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Coexistence of iron deficiency anemia with Helicobacter pylori infection among children aged 6 to 12 years in Erbil city

ABSTRACT

Background: The cause of iron deficiency anemia (IDA) refractory to iron therapy is suggested the Helicobacter pylori (H. pylori) infection.

The aim of this study was to evaluate the relation between H. pylori infection and IDA among children aged between 6-12 years old.

Patients and Methods: This was a case-control study conducted for six months starting from August 2018 until February 2019 included 50 children with IDA and 50 age and sex-matched non-anemic controls, attending the pediatric outpatient clinic at Rapareen pediatric Hospital, Erbil, Iraq. All of the participants were subjected to clinical evaluation and the following investigations: CBP, serum iron, serum ferritin, and stool for H. pylori.

Results The results indicate that there was a statistically significant association between IDA and H. pylori infection. 12% of IDA cases had positive H. pylori antigen in stool in contrary to only 2% of healthy (control) group. Chi-square test was done and P-value was 0.04.

Conclusion The results of this study demonstrate an association between positive H. pylori infection and IDA in children between 6 and 12 years old. Moreover, the infection may increase the severity of anemia.

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Introduction

Iron deficiency anemia (IDA) has been recognized as a common nutritional problem in infants and young children in developing countries (1). It has been reported that more than half of children in developing countries suffer from IDA mainly due to poor nutrition in the majority of cases (2) Many studies have demonstrated that IDA is associated with poor learning ability, poor memory, lack of concentration, educational failure and affects child cognitive and motor development (3,4) Knowledge about the causes of IDA in order to develop treatment and prevention strategies should be in the top of health research agenda, especially in the developing countries. Numerous risk factors for IDA have been recognized such as inadequate iron intake and absorption, increased requirements of iron during growth, and excessive losses of iron.

The high prevalence of combined H. pylori infection and ID/IDA in developing countries suggests that infection with this bacterium may be a cause of ID/IDA. Possible mechanisms include increased iron uptake by the H. pylori bacterium (5), a considerable amount of researches have focused on the role of H. pylori infection on a wide spectrum of gastrointestinal disorders that vary from asymptomatic gastritis to peptic ulcer, and also gastric carcinoma and MALT (mucosa-associated lymphoid tissue) lymphoma(6). The prevalence rate of H. pylori infection was higher in developing countries than

in developed countries. Low socioeconomic status, crowded families and poor sanitary indications in childhood were related to the high prevalence of H. pylori infection (7) However, the rates of infection range from more than 80 percent in developing the world to less than 40 percent among industrial countries (8). On the other hand, the widespread use of treatment against H. pylori infection has led to decrease dramatically in the prevalence of infection in developed countries. High rates of H. pylori was reported from north and south area (>85%) in Iran which was associated with gastrointestinal ulcer and cancer (8-10). During the past three decades, it is reported that H. pylori may influence some extra-gastrointestinal diseases such as idiopathic thrombocytopenic purpura, anemia and allergic diseases.6,11 an association between pediatric IDA and H. pylori has been established(12). Dufour et al. (13). This possible relation between IDA and H. pylori infection was first noticed in 1993 and after that multiple studies were conducted to assess the role of this infection on IDA. However, it is still a controversial issue, despite many studies showing the negative impact of H. pylori on iron status (11). The aim of this study was to evaluate the association between H. pylori infection and IDA among school-aged children at Rapareen Pediatric hospital in Erbil, Some authors associate iron deficiency anemia with H. pylori infection, because of the chronic gastritis it produces and consequent malabsorption

of iron from food (14, 15) colonization by *H. pylori* occurs during childhood and, if left untreated, remains a chronic infection into adulthood. A multi-country study of Latin American school children found an *H.pylori* prevalence of 47.7%, but not associated with anemia(16)However, it is difficult to accurately estimate *H. pylori* infection's contribution to the development of anemia in children, since precision depends on the extent of infection, symptom severity and nutritional status(14,15)

Aim of the study

The aim of our study was to know the relationship between iron deficiency anemia and *H.pylori* infection among children their ages are between 6_12 years old.

Material & methods

This was a case-control study conducted for six months starting from August 2018 until February 2019 with prospective collection of demographic, clinical, diagnostic and laboratory data included 50 children with IDA and 50 age and sex-matched non-anemic controls, attending the pediatric outpatient clinic at Rapareen pediatric Hospital, Erbil, Iraq.

We studied the relation between IDA & *Helicobacter pylori* infection in these cases. All of the participants were subjected to clinical evaluation and the following investigations: CBP, serum iron, serum ferritin, and stool for *H. pylori*.

Those patients visited Rapareen pediatric hospital either for poor oral intake, pallor, and fatigue or for a routine checkup. The data were collected by an interview of patient's caregivers or from the patient him/herself through a prepared questionnaire, designed for this study, containing demographic description, nutritional status assessment. The aim of the study was explained well to each caregiver, and informed verbal consent was taken from all individuals. The protocol of the study was approved by the scientific and ethical committees of the Kurdistan Board for Medical Specialties.

In our study, the inclusion criteria were children between 6 &12 years

Exclusion criteria were::

1. Children with positive stool analysis for parasitic infestation
2. Anemic children due to causes other than IDA

All patients were assessed well by taking a thorough history regarding nutritional intake, physical examination including clinical features of pallor, also anthropometric measurements were measured including weight and height.

All the patients did the following investigations by taking two cubic centimeters of blood & a stool specimen were also taken from each of them

1. CBP. Done by two types of automated hematology analyzer apparatuses measuring the blood count (Coulter) named: (Medonic & Mythic 22) the analyzer was calibrated with

reference methods and had regular quality control program. Then had been read by a hematologist through a microscope.

2. IRON STUDY. (S.IRON, S.FERRITIN) the serum iron screened by a kit (POINTE SCIENTIFIC Inc., CA, USA), and serum ferritin was measured using immunoassay (Roche Diagnostics GmbH, Mannheim, Germany). The analyzer was calibrated with reference methods and had regular quality control program. The iron study done by two apparatuses named (Gesam chem 400 & Cobas c 311 by Hitachi) and both are worked as auto analyzers.

3. STOOL FOR H.pylori

Done by H. pylori extraction buffer that mixed with the stool sample then

measured by special kit named (ATG Biotech Co., Ltd. RAPID diagnostic test)

Stool antigen test (SAT) is a noninvasive method with good sensitivity and specificity, 94% and 97% respectively in the global meta-analysis, in the diagnosis of H. pylori infection (17)

The data recorded on a specially designed direct questionnaire, collected and entered in the computer and then analyzed using the Statistical Package for Social Sciences (SPSS, version 22). Chi-square test of association was used to compare proportions. Any p-value of ≤ 0.05 was considered statistically significant.

Result

Table 1: Relationship between H. pylori infection & the study groups (IDA patients & healthy control

H. pylori	Study groups		Total
	IDA	Control group	
Negative	44	49	93
	88%	98%	93%
Positive	6	1	7
	12%	2%	7%
Total	50	50	100
	100%	100%	100%

The results of Table 1 indicate that there was a statistically significant association between IDA and H. pylori infection. 12% of IDA cases had positive H. pylori antigen in stool in contrary to only 2% of healthy (control) group. Chi-square test was done and P-value was 0.04.

Table 2: Relationship between gender and H. pylori among IDA patient

Gender	H. pylori		Total
	Negative	Positive	
Male	26	3	29
	89.7%	10.3%	100%
Female	18	3	21
	85.7%	14.3%	100%
Total	44	6	50
	88%	12%	100%

The results show no significant association between gender (male & female) & H.pylori infection among IDA patients and the P-value was (P: 0.67)

Table 3 Relation between nutritional status in healthy and failure to thrive and H.pylori among IDA patients

Nutritional status	H. pylori		Total
	Negative	Positive	
Healthy	28	3	31
	90.3%	9.7%	100.0%
Failure to thrive	16	3	19
	84.2%	15.8%	100.0%
Total	44	6	50
	88.0%	12.0%	100.0%

In our study, there was no significant association between nutritional status in (healthy 31 cases) and (failure to thrive 19 patients) & H.pylori infection among IDA patients. P: 0.51

Table 4: The relation between H. pylori infection & age, anthropometric measures, blood indices & iron study

Variables	H. pylori	N	Mean	Std. Deviation	P-value
Age	Negative	44	8.32	1.70	0.99
	Positive	6	8.31	0.51	
weight Kg	Negative	44	24.30	5.20	0.45
	Positive	6	22.66	2.52	
Height cm	Negative	44	124.98	8.95	0.98
	Positive	6	124.91	2.97	
RBC	Negative	44	4.97	0.27	0.98
	Positive	6	4.97	0.15	
Hb	Negative	44	10.59	0.58	0.10
	Positive	6	10.13	0.93	

PLT	Negative	44	359.06	73.46	0.45
	Positive	6	336.16	37.34	
MCV	Negative	44	68.24	2.46	0.36
	Positive	6	67.31	0.95	
MCH	Negative	44	19.28	1.43	0.26
	Positive	6	18.56	1.66	
RDW	Negative	44	18.60	1.61	0.03
	Positive	6	15.85	7.89	
Ferritin	Negative	44	4.58	1.49	0.76
	Positive	6	4.35	1.77	
Iron	Negative	44	32.38	7.13	0.66
	Positive	6	33.71	5.61	

In our study showed that there was a significant relationship between RDW level and H.pylori infected patients and the p-value was (0.03) while there was no any significance between H.pylori infection and age, weight, height, RBC, Hb, PLT, MCV, MCH, Ferritin & Iron.

Table 5 shows the relation between growth parameters, blood indices & iron study among control healthy children.

Variable	H. pylori	N	Mean	S.D	P-value
Age	Negative	49	8.31	1.54	0.90
	Positive	1	8.50	0	
Weight	Negative	49	25.80	5.07	0.95
	Positive	1	25.50	0	
Height	Negative	49	127.83	8.65	0.89
	Positive	1	129.00	0	
RBC	Negative	49	4.93	0.22	0.73
	Positive	1	5.01	0	
Hb	Negative	49	12.89	0.70	0.99
	Positive	1	12.90	0	
PLT	Negative	49	346.89	61.16	0.88
	Positive	1	338.00	0	
MCV	Negative	49	85.22	4.29	0.84
	Positive	1	86.10	0	
MCH	Negative	49	28.91	1.79	0.54
	Positive	1	27.80	0	
RDW	Negative	49	13.48	0.92	0.90
	Positive	1	13.60	0	.
Ferritin	Negative	49	53.66	23.67	0.95
	Positive	1	55.00	0	
Iron	Negative	49	86.79	14.81	0.68
	Positive	1	93.00	0	.

In table 5 there was no significant association between age, weight, height, RBC, Hb, PLT, MCV, MCH, RDW, Ferritin, Iron & H. pylori infection among control healthy children.

Discussion:

In this study, we aimed to evaluate the association between H. pylori infection and IDA among children between 6-12 years old. The results of this study revealed that there was a significantly higher rate of H. pylori infection among studied group than healthy controls, demonstrating a significant association between H. pylori infection and IDA among children aged between 6 and 12 years old. This came in agreement with Darvishi et al(18).who reported an association between H. pylori infection and IDA among pediatric patients where they found that 80.3% of IDA cases and 14% of non-anemic controls had a positive H. pylori infection and the difference between two groups was statistically significant ($P < 0.0001$).also, our study resembled an Iranian cross-sectional study was carried out by Zamani et al., during the year 2005 and 2006 on 1665 students age of them between 6 and 12 years old in Tehran to assess the relationship between serum ferritin levels and H. pylori infection(19). The rate of H. pylori seropositivity was 26 percent and 29 percent of children had IDA. They found that there is no real association between H. pylori infection and low serum ferritin levels or iron deficiency anemia. This finding is comparable to another study

in Tehran on children aged 2-14 (median: 7.1) years with a case-control design including 100 consecutive cases with H. pylori infection and 109 age-matched consecutive non-infected controls (20). They reported that 19% of cases and 21.1% of controls had iron deficiency anemia ($P=0.7$), and there was no relation between H. pylori infection and IDA However, an analytical study in 2008 on 100 IDA children aged 7- 12 years in Ilam city (located in west of Iran) found a significant negative correlation of H.pylori antibody level with serum iron and ferritin and its positive correlation with TIBC levels ($P < 0.001$) (21).Furthermore, recent meta-analyses have indicated that H. pylori infection is associated with IDA. The present work showed NO significance male predominance in H. pylori positive IDA patients. This came against the study done by Zamani et al., who reported that H. pylori infection was significantly more common in boys than girls ($p = 0.029$) (19)

The current study showed that parameters of iron deficiency anemia (Hb, MCV, HCT, and serum ferritin) were lower in H. pylori positive IDA patients than those of H. pylori negative IDA cases. And our study was resemble about –Talib et al.(11) This finding showed that there is a

negative effect of *H. pylori* infection on iron stores and confirmed that *H. pylori* infection could increase the severity of anemia and support the findings of other studies which suggested that eradication of *H. pylori* infection improve IDA treatment and help improvements in iron status(18,22,23).

In 2010, Zhang et al., in a meta-analysis (24), found that *H. pylori* infection may affect the absorption of oral ferrous and eradication of the infection may improve the treatment of iron-deficiency. Also, in another meta-analysis, Yuan et al (25) had reported a similar result. Regarding the diagnosis of iron deficiency anemia, a low hemoglobin level along with a high level of anisocytosis detectable by red cell distribution width (RDW) prove to be good indicators of changes in the blood due to depleted iron stores (26). In this study, we found that there was a significant relationship between RDW level and *H. pylori* infected patients while there was no relationship between RDW level and *H. pylori* infection among control healthy children. In a study done in Turkey 2015 revealed that erythrocyte distribution width (RDW) is the first variable which changes in iron deficiency anemia seen in children by complete blood count. (27)

Conclusion

In conclusion, the results of this study demonstrate an association between positive *H. pylori* infection in stool and IDA in children between 6 and 12 years old in Rapareen pediatric hospital in -Iraq-Erbil city. Moreover, the infection may increase the severity of anemia. 12% of IDA cases had positive *H. pylori* antigen in stool in contrary to only 2% of healthy (control) group.

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