

# Differences of Hemoglobin and Transferrin Level between Helicobacter Pylori Gastritis and Non-Helicobacter Pylori Gastritis in Children

Hensen<sup>a</sup>, Supriatmo<sup>b</sup>, Oke Rina Ramayani<sup>c</sup>, Isti Ilmiati Fujiati<sup>d</sup>,  
Bidasari Lubis<sup>e</sup>, Gema Nazri Yannif<sup>f</sup>

<sup>a</sup>hensenmd@gmail.com

<sup>a</sup>Resident of Paediatrics, Medical School, Universitas Sumatera Utara/ Adam Malik Hospital, Medan, Indonesia

<sup>b</sup>Department of Paediatric, Medical School, Universitas Sumatera Utara/ Adam Malik Hospital, Medan, Indonesia

<sup>c</sup>Department of Paediatrics, Medical School, Universitas Sumatera Utara/ Adam Malik Hospital, Medan, Indonesia

<sup>d</sup>Department of Community Medicine, Medical School, Universitas Sumatera Utara/ Adam Malik Hospital, Medan, Indonesia

<sup>e</sup>Department of Paediatric, Medical School, Universitas Sumatera Utara/ Adam Malik Hospital, Medan, Indonesia

<sup>f</sup>Department of Paediatrics, Medical School, Universitas Sumatera Utara/ Adam Malik Hospital, Medan, Indonesia

## Abstract

**Background:** Gastritis can reduce the hemoglobin level. Based on previous study, gastritis resulted from Helicobacter pylori infection often correlated to anemia as the capability of Helicobacter pylori to obtain iron from hemoglobin and transferrin. **Objective:** To analysis the differences of hemoglobin and transferrin level between Helicobacter pylori gastritis and non-Helicobacter pylori gastritis in children. **Method:** A cross sectional study was conducted on outpatient and inpatient in Haji Adam Malik General Hospital, Medan and network hospitals on March – April 2020, subject ages from 2 to 18 years, diagnosed with Helicobacter pylori gastritis and non-Helicobacter pylori gastritis based on CLO test. Blood sample was taken from subjects to evaluate hemoglobin and transferrin level. **Result:** 54 subjects with gastrointestinal complaints were recruited. Subjects were divided into 2 groups based on CLO test, 32 subjects with Helicobacter pylori and 22 subjects without Helicobacter pylori. From blood sample analysis, mean hemoglobin and transferrin value from Helicobacter pylori group was 10.9 gr/dL and 253.5 mg/dL. Meanwhile, mean hemoglobin and transferrin value from non-Helicobacter pylori group was 10.8 gr/dL and 261.9 mg/dL. ( $p>0.05$ ). **Conclusion:** No difference in hemoglobin and transferrin level between Helicobacter pylori gastritis and non-Helicobacter pylori gastritis in children.

**Keyword:** gastritis, Helicobacter pylori, hemoglobin, transferrin

## Introduction

Gastritis is a condition characterized by histologically confirmed inflammation or inflammation of the gastric mucosa. Based on etiology, there are several gastritis types such as H. pylori gastritis, chemical gastritis, and autoimmune gastritis, and the most common type of gastritis is H. pylori.<sup>1</sup> H. pylori is a negative gram bacteria that can cause gastritis, peptic ulcers, and gastric cancer, and is considered a bacterial infection that the most common appears in the world.<sup>2</sup> The prevalence estimation of H. pylori show a significant variation, Uwan et al. in 2014 found prevalence in Makassar was 55%, Solo 51.8%, Yogyakarta 30.6%, Surabaya 23.5% and the lowest in Jakarta 8%.<sup>3</sup> Besides gastritis and peptic ulcers, Helicobacter pylori infection is often associated with various extra-intestinal disorders, including anemia, especially iron-deficiency anemia.<sup>4,5</sup> From small randomized trials and cross-sectional epidemiological studies multiple cases, evidence shows the H. pylori's role in anemia.<sup>6</sup> A cross-sectional study by Cardenas et al. found that anemia in H. pylori gastritis patients occurs because of multifactorial such as decreasing iron absorption due to reducing acid secretion and iron loss from micro-bleeding, disturbance of up taking of iron from hemoglobin and transferrin in the gastrointestinal tract.<sup>7</sup> Currently, in Indonesia, there are no studies or data regarding the differences in the value of hemoglobin and transferrin in patients with H. pylori gastritis and non-H. pylori gastritis, so the author curious to study further more about differences between hemoglobin and transferrin level between H. pylori gastritis and non-H. pylori gastritis in children.

## Material and Method

Our cross sectional study was conducted at Gastroenterology Polyclinic H. Adam Malik Medan Hospital, University of North Sumatera Hospital, and Satellite Education Hospital Medan in March – April 2020 after obtaining ethical clearance from Universitas Sumatera Utara, with inclusion criteria: children 2 – 18 years old with diagnosed with *H. pylori* gastritis and non- *H. pylori* gastritis by endoscopy and rapid urea test/ Campylobacter-like organism test (CLO) and parents willing to join the study. Patients with malnutrition, metabolic disease, immunosuppression disease and malignancy are excluded and the patients using proton pump inhibitor (PPI), H2 receptor antagonist, antibiotic or non-steroid anti-inflammatory drugs (NSAID) within 14 days, with a history of gastric operation, gastric bleeding, hepatic cirrhosis, a renal failure that need dialysis, cardiac failure and early or advance gastric cancer and refuse to join the study also excluded. The subject appropriate with inclusion criteria will be noted in case report form for being analysed. All the *H. pylori* gastritis and non- *H. pylori* gastritis patient will be done complete blood count using a standardized machine and transferrin checking with immunoturbidimetry. Data will analyzed by using SPSS version 23 with Mann Whitney for hemoglobin data and T-independent test for transferrin data (figure 1). The significance of the statistical test results in the test between the group with *H. pylori* gastritis and the group non-*H. pylori* gastritis was determined based on a P value <0.05 with a 95% confidence interval.

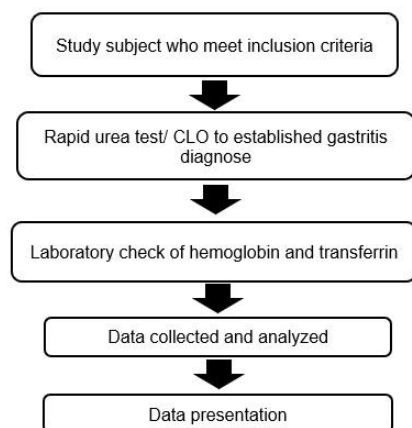


Figure 1. Subject recruitment

## Result

Figure 2 shows the subject of recruitment who met inclusion perform endoscopy and rapid urea test/ CLO to establish positive and negative *H. pylori*. All the positive and negative *H. pylori* perform complete blood check using a standardized machine for hemoglobin and transferrin with immunoturbidimetry. All data are shown in the subject characteristic grouping that can be shown in table 1. Positive *H. pylori* found greater than negative with the most in females 24 children. Boys age between 2 – < 5 years old found 75% than female, while in 5 – < 6 years old equal in both groups, and boys in 6 – 18 years old found 60% than the female with bodyweight mean 38,9 kg in the positive group and body height mean 139,7 in positive groups. In comparison, bataknese ethnic found the greatest among other ethnicities with 13 children. In child educational level, primary school found the greatest among other educational levels with 20,3% children. The majority of educational levels in the patient's father and mother are college with 85,2% and 90,7% while most of the patient's father and mother occupation status are private employees with 48,1% and 33,3%. 40 children with a

previous family history of gastritis.

Our study shows the hemoglobin mean of *H. pylori* gastritis  $10,9 \pm 2,1$  gr/dL while in non-*H. pylori* gastritis  $10,8 \pm 2,2$  gr/dL (figure 3) and the transferrin mean  $253,5 \pm 30,3$  mg/L while in non-*H. pylori* gastritis  $261,9 \pm 43,2$  mg/L (figure 4). We perform the Mann Whitney test and t-independent test to know the differences in the mean of hemoglobin and mean of transferrin between two groups (Table 2). With the Mann Whitney test, we found no significant difference mean of hemoglobin between two groups ( $p = 0,785$ ), while with the t-independent test, we found no significant difference mean of transferrin between two groups ( $p = 0,405$ ).

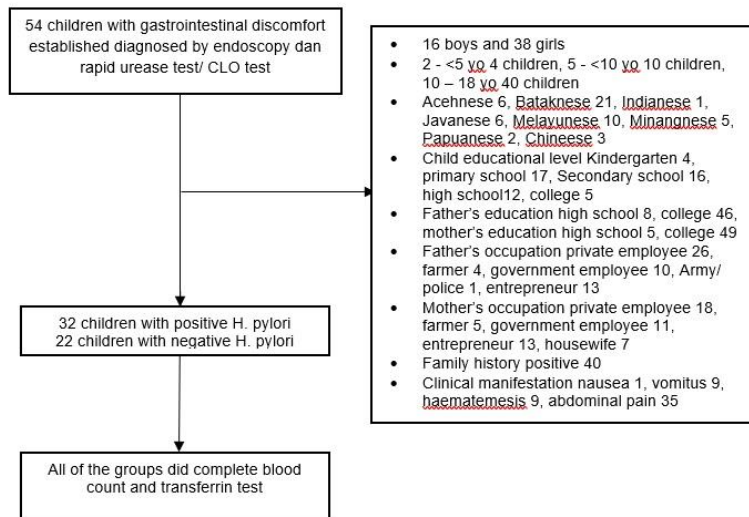


Figure 2. Subject recruitment

## Discussion

*H. pylori* is a gram-negative bacteria with spiral-shaped, 2 - 4  $\mu\text{m}$  of length and a 0.5 - 1  $\mu\text{m}$  of width, 2 - 6 unipolar flagella with 3  $\mu\text{m}$  of length that makes fast movement in the mucosal layer of gastric epithelial cells. *H. pylori* can also be found in basil and coccus shaped, especially after in-vitro culture and antibiotics treatment. *H. pylori* has heterogeneous genes, and all strains do not necessarily have the same role in gastritis disease, and each person with *H. pylori* infection has different strains.<sup>8,9</sup>

Gastritis, which means inflammation of the gastric mucosa, is a condition, not a disease. The gastritis term can only be established if there is microscopic inflammation of stomach and represents histologically not only clinically, and mostly patient with gastric inflammation are asymptomatic. The most common cause of gastritis is infection of *H. pylori*, a bacterium resides in the mucus gel layer overlaying the mucosa of the gaster. *H. pylori* gastritis has link to ulceration of duodenal and gastric, adenocarcinoma of gaster, mucosa-associated lymphoid tumor (MALToma), and non-Hodgkin lymphoma in gaster.<sup>10</sup> The colonization of *H. pylori* in the stomach for years or decades, not only days or weeks, and this organism always induces chronic gastritis. However, only fraction colonization of *H. pylori* can develop the disease.

Acute gastritis is characterized by mucosal hyperemia and changes in erosions with symptoms include sudden abdominal pain in the epigastric region, nausea, and vomiting. The histological features of acute gastritis are characterized by neutrophil infiltration, edema, and hyperemia. If untreated, acute gastritis will develop into a chronic one.<sup>11</sup> Chronic gastritis is histologically characterized by infiltration of inflammatory

Subject Characteristic	H. pylori	
	Positive n = 32	Negative n = 22
Gender, n (%)		
Male	8 (50)	8 (50)
Female	24 (63,2)	14 (36,8)
Age, n (%)		
2 – < 5 years old	3 (7,5)	1 (2,5)
5 – < 6 years old	5 (50)	5 (50)
6 – 18 years old	24 (60)	14 (40)
Body Weight, mean (SD), kg	38,9 (17)	36 (13)
Body Height, mean (SD), cm	139,7 (21,5)	137,6 (18,1)
Ethnic Group, n (%)		
Acehnese	4 (66,7)	2 (33,3)
Batakese	13 (61,9)	8 (38,1)
Indonesian	1 (100)	0 (0)
Javanese	5 (83,3)	1 (16,7)
Malaynes	4 (40)	6 (60)
Minangnese	2 (40)	3 (60)
Papuanese	2 (100)	0 (0)
Chinese	1 (33,3)	2 (66,7)
Child educational level, n (%)		
Kindergarten	3 (5,5)	2 (3,7)
Primary school	11 (20,3)	6 (11,1)
Secondary school	8 (14,8)	8 (14,8)
Senior high school	7 (12,9)	4 (7,4)
College	3 (5,5)	2 (3,7)
Father educational level, n (%)		
Senior high school	6 (11,1)	2 (3,7)
College	26 (48,1)	20 (37,0)
Mother educational level, n (%)		
Senior high school	4 (40)	1 (16,7)
College	28 (51,8)	21 (38,8)
Father's occupation, n (%)		
Private employee	15 (27,7)	11 (20,3)
Farmer	3 (5,5)	1 (1,8)
Government employee	5 (9,2)	5 (9,2)
Army/ police	1 (1,8)	0 (0)
Entrepreneur	8 (14,8)	5 (9,2)
Mother's occupation, n (%)		
Private employee	11 (20,3)	8 (14,8)
Farmer	4 (7,4)	1 (1,8)
Government employee	9 (16,6)	2 (3,7)
Entrepreneur	5 (9,2)	7 (12,9)
Housewife	3 (5,5)	4 (7,4)
Socioeconomic status, n (%)		
Scant(<5 million rupiah/month)	5 (9,2)	1 (1,8)
Good (>5 million rupiah/month)	27 (50,0)	21 (38,8)
Family history, n (%)		
Yes	25 (46,2)	15 (27,7)
No	7 (12,9)	7 (12,9)
Clinical manifestation, n (%)		
Nausea	1 (1,8)	0 (0)
Vomitus	6 (11,1)	3 (5,5)
Haematemesis	5 (9,2)	4 (7,4)
Abdominal pain	20 (37,0)	15 (27,7)

Table 1. Subject characteristic study

Subject characteristic	<i>Helicobacter pylori</i>		p
	(+) n = 32	(-) n = 22	
Hemoglobin, mean (SD), gr/dL	10,9 (2,1)	10,8 (2,2)	0,785 <sup>a</sup>
Transferrin, mean (SD), mg/L	253,5 (30,3)	261,9 (43,2)	0,405 <sup>b</sup>

<sup>a</sup>Mann Whitney, <sup>b</sup>T. Independent

Table 2. Hemoglobin and transferrin analysis

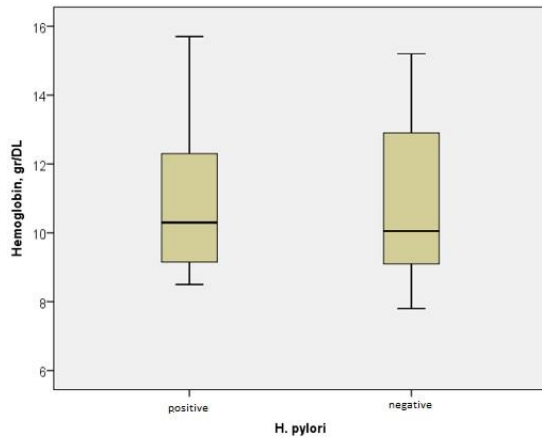


Figure 2. Boxplot of Hemoglobin value

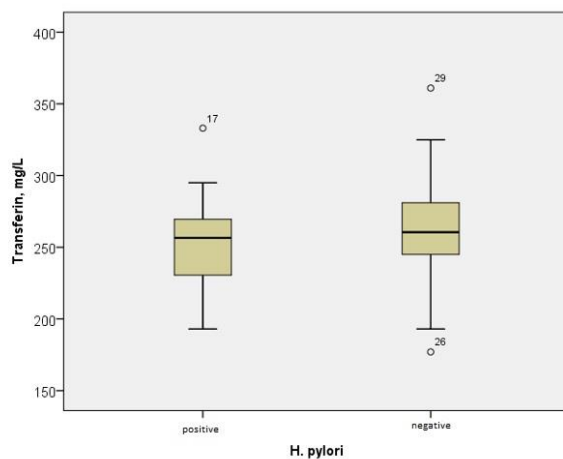


Figure 2. Boxplot of Transferrin value

cells consisting of lymphocytes and plasma cells. The initial phase of chronic gastritis is called superficial gastritis. Inflammatory changes are confined to the mucosal surface of the lamina propria, with edema and cell infiltration limiting the intact gland. The next stage is atrophic gastritis; the inflammation extends more

in-depth into the mucosa, distortion, and destruction of the glands. The final step in chronic gastritis is gastric atrophy, characterized by the loss of the glandular structure, reduced inflammatory infiltration, and endoscopic examination, the mucosa appears very thin.<sup>12</sup> *Helicobacter pylori* can survive in an acidic environment in the gaster by its high ability to form urease, in which urease can convert urea that can be found in gastric acid into alkaline ammonia and carbon dioxide.<sup>13,14</sup>

There are differences in the prevalence of *H. pylori* infection in various countries. In developed countries have lower prevalence rates. In Bangladesh, the mean prevalence of *H. pylori* was reported 92%, in India it was 79%, in Vietnam, it was 74.6%. In contrast, in countries that are considered developed, such as Australia, the seroprevalence rate is approximately 15.1%. The reported seroprevalence rate in East Asia was 59.6% in South Korea, 58.07% in China, 54.5% in Taiwan, and 39.3% in Japan. Meanwhile, in Southeast Asia, the reported prevalence rates were 57% in Thailand, 35.9% in Malaysia, and 31% in Singapore.<sup>15</sup> Two factors that highly predispose to a high colonization rate of *H. pylori* are low socioeconomic status and low education level and other critical factor is the mode of transmission of *H. pylori* that can be via fecal-oral, oral-oral, or environmental transmission from contaminated water sources.<sup>12</sup> A systematic meta-analysis study by Hooi JKY et al. in 2017 reported that more than half of the world's population in 62 countries is still infected with *H. pylori*. Another study in 2015 estimated the prevalence of *H. pylori*, about 4.4 billion people infected by *H. pylori* infection worldwide, with asymptomatic clinical manifestation. Another meta-analysis and comprehensive studies of healthy children by Torres et al. from 2011 to 2016 estimated the overall seroprevalence rate of 33%. In the same study, a review of 7 cohort studies concluded that the infection rate in healthy children under five years of age is still around 20 - 40% in high-income countries and 30-50% in middle and upper-income countries.<sup>13</sup>

Clinical manifestation of *H. pylori* gastritis is divided into two parts related to the gastrointestinal tract and non-gastrointestinal tract. Clinical manifestation related to the gastrointestinal tract commonly consist of nocturnal pain, abdominal pain in the epigastric region that relief with antacid treatment, and acute or chronic gastrointestinal bleeding (hematemesis, hematochezia, or melena).<sup>16,17</sup> Clinical manifestation *H. pylori* infection non-gastrointestinal tract, especially iron-deficiency anemia, idiopathic thrombocytopenia purpura (ITP), vitamin B12 deficiency, and allergies.<sup>18</sup> A systematic review and meta-analysis by Muhsen et al. in 2008 found *H. pylori* is the main factor causing iron deficiency anemia.<sup>19</sup> A cross-sectional study by Cardenas et al. in 2005 found that *H. pylori* infection was associated with the onset of iron deficiency anemia.<sup>7</sup>

Anemia defines as the concentration of hemoglobin is below the cut-off value. Based on the World Health Organization (WHO) criteria, the cut off depends on the child's age : in children aged 6 - 59 months the cut-off if below 11 gr/ dL, children aged 5 - 11 years the cut-off if below 11,5 gr/ dL and in children aged 12-14 years the cut-off if below 12 gr/ dL, in children over 15 years the cut-off if below 12 gr/ dL for girls and below 13 gr/ dL for boys.<sup>20</sup> The emersion of anemia in *H. pylori* infection is caused by decreased iron absorption, gastrointestinal bleeding, and the presence of iron uptake by the *Helicobacter pylori* bacteria. In a cohort study conducted by Taye B et al. in Ethiopia on children under 6.5 years, there was an association between anemia and *H. pylori* infection with age.<sup>21</sup> Other study in South Korea by Choe YH et al. found a greater incidence of anemia in the *Helicobacter pylori*-infected adolescent group of subjects.<sup>22</sup>

Our study found no difference in hemoglobin values between *H. pylori* infection and non-*H. pylori* infection. Our study in line with case-control study by Haghi-Ashtiani MT et al. in Iran on children with gastritis, they found no significant difference in hemoglobin values between children with *H. pylori* infection and non-*H. pylori* infection<sup>23</sup> and a cross-sectional study by Zahmatkeshan M et al. in Iran on children under 18 years of age also found no significant relationship between *H. pylori* infection and anemia.<sup>24</sup> In our study, a rapid urease test or *Campylobacter*-like Organism test (CLO test) was used to determine whether a subject infected with *Helicobacter pylori* or not because this in some study has higher sensitivity and specificity test.<sup>25</sup> Our study showed no difference in transferrin values between groups with *H. pylori* infection and non-*H. pylori* infection. Our study can be used as a reference that there is no relationship between transferrin value with the incidence of *H. pylori* infection.



## Conclusion

*H. pylori* is a gram-negative bacteria with spiral-shaped and also can be found in basil and coccus shaped, especially after in-vitro culture and antibiotics treatment. *H. pylori* can cause gastritis with clinical manifestation divided into two parts related to the gastrointestinal tract and non-gastrointestinal tract. Clinical manifestation *H. pylori* infection non-gastrointestinal tract, especially iron-deficiency anemia, idiopathic thrombocytopenia purpura (ITP), vitamin B12 deficiency, and allergies.

Our study found no significant difference in hemoglobin and transferrin levels between *H. pylori* and non-*H. pylori* gastritis in children. However, more studies and larger sample sizes are needed to evaluate eradication on *H. pylori* gastritis patients against hemoglobin and transferrin levels in children with *H. pylori* gastritis.

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## Conflicts of interest

The author declares that there are no conflicts of interest.

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