Helicobacter Pylori Infection in Children: Prevalence of Anemia and Impact on Growth Parameters

Barakat SH. ; Hanafy HM. ; Guimei M. ; Khalifa EH.* ; Khalil AFM.

*Pediatric Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt***.**

Corresponding authors: El-Said Hamdy Khalifa**,**

e_elsawy17@alexmed.edu.eg

ABSTRACT

Background: Helicobacter pylori (H. pylori) infection in children can be associated with various clinical conditions. The infection is the major contributor to peptic ulcer disease in children. In addition, it was suggested by some researchers to be a risk factor for iron deficiency anemia and growth impairment. **Aim:** To determine the prevalence of anemia, and the anthropometric measurements (weight for age and height for age z-scores) in children with H. pylori infection. **Patients and methods**: Two hundred children with confirmed H. pylori infection were included. The infection was diagnosed based on histopathological detection of H. pylori in gastric biopsies and a positive rapid urease test during upper gastrointestinal endoscopy. Clinical data, anthropometric measurements, and a complete blood picture (CBC) were obtained for all patients. **Results:** Seventy-nine percent of patients had epigastric pain. The means (SD) of weight for age z-score (WAZ), height for age z-score (HAZ), and body mass index z-score (BMIZ) were -0.86 ± 0.82, -0.93 ± 0.69, and -0.38 ± 0.73, respectively. The anthropometric measurements WAZ, HAZ, and BMIZ were negatively correlated with the duration of symptoms before presentation (r = -0.729, r = -0.820, and r = -0.413, respectively). Hypochromic microcytic anemia was present in 58.5% of all cases. The mean hemoglobin concentration among the studied children was 10.48 ± 1.11 g/dl. Conclusion: In children with H. pylori infection, a high prevalence of iron deficiency anemia, and lower anthropometric measurements were observed.

Keywords: helicobacter pylori, anemia, children, growth parameters.

DOI: 10.48047/ecb/2023.12.8.719

Background

H. pylori infection is a common worldwide health problem, especially in developing countries. The infection has been linked to poor growth in children in some studies. Some postulated mechanisms include impaired absorption of nutrients and vitamins and reduced food intake as a result of dyspepsia. The infection and eradication therapy are also reported to affect circulating ghrelin and leptin levels.[1, 2]

Iron deficiency anemia is frequent in children, and it can be caused by a variety of causes. It is still debatable whether H. pylori infection is one of them. Reduced iron absorption due to hypochlorhydria is one possible explanation. Also, iron loss is probably increased due to occult bleeding from H. pylori gastritis.[3] The consensus guidelines recommend endoscopic evaluation

in children with refractory iron deficiency anemia to rule out not only the presence of H. pylori but also other causes of iron deficiency anemia.(4)

The aim of this study was to determine the prevalence of anemia, and the anthropometric measurements (weight for age and height for age z-scores) in children with H. pylori infection.

Patients and Methods:

This cross-sectional study was conducted at the Pediatric Gastroenterology Clinic of Alexandria University Children's Hospital (AUCH), Egypt. Written consent was obtained from the parents before inclusion in the study. The study protocol has been approved by the Ethical Committee of the Faculty of Medicine, Alexandria University, Egypt. The study included children who were proven to have H. pylori infection by both histopathological detection of H. pylori in gastric biopsies and a positive rapid urease test during upper gastrointestinal endoscopy.(5)

All included patients were subjected to full history taking and detailed clinical examination. Weight, height and body mass index were measured and their appropriate z-scores for age and sex were obtained. The anthropometric measurements were correlated with the duration of disease condition before presentation. Complete blood picture was obtained for all patients. The presence of anemia, type of anemia and hemoglobin level were recorded. The presence of anemia was defined based on hemoglobin level according to the World Health Organization's (WHO) age criteria.(6) Patients with hematemesis were divided into two groups; severe hematemesis and non-severe hematemesis group. The presence of a severe hematemesis was indicated by the presence of one or more of the following: a large amount of hematemesis, heart rate (HR) >20 bpm above the mean heart rate for age, prolonged capillary refill time, a hemoglobin drop of >2 g/dl, the need for blood transfusion, and hemoglobin< 8 g/dl.(7) The hemoglobin levels in children with severe and non-severe hematemesis were estimated and compared with the hemoglobin levels in children without hematemesis.

Statistical analysis:

Data were analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Categorical data were represented as numbers and percentages. Chi-square test was applied to compare between different groups. Continuous data were tested for normality by Shapiro-Wilk test. Quantitative data were expressed as mean and standard deviation for not normally distributed quantitative variables. Significance was judged at the 5% level.

Results:

The age of the patients ranged from 3–16 years (102 girls and 98 boys), with a median of 7.5 years and a mean of 7.69 ± 3.64 years. The socioeconomic status was low to middle for most of the studied children (52% low, 31% middle, and 17% high). Sixty-three percent of the children were from rural areas.

The median duration of clinical symptoms before presentation was 8 months. Abdominal pain, vomiting, and hematemesis were the common causes for endoscopic referral. Seventy-nine percent of patients had epigastric pain. Epigastric pain was the sole presenting cause in 27% of cases and was associated with either vomiting or hematemesis in 52% of cases. Vomiting was present in about 60% of cases. Hematemesis was present in about 36% of cases. Among patients with hematemesis, nine patients had severe hematemesis; only three patients required blood transfusions. Endoscopic examination of these three patients revealed peptic ulcers. A gastric ulcer was present in one patient, while a duodenal ulcer was present in two cases. Refractory iron deficiency anemia with positive occult blood in the stool was the cause of presentation in six patients (3%).

A family history of either present or past history of H. pylori infection was present in 39% of patients. Mothers were the most common infected family members, representing 57.7% of the cases with positive family history of infection. The mean age of the studied patients was significantly lower among cases with positive family history of infection (p=0.010) as seen in Table (1).

The means (SD) of weight for age z-score (WAZ), height for age z-score (HAZ), and body mass index z-score (BMIZ) were -0.86 ± 0.82, -0.93 ± 0.69, and -0.38 ± 0.73, respectively (Table 2). The anthropometric measurements WAZ, HAZ, and BMIZ were negatively correlated with the duration of symptoms (r = -0.729, r = -0.820, and r = -0.413, respectively).

Table (1) The relation between age and family history in the studied patients (n = 200).

Age (years)	**Family history of H. pylori**		**p**
	Negative (122)	**Positive (78)**	
Mean ± SD. **Median (Min. – Max.)**	8.20 ± 3.69 8.50 (2.0 – 16.0)	6.88 ± 3.42 6.75(3.0 – 15.0)	0.010*

SD: Standard deviationp: p value for relation between age and duration of symptoms with different parameters
**: Statistically significant at p ≤ 0.05*

Table (2): The anthropometric data, prevalence of hypochromic microcytic anemia and hemoglobin level in the studied cases (n = 200).

Anthropometric data, anemia and hemoglobin level	
WAZ (mean ± SD.)	-0.86 ± 0.82
HAZ (mean ± SD.)	-0.93 ± 0.69
BMIZ (mean ± SD.)	-0.38 ± 0.73
Anemia	117 (58.5%)
Hemoglobin level – Min. – Max.	6.50 – 13.0

– Mean ± SD.	10.48 ± 1.11
– Median (IQR)	10.50 (10.0 – 11.20)

IQR: Inter quartile range, SD: Standard deviation

Hypochromic microcytic anemia was detected in 58.5% of all cases. The mean hemoglobin concentration among the studied cases was 10.48 ± 1.11 g/dl (Table 2). Children with severe hematemesis had a lower hemoglobin concentration, with a mean of 8.59 ± 1.1 g/dl. The mean hemoglobin among peptic ulcer cases was 7.7± 0.85g/dl. Cases with severe hematemesis had significantly lower hemoglobin levels than those with non-severe hematemesis ($p<0.001$), and those with no hematemesis ($p<0.001$). There was no significant difference between children with non-severe hematemesis and those without hematemesis regarding the hemoglobin level ($p = 0.948$) as seen in Table (3).

Table (3) Relation between hematemesis severity and hemoglobin level (n = 200)

Hemoglobin level	**No hematemesis (n = 129)**	**Non- severe hematemesis (n = 62)**	**Severe hematemesis (n = 9)**	**p**
Mean ± SD.	10.55 ± 1.04	10.60 ± 1.01	8.59 ± 1.10	<0.001*
Median (Min. – Max.)	10.50 (8.0 – 13.0)	10.40 (8.50 – 13.0)	8.50 (6.50 – 10.0)	
Sig. bet. Categories	p_1=0.948, p_2<0.001*, p_3<0.001*			

SD: Standard deviation, F: F for One-way ANOVA test, pairwise comparison between each 2 groups was done using Post Hoc Test (Tukey)
p: p value for comparing hemoglobin level between the three different categories
p_1: p value for comparing between patients with No hematemesis and Non-severe hematemesis
p_2: p value for comparing between patients with No hematemesis and severe hematemesis
p_3: p value for comparing between patients with Non-severe hematemesis and severe hematemesis
**: Statistically significant at $p \leq 0.05$*

Discussion

H. pylori infection is the major cause of gastritis and peptic ulcer disease in children. Also, the infection has been linked to several extragastric pediatric disorders. In the present study, low and moderate socioeconomic status and rural residency were common among our patients. Similarly, Galal et al. reported that, in Egyptian children infected by H. pylori infection, poor socio-economic status, rural residency, and bad hygiene were among the main risk factors for infection.(8)

In the present study, interfamilial transmission of H. pylori was a possible route of infection acquisition. This was evidenced by our findings, as a family history of H. pylori infection was present in 39% of our cases, with mothers being the most common family affected member. Moreover, the mean age of children with a positive family history of infection was significantly lower than that of those without a family history of infection. This means that the occurrence of infection among family members, especially mothers, is a

probable risk factor for the early acquisition of infection. This was in agreement with several studies that reported mother-to-child transmission of H. pylori infection as an important risk factor for the acquisition of infection [9, 10]

H. pylori has been linked to a variety of gastric and extragastric pediatric health problems. Epigastric pain was the most common clinical manifestation among our cases (79%). Similarly, a high prevalence of abdominal pain (76%) was reported among Egyptian children with symptomatic H. pylori infection.[8] This was also in agreement with several studies that reported a significant association between epigastric pain and H. pylori infection.[10-12]

The relation between H. pylori infection and impaired growth was addressed in some pediatric studies.[13-18] In the current study, the growth parameters (WAZ, HAZ, and BMIZ) of the studied children were below the expected average for age and sex and were negatively correlated with the duration of symptoms, especially HAZ. Similarly, an Egyptian study reported that anthropometric data (WAZ and HAZ) among Egyptian children with symptomatic H. pylori infection were significantly lower than those without infection.[8] This was also in agreement with a pediatric meta-analysis study that found an association between H. pylori infection and poor growth outcomes, especially HAZ. One of the suggested mechanisms for growth impairment is that H. pylori can lower gastric acid secretion, which leads to enteropathogen infection and diarrhea, nutritional malabsorption, and decreased food intake. However, it is difficult to prove that H. pylori is the sole cause of impaired growth because other confounding factors, such as socioeconomic status and poor nutrition, frequently coexist.[8]

Iron deficiency anemia (IDA) is a global pediatric health problem, particularly in developing countries. Several studies have reported H. pylori infection as a potential cause of iron-deficiency anemia (IDA). In the current study, hypochromic microcytic anemia was a common associated finding (58.5%), while refractory iron deficiency anemia was the cause for endoscopic intervention in a minority of cases (3%). The mean hemoglobin concentration was 10.48 ± 1.11 g/dl among our studied cases. Similar to our results, a median hemoglobin concentration of 10.5 g/dl were reported among Egyptian children with symptomatic H. pylori infection.[8] In addition, Abo El-Naga et al. found a significantly increased incidence of H. pylori infection among Egyptian children with iron deficiency anemia and refractory iron deficiency anemia compared to healthy controls who had no anemia.[19] Even in the absence of anemia, iron stores were reported to be depleted in children infected with H. pylori.[20] H. pylori-related anemia is probably due to impaired iron absorption as a result of chronic gastritis and decreased acid secretion.[21]

The current study evaluated the relation between upper GI bleeding and the occurrence of anemia among the studied cases. With the exception of cases with severe hematemesis, there was no significant difference between children with hematemesis and those without hematemesis regarding the hemoglobin level. Our results support that H. pylori-related anemia is probably due to the disease condition itself rather than the occurrence of hematemesis.[22-24]

The current study highlighted a possible relation between H. pylori infection and some of the pediatric public health problems in Egypt. Our study had its own strengths, being a big single-center study in a developing country with relatively limited resources. However, we had some limitations. One of these limitations is the lack of H. pylori-negative controls. Despite these limitations, the study expands the field of research for a condition with high morbidity and advocates for early diagnosis and treatment of symptomatic infections before the occurrence of complications.

Conclusion

A high prevalence of iron deficiency anemia was observed among children suffering from H. pylori infection, irrespective of the presence of hematemesis. The growth parameters, especially HAZ, were negatively correlated with the duration of gastric symptoms.

Data Availability: The data used to support the findings of this study are available upon request.
Conflict of interest: None. No specific funding was received for this work.

References

1. Kasai C, Sugimoto K, Moritani I, et al. Changes in plasma ghrelin and leptin levels in patients with peptic ulcer and gastritis following eradication of Helicobacter pylori infection. BMC Gastroenterol. 2016;16.

2. Taye B, Enquselassie F, Tsegaye A, et al. Effect of Helicobacter pylori infection on growth trajectories in young Ethiopian children: a longitudinal study. Int J Infect Dis. 2016;50:57-66.

3. Pacifico L, Osborn JF, Tromba V, et al. Helicobacter pylori infection and extragastric disorders in children: a critical update. World J Gastroenterol. 2014;20(6):1379-401.

4. Jones NL, Koletzko S, Goodman K, et al. Joint ESPGHAN/NASPGHAN Guidelines for the Management of Helicobacter pylori in Children and Adolescents (Update 2016). J Pediatr Gastroenterol Nutr. 2017;64(6):991-1003.

5. Kalach N, Zrinjka M, Bontems P, et al. Systematic Review and Meta-analysis of Histological Gastric Biopsy Aspects According to the Updated Sydney System in Children. J Pediatr Gastroenterol Nutr. 2022;74(1):13-9.

6. De Benoist B, Cogswell M, Egli I, et al. Worldwide prevalence of anaemia 1993-2005; WHO global database of anaemia. 2008.

7. Thomson MA, Leton N, Belsha D. Acute upper gastrointestinal bleeding in childhood: development of the Sheffield scoring system to predict need for endoscopic therapy. J Pediatr Gastroenterol Nutr. 2015;60(5):632-6.

8. Galal YS, Ghobrial CM, Labib JR, et al. Helicobacter pylori among symptomatic Egyptian children: prevalence, risk factors, and effect on growth. J Egypt Public Health Assoc. 2019;94(1):17.

9. Okuda M, Lin Y, Kikuchi S. Helicobacter pylori Infection in Children and Adolescents. Adv Exp Med Biol. 2019;1149:107-20.

10. Aguilera Matos I, Diaz Oliva SE, Escobedo AA, et al. Helicobacter pylori infection in children. BMJ Paediatr Open. 2020;4(1):e000679.

11. Spee LA, Madderom MB, Pijpers M, et al. Association between helicobacter pylori and gastrointestinal symptoms in children. Pediatrics. 2010;125(3):e651-69.

12. Al Kirdy F, Rajab M, El-Rifai N. Helicobacter pylori Infection: Clinical, Endoscopic, and Histological Findings in Lebanese Pediatric Patients. Int J Pediatr. 2020;2020:4648167.

13. Vilchis J, Duque X, Mera R, et al. Association of Helicobacter pylori infection and height of Mexican children of low socioeconomic level attending boarding schools. Am J Trop Med Hyg. 2009;81:1091-6.

14. Mera RM, Correa P, Fontham EE, et al. Effects of a new Helicobacter pylori infection on height and weight in Colombian children. Ann Epidemiol. 2006;16:347-51.

15. Egorov AI, Sempertegui F, Estrella B, et al. The effect of Helicobacter pylori infection on growth velocity in young children from poor urban communities in Ecuador. Int J Infect Dis. 2010;14e:788-91.

16. Mera RM, Bravo LE, Goodman KJ, et al. Longterm effects of clearing Helicobacter pylori on growth in schoolage children. Pediatr Infect Dis. 2012;31:263-6.

17. Richter T, List S, Muller DM, et al. Five- to 7-year-old children with Helicobacter pylori infection are smaller than Helicobacter-negative children: a cross-sectional population-based study of 3,315 children. Pediatr Gastroenterol Nutr. 2001;33:472-5.

18. Thomas JE, Dale A, Bunn JE, et al. Early Helicobacter pylori colonisation: the association with growth faltering in The Gambia. Arch Dis Child. 2004;89:1149-54.

19. Abo El-Naga AM, Abd El-laatef AM, Khalifa NA, et al. Association between Helicobacter pylori and Iron Deficiency Anemia in Preschool Children. Egypt J Hosp Med. 2020;81(3):1597-602.

20. Queiroz DMM, Harris PR, Sanderson IR, et al. Iron status and Helicobacter pylori infection in symptomatic children: an international multi-centered study. PLoS One. 2013;8(7):e68833.

21. Haile K, Yemane T, Tesfaye G, et al. Anemia and its association with Helicobacter pylori infection among adult dyspeptic patients attending Wachemo University Nigist Eleni

Mohammad Memorial Referral Hospital, Southwest Ethiopia: A cross-sectional study. PLoS One. 2021;16(1):e0245168.

22. Xu MY, Cao B, Yuan BS, et al. Association of anaemia with Helicobacter pylori infection: a retrospective study. Sci Rep. 2017;7(1):13434.

23. Lupu A, Miron IC, Cianga AL, et al. The Relationship between Anemia and Helicobacter Pylori Infection in Children. Children (Basel). 2022;9(9).

24. Demerdash DME, Ibrahim H, Hassan DM, et al. Helicobacter pylori associated to unexplained or refractory iron deficiency anemia: an Egyptian single-center experience. Hematol Transfus Cell Ther. 2018;40(3):219-25.