urea breath test, was achieved in 73.4% by omeprazole + amoxicillin with metronidazole and in 62.6% by omeprazole + amoxicillin with claritromycin.<sup>16</sup>

Many literatures reported that eradication therapy give real effect in *H. pylori* infection with peptic ulcer. Since this time, the patient never had abdominal pain and vomit symptom. For the future, a good hygiene and sanitation is still become attention to prevent eradication.<sup>12</sup>

Many literatures also have reported that eradication therapy may provide actual effective results for patients who have both *H. pylori* infection and peptic ulcer. Therefore, after having the eradication treatment, our patient had no further complaint of abdominal pain and vomiting. For the future, a good hygiene and sanitation is still become attention to prevent eradication.<sup>12</sup>

Our patient has received first line therapy of *H. pylori* eradication to provide total elimination of *H. pylori* and to neutralize the hypersecretion of gastric acid into normal state. Antimicrobial resistance may cause treatment failure.<sup>17</sup> Triple therapy is a combination of anti-secretory agent and antimicrobial agent for 7-14 days. A meta-analysis conducted by Laheij et al of 666 studies with 53,228 adults sample indicated that eradication therapy with PPI combination 2 of 3 antibiotics (claritromycin, amoxicillin, and metronidazole) gives survival rate of 79%-83%.<sup>18</sup> Another meta-analysis study about eradication therapy *H. pylori* in children by Khurana et al, concluded that metronidazole and amoxicillin for 2-6 weeks, clarithromycin for 1-2 weeks, amoxicillin and proton pump inhibitor and macrolides for 2

weeks are the best regimens in developing country.<sup>19</sup> Faber et al, who conducted a study in Israel showed that eradication was achieved in 73.4% cases by omeprazole plus amoxicillin with metronidazole and in 62.6% cases by omeprazole plus amoxicillin with claritromycin ( $p = 0.078$ ).<sup>16</sup>

Good nutrition is very important for growth and developmental of children. Optimal intake dietary is necessary for patients to protect them against severe nutritional problem. Our patient was undernourished due to her inadequate dietary intake at home. The prognosis depends on the management of the disease, early detection and adequate therapy, which are important to prevent complication including gastrointestinal bleeding and ulcer, as well as providing better survival rate. If the establishment of diagnosis is delayed and the treatment is inadequate, gastrointestinal ulcer, bleeding, and cancer may occur. Moreover, it may also easily cause relapse and drug resistance.<sup>20</sup>

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