

Helicobacter Pylori as a Cause of Iron Deficiency Anemia

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Abstract: Male 63 years old came with hematemesis and melena. Hypochromic micrositic anemia present and need to blood transfusion therapy. On histopathologic examination of gaster biopsy, revealed *H. pylori* positive chronic gastritis. Treatment with triple drug as a eradication therapy improved the patient clinically.

Keywords: Helicobacter pylori, iron deficiency anemia, PPI.

1. Background

Anemia, defined as a hemoglobin concentration below established cut-off levels, is a widespread public health problem with major consequences for human health as well as social and economic development. The World Health Organization (WHO) estimates that about 2 billion people in the world are suffering from this disease, and that approximately 50% of all anemia cases are diagnosed as iron deficiency anemia (IDA).¹ Many risk factors for IDA have been identified, most of which are related to dietary habits. In the past decades, the association between Helicobacter pylori (*H. pylori*) infection and IDA has been controversial.^{2,3,4}

Helicobacter pylori (*H. pylori*) is a Gram-negative bacterium that colonizes human gastric mucosa, leading to chronic antral gastritis and peptic ulcer disease. The overall prevalence varies globally from one geographical region to another with occurs mainly in developing countries. In the United States, *H. pylori* infection was associated with IDA regardless of the presence or absence of peptic ulcer disease.³ As a developing country in Southeast Asia, Indonesia is an archipelago with a multi-ethnic society (more than 1,000 ethnic and sub-ethnic groups). Indonesia, with its different ethnicities, cultures, life-styles and religions, presents an appropriate model to examine the effects of migration and co-evolution on the bacteria-host interactions involved in the *H. pylori* infection. The overall *H. pylori* prevalence in Indonesia was only 14.3% for adults and 3.8% for children.⁴

Previous studies have shown that *H. pylori* colonization of the gastric mucosa may impair iron uptake and increase iron loss, potentially leading to iron deficiency anemia.^{1,5} However, eradication of *H. pylori* has not been clearly demonstrated to improve IDA. The American College of Gastroenterology suggests adequately powered research studies are needed to assess whether *H. pylori* eradication offers benefit to patients with IDA, especially unexplained IDA.^{5,7}

2. Case Presentation

A 65 years old, male, was admitted in emergency room (ER) Wangaya Hospital because of bloody vomiting and black stool. Vomiting was occurred since 3 days before admitted to the hospital. The colour was dark red and dark brown like coffee grounds. The patient said that volume of vomit was 50ml. He also had black stool since 1 day prior to admission. The stool was sticky and putrid odor. The patient usually complained a heartburn and nausea. Heartburn was food relieve. History of NSAID or herbal medicine consumer was denied by this patient. Any history of alcohol consumer also denied. This patient often return to hospital with the same complaints and the last episode was 1 week before this admission. And his family bring out endoscopic result that was done 4 months before with the result was superficialispangastritis.

On examination, his vital sign was normal with no sign of infection and inflammation. But on the physical examination his eyes was anemic and there were epigastric tenderness on palpation. There's no hepatomegaly and splenomegaly. Cardiac and pulmonary examination also normal. The laboratory result showed an anemia with hypochromic microcytic type Hb 7,2; MCV 79,3; MCH 26,2; MCHC 33. Serum Iron (SI) 12, TIBC 104 and Ferritin was 23. Liver function and kidney function was normal. In stool analysis, the color was dark brown with positive erythrocyte +3, there's no parasite in the stool. Urin analysis was normal. Peripheral blood smear was done to confirm what type of this anemia, and the result was iron deficiency anemia.

Abdominal ultrasonography revealed a normal result, with no sign of any chronic liver disease. We also done endoscopy again and the result was still the same just superficialispangastritis only. Pathologic examination reported active chronic gastritis with positive (+) result for *H. Pylori*.

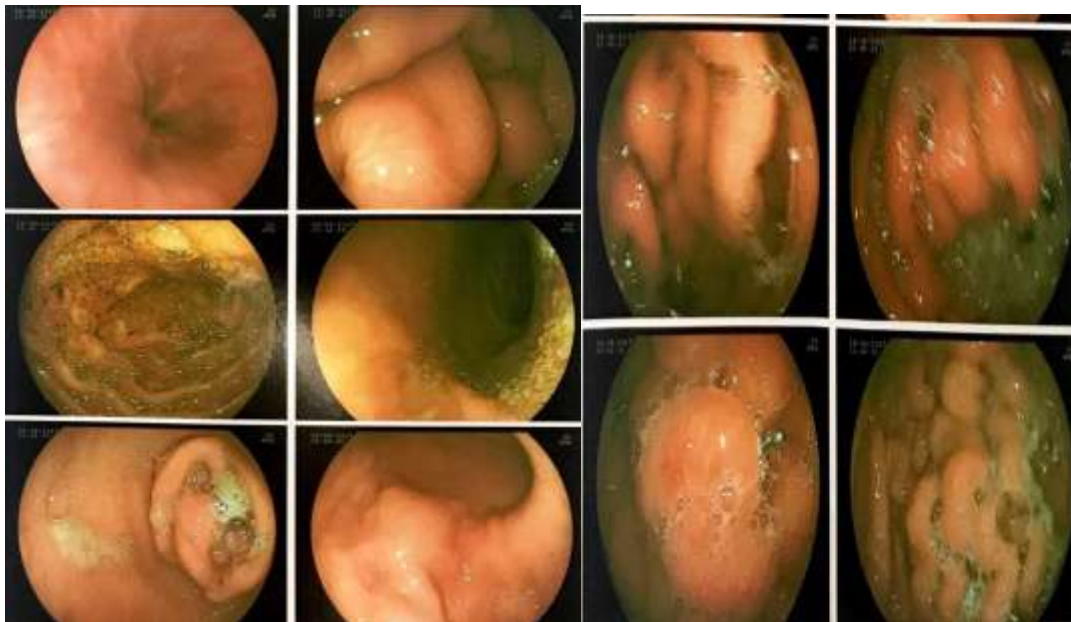


Figure 1: Esophagogastroduodenoscopy result

This patient was diagnosed and managed in line of Pangastritisuperficialis caused by *H. pylori* with iron deficiency anemia (IDA). This patient was treated with triple *H. pylori* eradication therapy (amoxicillin, omeprazole, and clarithromycin for 14 days). The patient also got therapy for IDA with PRC transfusion, and ferrous sulfate. He also got therapy for his upper GI bleeding with tranexamic acid, sulcrat syrup, and antacid syrup. After 2 days of admission bloody vomiting stopped.

3. Discussion

This case illustrated about iron deficiency anemia (IDA) in patient with pangastritisuperficialis which caused by *H. pylori*. While *Helicobacter pylori* infection was initially revealed to be associated only with some gastroduodenal diseases, further studies have shown its possible role in several extragastric diseases.^{1,6} The role of *H. pylori* infection in unexplained iron deficiency anemia (IDA) has already been confirmed. A study showed that while prevalence of *H. pylori* in patients with IDA is higher compared with that of the general population, 64–75% of the

patients reported a complete disappearance of IDA after *H. pylori* eradication.^{6,7}

Although the mechanisms remain unclear, clinical and epidemiologic studies suggest that infection with *H. pylori* has emerged as a new cause of refractory iron deficiency anemia (IDA), unresponsive to iron therapy, malabsorption or diversion of iron in the reticuloendothelial system. Barabino hypothesized that gastritis increased levels of neutrophil derived lactoferrin, and since *H. pylori* has a lactoferrin-binding protein receptor, the infection would result in increased iron losses related to bacterial turnover.^{3,6,8,10} *H. pylori* takes up iron from human lactoferrin through a receptor-mediated method, and lactoferrin secretion in the gastric mucosa appears to be influenced by the *H. pylori* organism. Lactoferrin may play a role in IDA, since gastric mucosa lactoferrin levels have been shown to be significantly higher in *H. pylori*-positive IDA persons compared to persons who are non-anemic *H. pylori*-negative, non-anemic *H. pylori*-positive, and *H. pylori*-negative with IDA.^{9,10}

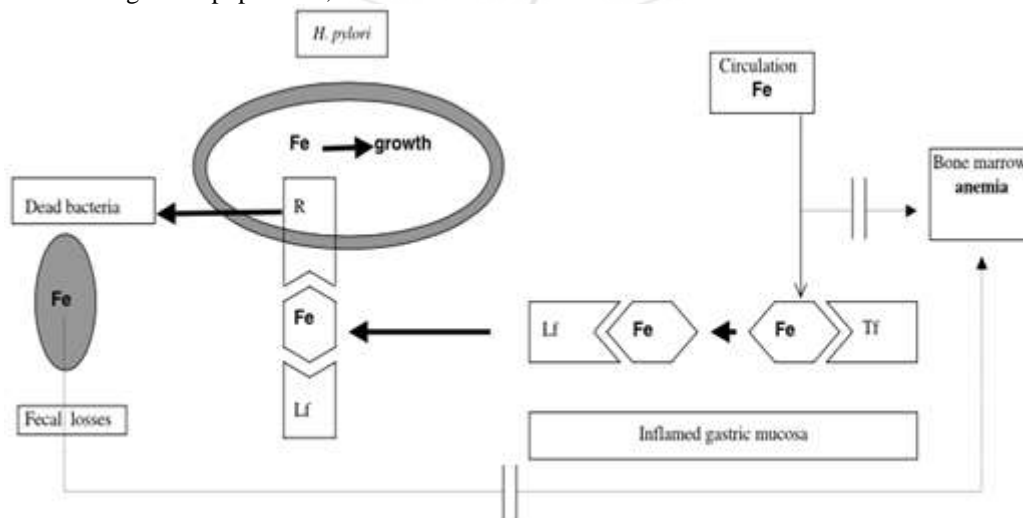


Figure 2: Possible physiopathologic mechanism of the anemia. Lf = lactoferrin; Tf = transferrin; R = outer membrane receptor.⁹

People with *H. pylori* infection and IDA appear more likely to have corpus gastritis as compared to *H. pylori*-infected patients without anemia.^{8,9} Corpus gastritis results in decreased gastric acid secretion and increase in intragastric pH that may impair iron absorption. Acid secretion returns to the normal range after eradication of *H. pylori*. Another important effect of *H. pylori* gastritis that may cause reduced iron absorption is a decrease in gastric juice ascorbic acid concentration.^{6,9,11} Ascorbic acid facilitates iron absorption by reducing iron to the ferrous form. Ascorbic acid is secreted into gastric juice, and it has been shown that gastric juice ascorbic acid levels are significantly lower in *H. pylori*-infected vs. uninfected persons, and that ascorbic acid level increases after cure of *H. pylori* infection.^{10,11,13}

According to the literature, there are some studies which have shown the benefits of *H. pylori* treatment on iron deficiency anemia. For example, improved iron deficiency was reported after the eradication of *H. pylori*.^{11,12,14} While choosing a treatment regimen for *H. pylori*, patients should be asked about previous antibiotic exposure and this information should be incorporated into the decision-making process. For first line treatment, clarithromycin triple therapy should be confined to patients with no previous history of macrolide exposure who reside in areas where clarithromycin resistance amongst *H. pylori* isolates is known to be low. Most patients will be better served by first-line treatment with bismuth quadruple therapy or concomitant therapy consisting of a PPI, clarithromycin, amoxicillin, and metronidazole.^{5,16}

In Malik et al.'s study, they have shown that the eradication of *H. pylori* resulted in a significantly better response to oral iron supplementation among *H. pylori* infected pregnant women with iron deficiency anemia.¹¹ Nevertheless, gastrointestinal endoscopy was not performed in this study; additionally, antiulcer treatment was given to the patients in the study group. Duque et al. also reported that change observed on the hemoglobin concentration as a result of *H. pylori* eradication and/or iron supplementation may reflect the effect of the infection on iron metabolism. Choe and Barabino reported that iron supplementation without eradication of the infection is insufficient to improve iron status.⁹ Other authors have reported correction of megaloblastic or iron deficiency anemia after eradication of *H. pylori*.^{11,12,15}

In another study, Huang *et al.*, reported that *H. pylori* eradication therapy combined with iron administration is more effective than iron administration alone for the treatment of iron deficiency anemia.¹⁶ They also stated that bismuth based triple therapy has a better response in terms of increased hemoglobin and serum ferritin concentrations than proton pump inhibitor based triple therapy. It is understood that all patients in their study had gastrointestinal problems because they were given bismuth or a proton pump inhibitor based triple therapy.^{15,16}

4. Conclusion

The causes of iron deficiency anemia is a lot. *H. pylori* infection is a frequent cause of IDA in men and postmenopausal women with either iron refractoriness or

iron dependency, in whom other causes of IDA have been previously ruled out. *H. pylori* eradication therapy produces long-term resolution of IDA in such patients. *H. pylori* eradication can improve IDA. These findings support the guidelines of the American College of Gastroenterology. Refractory IDA patients should be considered for assessment and treatment of *H. pylori*.

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