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Prevalence of *Helicobacter Pylori* infection in children with iron deficiency anemia admitted in tertiary care hospital

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ABSTRACT

Background: Iron deficiency anemia (IDA) can result from both physiological and pathological events, the etiology of underlying IDA should be determined. *Helicobacter pylori* infection in children has mostly been associated with recurrent abdominal pain, gastric dyspepsia, or duodenal-ulcer. Other extra-digestive tract conditions such as iron deficiency or IDA have been recently related to the *H. pylori* infection. **Aims and Objectives:** To find out the prevalence of *H. pylori* infection in children aged 2–18 years with IDA in a tertiary care hospital. **Materials and Methods:** A cross-sectional observational study was carried out in the Department of Paediatrics, Dr. S.N. Medical College, Jodhpur for a period of 1 year. A total of 52 children aged between 2 and 18 years with anemia (as per the WHO criteria of anemia) were evaluated for complete blood count, peripheral blood film and serum ferritin, serum iron, total iron-binding capacity (TIBC), Upper gastrointestinal endoscopy and two biopsy specimen evaluated for *H. pylori* and histopathological changes. Normally distributed data means were compared using student's t-test unpaired and paired. Proportions were compared using Chi-square or Fisher's exact test. **Results:** The prevalence of H. pylori in our study population was 32.69%.In children with H. pylori infection mean S.iron was 25.78 ± 10.24 µg/dl, mean S.TIBC 544.66 ± 91.68 µg/dl, and mean S.ferritin was 6.07 ± 3.00 µg/dl. There was statistically significant difference in serum iron, S.TIBC and S.ferritin between children having *H. pylori* infection and without *H. pylori* infection ($P < 0.001$). **Conclusion:** There is an association of IDA and *H. pylori* infection. Therefore prevention and eradication of *H. pylori* infection might be helpful to prevent IDA, especially in those patients who are not responding to usual treatment.

Key words: *Helicobacter pylori* infection; Iron deficiency anemia; Serum iron

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INTRODUCTION

According to the World Health Organization (WHO), anemia is the ten most serious health problem in the world.[1] Several factors contribute to the occurrence of anemia and nearly half of (43%) the anemia cases in childhood are due to iron deficiency (ID) which is thought to be the most common cause of anemia globally.[2] The exact cause of ID anemia (IDA) could not be identified in 20% of cases, despite all routine examinations even including gastrointestinal (GI) endoscopy and serologic markers for celiac disease. The global prevalence of *Helicobacter pylori* (*H. pylori*) infection is more than 50%.[3] *H. pylori* infection is very prevalent in developing countries and it is markedly more prevalent at younger groups and in lower socioeconomic status.[4] However, most of the infected people (>70%) are asymptomatic while <30% symptomatic.[5,6] In developed countries, the overall prevalence of this infection in young

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children is <10% and up to 50% of children living in poor socio-economic conditions are infected and 80% of children <10 years are infected in developing countries. Prevalence of infection in India is 22%, 56%, and 87% in 0–4, 5–9, and 10–19 years age group, respectively. The exact relationship between *H. pylori* infection and IDA is still a matter of debate. In many studies, it was found that infection with *H. pylori* causes chronic gastritis. Chronic infection of *H. pylori* is usually asymptomatic but it may predispose infected persons to gastric and duodenal ulcers, gastric cancers, and mucosal-associated lymphoid tissue lymphomas. These lesions can cause chronic GI bleeding, resulting in IDA.[7]

As most studies in which *H. pylori* infection detected as a cause of IDA has been done in adults and *H. pylori* causing IDA in children, literature regarding this is limited. Hence, we have planned this study to know the prevalence of *H. pylori* infection in iron-deficient anemic children.

Aims and objectives

To find out the prevalence of *H. pylori* infection in children aged 2–18 years with IDA in a tertiary care hospital.

MATERIALS AND METHODS

A cross-sectional observational study was carried out in the Department of Paediatrics, Dr. S.N. Medical College, Jodhpur for a period of one year after approval from the institutional review committee of Dr. S.N. Medical College, Jodhpur. 52 Children admitted with IDA aged 2–18 years with S. Ferritin level <12 μg/L, S. Iron levels <50 μg/dL, and parents who gave written consent for the upper GI endoscopy (gastric biopsy) of their children were included in the study. Children with peptic ulcer, celiac disease, and intestinal parasites and children with a present or past history of GI bleeding, esophageal varices, coagulation disorders, inflammatory diseases, acquired or congenital immunosuppression, hematologic disorders, neoplasia or an anatomical obstacle preventing endoscopy Upper GI endoscopy performed to look for atrophy or gastritis in the stomach were excluded from the study.

All children after complete history and clinical examination evaluated for complete blood count, peripheral blood film and serum ferritin by Roche E-170 Ferritin "ECLIA" method, serum iron,and total iron-binding capacity(TIBC) by Modification of the Automated AAII-25 Colorimetric Method. Upper GI endoscopy were done with (Olympus endoscope CV- 15/GIF- XP 150 W (for children <5 years)/Karl Storz-Endoscope (>5 years children). Two gastric biopsies of all included patients, one from the antrum and the other from corpus of the stomach taken during endoscopy and sent in formalin solution to be examined after staining with Haematoxylin-Eosin stain for histopathological changes (will be classified as normal, inflammation, atrophy, and intestinal metaplasia) by a pathologist, who will be blinded to the study design. Biopsy specimens were also evaluated for *H. pylori* density which is classified according to the Sydney system[8] as chronic inflammatory infiltrate, inflammatory activity (polymorphonuclear cells), glandular atrophy, and intestinal metaplasia were score (0; none, 1; mild, 2; moderate, or 3: severe). Gastritis that was limited strictly to the antrum or corpus was classified accordingly as antrum or corpus- predominant. For each location (corpus and antrum) the severity score for gastritis is equal to the highest score for inflammation (or atrophy) in the biopsy sections.

SPSS Inc., Chicago IL, version 24.0 for windows used for data analysis. Quantitative variables were estimated using mean, median, and standard deviation. Normality of data was checked by measures of Kolmogorov Smirnov tests of normality. For normally distributed data means were compared using student's t-test. Proportions were compared using Chi-square or Fisher's exact test. $P<0.05$ is considered significant.

RESULTS

In our study 17 (32.69%) out of 52 children were *H. pylori* positive. The prevalence of *H. pylori* in our study population was 32.69%. The baseline characteristics of the patients are summarized in Table 1. Maximum (35.29%) *H. pylori* positivity was found in 2–5 years of age group and mean age was 8.67±5.26 years in these cases. In children with *H. pylori* infection mean serum iron was 25.78±10.24 μg/dl, mean S.TIBC 544.66±91.68 μg/dl, and mean serum ferritin was 6.07±3.00 μg/dl. There was statistically significant difference in serum iron and serum TIBC and serum ferritin between children having *H. pylori* infection and without *H. pylori* infection ($P<0.001$) (Table 1).

The most common presenting symptom was pain abdomen (40.38%) followed by weakness (32.69%), loss of appetite (19.23%) in both *H. pylori* positive and negative patients and pain abdomen (41.18%) was the most common presentation in children with *H. pylori* infection. On endoscopic examination, 64.71% cases were having gastric pallor (64.71%) followed by esophageal pallor in 52.94% while 41.18% cases were having mild villous atrophy in the duodenum (Table 2).

Children with *H. pylori* infection 58.82% had mild chronic antral gastritis followed by 23.53% had moderate chronic

Table 1: Baseline characteristics of study population

Parameter	*Helicobacter Pylori* status			P-value
	Positive (%)	Negative (%)	Total	
	17 (32.69%)	25 (67.31%)	52 (100%)	
Mean Age (years)	8.67±5.26	9.18±4.15	9.01±4.50	0.79
BMI (kg/m^2)	15.52±3.40	15.46±2.82	15.48±2.99	0.9991
Hb (g/dl)	4.73±1.54	5.06±1.60	4.84±1.55	0.03
MCV(µm^3)	52.97±9.11	51.74±7.40	52.57±8.54	0.69
Mean Iron(µg/dl)	25.78±10.24	34.69±19.93	30.50±15.03	<0.0001
Mean TIBC(µg/dl)	544.66±91.68	497.65±75.87	521.50±83.93	<0.0001
Mean Ferritin(µg/dl)	6.07±3.00	6.70±2.26	6.55±2.53	<0.0001

BMI: Body mass index, MCV: Mean corpuscular volume, TIBC: Total iron binding capacity

Table 2: Endoscopy findings in study population

Endoscopy findings	*Helicobacter Pylori* (n=52)		P-value
	Present (n=17)	Absent (n=35)	
	n (%)	n (%)	
Oesophagus			
Normal	6 (35.29)	27 (77.14)	0.01
Hyperaemic	5 (29.41)	2 (5.71)	0.02
Pallor	6 (35.29)	7 (20.00)	0.03
Stomach			
Normal	6 (35.29)	26 (74.28)	0.60
Pallor	11 (64.71)	9 (25.71)	0.02
Duodenum			
Normal	8 (47.06)	26 (74.28)	0.03
Mild villous atrophy	7 (41.18)	6 (17.14)	0.01
Moderate villous atrophy	1 (5.88)	1 (2.85)	0.86
Scalloping	1 (5.88)	2 (11.43)	0.02

antral gastritis and 5.88% had severe chronic antral gastritis. There was statistically significant (P<0.05) difference seen in the all grades of antral gastritis in *H. pylori* positive and negative patients. Patients with mild chronic antral gastritis had maximum *H. pylori* positivity (58.82%) (Table 3).

Patients with severe chronic antral gastritis had lowest mean S.iron and mean S.ferritin and S.TIBC but their correlation was found statistically non-significant (Table 4).

According to updated Sydney system *H. pylori* density was mild in 19.23% cases, moderate in 11.54% and severe in 1.92%cases.

DISCUSSION

In the present study prevalence of *H. pylori* infection was 32.69%. Choe YH et al[16] did a study in 216 children of IDA, aged 3–14 years, who were tested for *H. pylori* infection by 13C-urea breath test and *H. pylori* positivity was 22.7%. Zahmatkeshan et al[9] did study in 71 children to find out association between *H. pylori* and IDA. *H. pylori* infection was detected in 59.1% of patients which was more than that of our study.

Maximum (35.29%) *H. pylori* positivity was found in 2–5 years of age group. Mean age was 8.67±5.26 years in *H. pylori*-positive patients. Study conducted by Goldman et al[10] in 395 children in the age group of 2–17 years were having mean age of 9.91±3.1 years and similar study conducted by Gulen et al[11] in the age group between 9 and 17 years and mean age was 14.6±9.5 years.

In the present study most common presenting symptom was pain abdomen (40.38%) followed by weakness (32.69%) and in children with *H.pylori* infection most common presenting symptom was pain abdomen (41.18%). Kurekci et al[12] found that IDA children with *H. pylori* infection had complaints of chronic abdominal pain, nausea, vomiting, and loss of appetite. Study conducted by Goldman et al[11] in children who were having with *H. pylori* infection, most common presenting symptom was abdominal pain and results of these studies are same as that of our study.

In our study, there was statistically significant difference in serum iron and S.TIBC and S.ferritin between children having *H. pylori* infection and without *H. pylori* infection (P<0.001). Qujeq et al[13] found serum iron and total iron-binding capacity in *H. pylori* positive group were lower than in the control group (P=0.153). The mean of ferritin was significantly lower in *H. pylori* positive group than *H. pylori* negative group (P=0.047) but we have documented significant correlation with all three parameters in *H. pyroli* positive and negative patients which shows that with decrease in serum levels of iron and ferritin, there are more probability of detection of *H. pylori* infection.

We have found on histopathological examination that patients with positive *H. pylori* infectivity have mild chronic antral gastritis (58.82%) as the most common histopathological finding which showed that *H. pylori* positivity does not depend on the severity of antral gastritis. Gulen et al[11] conducted similar study in pediatric

Table 3: Histopathological findings of study population

Histopathological finding	*Helicobacter Pylori*		Total	P-value
	Present	Absent		
	n-17 (%)	n-35 (%)	n-52 (%)	
Normal	2 (11.76)	16 (45.71)	18 (34.62)	0.0021
Mild chronic antral gastritis	10 (58.82)	13 (37.14)	23 (44.23)	0.0032
Moderate chronic antral gastritis	4 (23.53)	6 (17.14)	10 (19.23)	0.0001
Severe chronic antral gastritis	1 (5.88)	0 (0.00)	1 (1.92)	0.034

Table 4: Correlations between mean S.iron, S.TIBC, S.ferritin and Histopathological findings

Histopathological finding	Iron (µg/dl)	TIBC (µg/dl)	Ferritin (µg/dl)
	Mean±SD	Mean±SD	Mean±SD
Normal	26.96±11.02	552.44±104.98	6.23±2.84
Mild chronic antral gastritis	29.54±13.29	519.48±78.06	6.69±2.82
Moderate chronic antral gastritis	30.13±23.04	521.00±79.91	5.70±2.67
Severe chronic antral gastritis	26.1±0	421±0	3.5±0
P-value	0.9363	0.3219	0.6289

TIBC: Total iron binding capacity

population suffering from IDA. They found 56% abnormal endoscopic finding in their study and demonstrated antral gastritis in 21%, duodenal polyps 2%, active duodenal ulcers in 2% of patients. Pacifico et al[14] also demonstrated an association between *H. pylori* infection and antral gastritis and duodenal ulcer in children. In our study patients with severe chronic antral gastritis had lowest mean S.iron and mean S.ferritin and S.TIBC followed by moderate and mild chronic antral gastritis.

35.29% cases in our study with *H. pylori* infection patients with mild density had mild chronic antral gastritis. There was no significant statistical difference (P=0.772) in between histopathological finding and density of *H. pylori*. Sayin et al[15] in their study found *H. pylori* density in 68.6% of patients according to Sydney scoring and relation between the density of *H.pylori* and the severity of the inflammation was statistically significant (P<0.0001). This is different from our study as they included adult population in which yield of *H. pylori* bacteria is more than children.

CONCLUSION

There is an association of IDA and *H. pylori* infection, therefore prevention and eradication of *H. pylori* infection might be helpful to prevent IDA, especially in those patients who are not responding to usual treatment. We suggest screening of *H. pylori* infection and appropriate treatment in any case of refractory moderate to severe IDA, especially with clinical manifestations of GI tract in children. These results should be interpreted with caution in view of small sample size and observational data. Larger studies and interventional trials may further clarify association between ID and *H. Pylori infection* in children.

Limitations of the study

Sample size of the study was small to prove our results.

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RJ and SK-Concept and design of the study; prepared first draft of manuscript; **MU and MG-** Interpreted the results; reviewed the literature and manuscript preparation; **SV and MK-** Concept, coordination, review of literature and manuscript preparation; **SC and VSK-** Statistically analyzed and interpreted, preparation of manuscript and revision of the manuscript.

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