Journal of the Egyptian Society of Parasitology, Vol.44, No.3, December 2014
J. Egypt. Soc. Parasitol. (JESP), 44(3), 2014: 695- 708

ASSESSMENT OF DIAGNOSTIC AND THERAPEUTIC APPROACHES OF *HELICOBACTER PYLORI*-ASSOCIATED IRON DEFICIENCY AND ANEMIA IN CHILDREN WITH DYSPEPTIC SYMPTOMS

By
MOHIEE EL-DEEN ABD EL-AZIZ AWAD[1], SALEH MOHAMED AMIN[1] AND SAIED MOHAMED ABDOU[2]
Departments of Pediatrics[1] and Clinical Pathology[2], Faculty of Medicine, Tanta University, Tanta, Egypt

Abstract

This study assessed the diagnostic approaches of *Helicobacter pylori* (HP)-associated iron deficiency (ID) and anemia (IDA) in children with dyspeptic symptoms and evaluated the effects of simultaneous anti-*H. pylori* (anti-HP) therapy and oral iron in comparison with each of anti-HP therapy and oral iron therapy alone, on iron status as assessed by serum soluble transferrin receptor (sTfR) level.

Two hundreds children with dyspeptic symptoms were subjected to clinical evaluation, stool examination, CBC, biochemical assays for serum iron parameters and measurements of serum IgG antibodies to HP and serum sTfR level by ELISA. Sixty children were found to have HP-associated ID or IDA and were randomly divided into 3 groups (20 children each). GA received 2-week anti-*HP* therapy plus 90-day oral iron, and GB received 2-week anti-*HP* therapy alone whereas group C received 90-day oral iron alone. Re-evaluation of the 3 groups was performed after 3 months of treatment initiation by repeat CBC and serum sTfR level.

Children (45%) were *HP*-seropositive. The mean values of serum sTfR were significantly higher in *HP*-positive group and in *HP*-positive children with IDA than in *HP*-negative group and in *HP*-negative children with IDA although no significant differences were noted in hematologic variables and iron parameters between the corresponding groups and children. As regard treatment groups, there were significant improvements in the mean values of indices of IDA status (Hb, MCH, MCV, sTfR) and ID status (sTfR) at 3 months of treatment initiation compared with their baseline values after anti-*HP* triple therapy either with oral iron or without oral iron whereas the control children who were treated with oral iron alone showed insignificant changes despite oral iron administration. The improvements in these parameters were significantly greater in groups of children who received anti-*HP* therapy either combined with iron or alone when compared with those who did not receive anti-*HP* therapy. Their magnitudes were significantly higher among children receiving anti-*HP* therapy combined with oral iron when compared with that receiving anti-*HP* therapy alone.

Key words: *Helicobacter pylori*, iron deficiency, iron deficiency anemia, serum soluble transferrin receptor, children.

Introduction

Several clinical reports have demonstrated that *Helicobacter pylori* (*HP*) gastric infection has emerged as a new cause of refractory *HP*- associated iron deficiency anemia (IDA) (Barabino, 2002). The role of *HP* and its eradication in IDA patients with *HP*-positive gastritis has been unclear (Chen *et al,* 2007). Although the mechanisms by which *HP* infection can cause IDA are still unclear, several possibilities have been suggested. Besides the occult gastrointestinal bleeding and the competition for dietary iron, *HP* infection can affect the gastric body and initiate development of atrophic body gastritis that can in turn cause decreased gastric acid secretion and increased intragastric pH. Infection with HP adversely influences the composition of the gastric juice; for example, in terms of its acidity and ascorbate content, both of which are critical for normal iron absorption (Bini, 2001; Ciacci *et al,* 2004; Ashorn, 2004; Koike *et al,* 2001). These findings suggest that the physiological mechanisms that are necessary for the absorption of alimentary iron in the duo-

denal mucosa are impaired in patients with HP-positive gastritis and IDA (Chen *et al*, 2007; Konno *et al*, 2000).

It was demonstrated that refractory IDA is not sensitive to oral iron treatment, especially in patients with HP-positive gastritis. It is important to elucidate the relation of IDA to HP infection and the effect of HP eradication on the treatment of IDA (Chen et al 2007). It has been suggested that HP eradication can reverse the negative effect of HP infection on iron absorption and lead to improvement of IDA and several authors have reported that eradication of HP may be followed by an improved response to oral iron in previously refractory IDA patients with HP-positive gastritis in both children and adults. Therefore, it has been proposed that HP infection needs to be eradicated to treat absolutely IDA in such patients (Chen et al 2007; Konno *et al*, 2000; Hacihanefioglu et al, 2004; Kurekci et al, 2005; Choe et al, 1999; Choe et al, 2001).

However, some studies have demonstrated that HP infection does not induce IDA in prepubescent children under 12 years of the age (Santos *et al*, 2009). However, most of the studies regarding HP-associated IDA were focused on estimation of serum ferritin level (Seo *et al*., 2001; UmaKiran *et al*, 2011). Although serum ferritin is used as an indicator of iron stores, its value is limited because ferritin is an acute-phase reactant and its level increases sharply in the presence of inflammation and infection (Dennison, 1999). On the other hand, serum soluble transferrin receptor (sTfR) has been recently introduced as a promising new tool for diagnosing iron deficiency (ID) and is considered a sensitive indicator of ID in inflammatory states and in anemia of chronic diseases because its concentration is not affected by the acute phase response (Ragab *et al,* 2002; Speeckaert *et al,* 2010; Wang *et al,* 2011)**.** It was reported that high concentrations of sTfR indicate iron-deficient erythropoiesis rather than levels of iron storage in the tissues in anemic patients with inflammation (Siebert *et al,* 2007) and is considered a characteristic feature of functional ID, a situation defined by tissue ID despite adequate iron stores (Suominen *et al,* 1998). Serum level of sTfR gradually decreased to normal with the restoration of normal iron status during the process of iron supplementation and could be used as a specific indicator for assessing efficacy of iron supplementation (Tian *et al,* 2004). Serum level of sTfR were examined as a specific indicator for assessing iron status in patients with *HP*-associated ID or IDA (Choi, 2006; Vendt *et al,* 2011) and as a specific indicator for assessing efficacy of HP eradication and iron supplementation on iron status in such patients (Sarker *et al,* 2008).

The work aimed to assess diagnostic approaches of *HP*-associated ID or IDA in children with dyspeptic symptoms and evaluated effects of simultaneous anti-*HP* triple therapy and oral iron supplementation as compared with each of anti-*HP* triple therapy and oral iron therapy alone, on iron status assessed by serum sTfR concentrations as a specific indicator for functional iron status.

Patients, Materials and Methods

A total of two hundreds (200) children with dyspeptic symptoms such as chronic upper abdominal pain, vomiting and anorexia who attended the Outpatient Gastroenterology Clinic of Pediatric Department of Tanta University Hospital were eligible for the present study from September 2010 to March 2012. Their ages ranged from 5 to 16 years. They were 104 males and 96 females. Exclusion criteria of this study included the following: children with parasitic infestations or any chronic diseases that may result in anemia; children who received anti-HP treatment or anti-secretory drugs during the previous month; children taking iron supplements during the last three months; children having upper or lower gastrointestinal bleeding; and children who did not complete the follow-up period. The study was approved by the Postgraduate Clinical Research and Ethics Committee of Faculty of

Medicine, Tanta University. Patients were enrolled after obtaining an informed consent from their parents. Clinical assessment was done with special emphasis on the manifestations of IDA.

Laboratory examinations: 1- Stool examination to exclude parasitic infestations. 2- CBC: Hb concentration, RBC count, reticulocytic count, MCV, MCH, MCHC and red cell distribution width (RDW). 3- ELISA serum IgG antibodies to *H. pylori* level. Samples with concentrations >20U/mL were considered positive for IgG antibodies to *H. pylori* (Choi, 2006) 4-Biochemical assays for serum ferritin level (SF), serum iron (SI) and total iron binding capacity (TIBC) 5- Serum level of sTfR by ELISA After Manufacturers' Recommendations.

Diagnosis of *H. pylori* infection was based on positive serum IgG antibodies to *H. pylori* by ELISA. Diagnosis of ID was based on elevation of sTfR concentrations (sTfR >8.3 mg/L in children aged 4-7 years, sTfR > 5.7 mg/L in children aged 7-12 years and sTfR > 4.5 mg/L in older children) in the presence of normal Hb level (Vendt *et al*, 2011). Diagnosis of IDA was based on elevation of sTfR concentrations as mentioned for ID in addition to decreased blood hemoglobin level below the thresholds determined by the WHO for IDA, reduced MCV < 75 fL and increased RDW > 14.5. Thresholds of Hb level determined by WHO: Hb < 110 g/L in children aged less than 6 years, Hb < 115 g/L in children aged 7-12 years, Hb < 130 g/L for boys and Hb < 120 g/L for girls in children aged 13-18 years (WHO 2004).

Sixty children had HP-associated iron deficiency (ID) or anemia (IDA) and were randomly divided into 3 groups of 20 children each. GA: received 2 weeks anti-*HP* plus 90-day oral iron, and GB: received 2-week anti- *HP* therapy alone whereas GC received 90-day oral iron alone. GC served as a control. Children within each G were divided into 2 subgroups (ID and IDA) based on Hb level and sTfR concentrations. Triple therapy for *HP* infection included a combination of omeprazole (0.7mg/kg/day divided into two doses, maximum dose 20mg twice daily), amoxicillin (50mg/kg/day in two doses, maximum dose 1.0 g twice daily), and clarithromycin (250mg twice daily for those less than 10 years old or 500mg twice daily for children more than 10 years old) for 2 weeks. Oral iron therapy as ferrous sulphate was given in a dose of 6 mg (elemental iron) /Kg/day for 3 months supplemented with ascorbic acid in a dose of 50 mg daily to enhance iron absorption (Sarker *et al*, 2008). Re-evaluation of the 3 Gs was performed after 3 months of treatment initiation by repeat CBC & measuring sTfR level.

Statistical analysis: Qualitative data were expressed as frequency and percentage whereas quantitative data were expressed as M±SD unless otherwise stated. Statistical significance between means was calculated by Student's t-test, analysis of variance followed by Tukey's test as appropriate. Qualitative data were analyzed by Chi-Square (X^2) test. P-value of <0.05 was significant.

Results

Children 90/200 (45%) were *HP*-seropositive and 110 (55%) children were *HP*-seronegative. The IDA was present in 40 (44.4%) among those who were *HP*-seropositive and in 36 children (32.7%) among those who were *HP*- seronegative without significant differences (Tab. 1). Iron deficiency (ID) based on elevated serum levels of sTfR were shown among non-anemic children according to HP seroreactivity (Tab. 2). Twenty children of non-anemic *HP*-positive and 24 of non–anemic *HP*-negative showed high sTfR levels consistent with elevated values of sTfR for ID status without significant differences. There were significant differences between *HP*-positive and negative children with respect to age, indices of pain severity, socioeconomic condition, family size, weight/age Z score, and weight/ height Z score. Compared with HP-negative children, HP-positive children were older in age, more often from large families and lower socioeconomic classes and had

growth impairment (Tab. 3). Mean sTfR conc. values were significantly higher in *HP*-positive than in HP-negative children (6.92±2.37 vs. 4.54±1.27 mg/L respectively), without significant differences in iron parameters and hematologic variables between two groups suggesting a higher occurrence of subclinical iron deficiency and anemia among *HP*-infected children (Tab. 4). Mean values of serum sTfR conc. were significantly higher in anemic *HP*-positive than in anemic *HP*-negative children (10.4±1.48 vs. 7.97±1.68 mg/L respectively) although, mean values of iron parameters and hematologic variables were not significant between 2 groups (Tab. 5). This showed that serum sTfR concentration proved useful in evaluating IDA in *HP* patients. sTfR serum levels (Fig. 1) in HP-positive & *HP*-negative and in anemic *HP*-positive & anemic *HP*-negative children.

Table 1: Distribution of iron deficiency anemia among children according *to H. pylori* seroreactivity.

H. pylori-positive children (n=90)		*H. pylori*-negative children (n=110)		χ^2	P-value
Anemic n(%)	Non-anemic No. (%)	Anemic No. (%)	Non-anemic No. (%)		
40 (44.4%)	50 (55.6%)	36 (32.7%)	74(67.3%)	2.41	2.41

Table 2: Distribution of iron deficiency among non-anemic children according *to H. pylori* seroreactivity.

H. pylori-positive children (n=50)		*H. pylori*-negative children (n=74)		χ^2	P-value
ID Patients No. (%)	Non- ID Patients No. (%)	ID Patients No. (%)	Non-ID Patients No. (%)		
20 (40%)	30 (60%)	24 (32.4%)	50 (67.6%)	0.45	0.501

Table 3: Clinical, demographic & anthropometric characteristics of children according *to H. pylori* seroreactivity

Variable	Positive (n=90)	Negative (n=110)	P-value
Age (years) mean ±SD	12.7 ±2.5	9.7± 2.6	< 0.05*
Sex (% M)	58	56	>0.05
Epigastric pain (%)	58	45	>0.05
Pain during night (%)	67	33	< 0.05*
Nausea and / or vomiting (%)	58	53	>0.05
Duration of symptoms (mo)	10.0±6.8	9.3± 4.9	>0.05
Duration of attack (>60min) %	42	17	< 0.05*
Frequency of attacks (≥1/wk) %	50	28	< 0.05*
Low socioeconomic status (%)	36	10	< 0.001*
No. of siblings(>3) %	83	17	< 0.001*
Family history of G.I complaints (%)	17	11	>0.05
Weight/age (z) mean ±SD	-1.1 ±1.7	-0.4± 1.2	< 0.05*
Height/ age (z) mean ±SD	-0.5 ±0.4	-0.4± 1.1	>0.05
Weight / height (z) mean ±SD	0.4±0.5	-0.1± 0.2	< 0.05*

*Significant

Table 4: Laboratory data of children according to *H. pylori* seroreactivity

Variable	Positive (n=90)	Negative (n=110)	P =value
Serum IgG titer (U/ml)	75.34±28.43	10.12±3.8	0.0001*
sTfR (mg/L)	6.92±2.37	4.54±1.27	0.001*
Iron parameters			
Serum ferritin (µg/ L)	33.6±12.1	30.2±18.4	0.425
Serum iron (µg/dl)	73.2±24.7	75.4±37.5	0.879
TIBC (µg/dl)	358.7±58.3	363.4±45.6	0.642
TS (%)	22.6±11.8	21.7±11.8	0.817
Hematologic variables			
Erythrocytes count(1012/L)	4.4±0.5	4.3±0.3	0.879
Reticulocytes count (%)	0.68.±0.24	0.66±0.28	0.815
Hb (g/dl)	11.26±1.69	11.62±1.15	0.625
MCV (fL)	78.85±5.17	77.46±6.95	0.465
MCH (pg)	28.57±3.06	29.08±2.38	0.501
MCHC (g/dl)	32.74±4.81	32.37±3.34	0.911

*Significant

Table 5: Laboratory data of children according to *H. pylori* seroreactivity and anemia

Variables	Postitive (n=90)		Negative (n=110)		Anemic+ve vs.- ve P-value
	Anemic (n=40)	Non-anemic (n=50)	Anemic (n=36)	Non-anemic (n=74)	
Serum IgG titer (U/ml)	76.05±28.34	63.97±24.97	11.21±4.9	10.12±3.8	0.0001*
sTfR (mg/L)	10.4±1.48	3.72±0.53	7.97±1.68	3.24±0.66	0.001*
Iron parameters					
Serum ferritin (µg/L)	11.0±7.3	34.1±9.6	9.4±6.8	36.7±17.3	0.817
Serum iron (µg/dl)	28.6±14.2	94.8±36.4	32.8±15.6	96.3±42.7	0.134
TIBC (µg/dl)	445.6±53.0	385.4±52.6	441.2±75.9	377.1±42.6	0.654
TS (%)	7.4±4.8	26.3±12.7	8.5±5.2	29.4±15.2	0.285
Hematologic variables					
Erythrocytes count (10^{12}/L)	4.2±0.3	4.8±0.7	4.3±0.2	4.7±0.6	0.754
Reticulocytic count (%)	0.66±0.24	0.70±0.11	0.65±0.12	0.67±0.22	0.912
Hb (g/dl)	9.31±0.90	12.25±0.62	9.12±0.43	12.19±0.42	0.605
MCV (fL)	71.21±4.92	79.37±6.21	70.57±7.21	79.59±3.27	0.724
MCH (Pg)	24.02±2.46	32.11±7.45	24.78±2.72	31.07±3.57	0.618
MCHC (g/dl)	27.66±2.48	33.99±1.87	28.31±1.49	34.98±1.54	0.542

Table 6: Hematological parameters before and after treatment among groups

Parameters	GA (n=20)	GB (n=20)	GC (n=20)
sTfR (mg/L)			
Pre-treatment	10.8±1.72	10.4±1.81	10.6±1.61
Post- treatment	3.7±0.61	6.4±1.72	9.2±1.44
p-value	<0.001*	0.022*	0.805
Hb (g/dl)			
Pre-treatment	9.6±0.98	9.6±0.25	9.5±0.24
Post-treatment	14.3±1.45	12.5±1.33	10.3±1.22
p-value	<0.001*	<0.001*	0.519
MCH (pg)			
Pre-treatment	24.6±3.2	23.4±2.3	24.7±2.3
Post-treatment	32.4±4.3	28.4±3.3	24.9±3.2
p-value	<0.001*	0.018*	0.774
MCV (f L)			
Pre-treatment	72.45±5.38	71.15±6.27	73.28±5.44
Post-treatment	85.55±6.44	80.33±5.32	74.82±6.33
p-value	<0.001*	<0.001*	0.695

Table 7: Comparison of hematological parameters before and after treatment among subgroups

Parameters	Patients with ID (n=20)			Patients with IDA (n=40)		
	GA (n=7)	GB (n=7)	GC (n=6)	GA (n=13)	GB (n=13)	GC (n=14)
sTfR (mg/L)						
Pre-treatment	9.4±1.35	9.6±1.53	9.7±1.65	11.5±2.61	11.4±2.41	11.6±2.71
Post-treatment	3.4±0.44	5.4±1.23	9.2±1.34	3.8±0.61	5.3±1.51	10.7±1.62
p-value	<0.001*	0.027*	0.654	<0.001*	<0.001*	0.841
Hb (g/dl)						
Pre-treatment	12.34±1.95	12.94±1.95	12.9±1.25	8.9±0.46	8.8±1.70	8.4±1.46
Post-treatment	12.2±1.4	12.9±1.6	12.9±1.1	13.9±1.26	11.6±1.15	9.5±1.26
p-value	0.905	0.870	0.988	<0.001*	0.031*	0.738
MCH (pg)						
Pre-treatment	28.5±2.2	28.7±2.7	28.8±2.4	22.5±4.38	22.8±3.4	21.6±2.3
Post-treatment	29.7±1.8	29.6±2.3	29.5±2.6	32.7±3.4	27.7±2.3	22.7±3.2
p-value	0.859	0.912	0.655	<0.001*	0.023*	0.551
MCV (f L)						
Pre-treatment	80.36±4.3	81.45±4.4	81.53±3.4	69.91±6.6	69.81±5.61	69.71±5.91
Post-treatment	81.91±4.4	81.7±3.6	81.63±3.5	81.45±4.5	75.96±3.85	70.18±5.19
p-value	0.438	0.933	0.789	<0.001*	0.033*	0.728

*Significant

Table 8: Comparison of hematological parameters among treatment groups after treatment,

Parameters		GA (n=20)	GB (n=20)	GC (n=20)	ANOVA test	
					F	P
sTfR (mg/L)	Mean+SD	3.7±0.61	6.4±1.72	9.2±1.44	92.29	<0.001*
	Tukey's test (P-value)	A vs C <0.001*, B vs C =0.012* A vs B =0.033*				
Hb (g/dl)	Mean+SD	14.3±0.45	12.5±0.33	10.3±0.22	785.14	<0.001*
	Tukey's test (P-value)	A vs C <0.001*,B vs C =0.011* A vs B =0.023*				
MCH (pg)	Mean+SD	32.4±4.3	28.4±3.3	24.9±3.2	21.64	<0.001*
	Tukey's test (P-value)	A vs C <0.001*, B vs C = 0.040* A vs B =0.01*				
MCV (fL)	Mean+SD	85.55±6.44	80.33±5.32	74.82±6.33	7.78	0.001*
	Tukey's test (P-value)	A vs C = 0.001*,B vs C =0.023* A vs B =0.014*				

*Significant

Table 9: Comparison of hematological parameters among treatment subgroups after treatment

Parameters		Patients with ID (n=20)				Patients with IDA (n=40)			
		GA (n=7)	GB (n=7)	GC (n=6)	P-value	GA (n=13)	GB (n=13)	GC (n=14)	P-value
sTfR (mg/L)	M±SD	3.4±0.44	5.4±1.23	9.2±1.34	<0.001*	3.8±0.61	5.3±1.51	10.7±1.62	<0.001*
	Tukey's P-value	A vs C <0.001*, B vs C =0.018* A vs B =0.043*				A vs C <0.001*, B vs C =0.010* A vs B =0.013*			
Hb (g/dl)	M±SD	12.2±1.4	12.9±1.6	12.9±1.1	0.292	13.9±1.2	11.6±1.1	9.5±1.26	<0.001*
	Tukey's P-value	A vs C =0.637,B vs C =0.781 A vs B =0.263				A vs C <0.001*, B vs C =0.012* A vs B =0.033*			
MCH (pg)	M±SD	28.7±1.8	29.6±2.3	29.5±2.6	0.054	32.7±3.4	27.7±2.3	20.7±3.2	<0.001*
	Tukey's P-value	A vs C =0.569, B vs C =0.169 A vs B =0.057				A vs C <0.001*, B vs C =0.004* A vs B=0.02*			
MCV (f L)	M±SD	81.91±4.4	81.7±3.6	81.63±3.5	0.959	81.45±4.5	75.96±3.8	70.18±5.1	<0.001*
	Tukey's P-value	A vs C = 1.000, B vs C =0.962 A vs B =0.964				A vs C <0.001*, B vs C =0.004* A vs B =0.021*			

Values of Hb, MCH & MCV (Tabs. 6, 7) rose significantly whereas sTfR values decreased significantly compared with baseline values after anti-HP therapy either with oral iron (GA and its subgroup with IDA) or without oral iron (GB and its subgroup with IDA). The subjects in the control group (GC and its subgroup with IDA) who were treated orally with iron alone showed no significant changes in parameters by day 90 from their baseline values. Regarding children with ID, only serum sTfR values decreased significantly in subgroups with ID included in GA and GB. Other parameters including Hb, MCH and MCV did not differ as their baseline values were normal among children with ID in three treated subgroups. No significant changes in these parameters were detected in subgroup with ID in GC when compared with their baseline values.

Hb level and sTfR values (Figs. 2, 3) before and after treatment among treatment groups, were shown. The most prominent increase in values (Tabs. 8, 9) of Hb, MCH, MCV and most prominent decrease in sTfR level were in children who received anti-HP therapy plus oral iron (GA and its subgroup with IDA) and children who received anti-HP therapy alone (GB and its subgroup with IDA) as compared with those who did not receive anti-HP therapy (GC and its subgroup with IDA) who showed continuing anemia despite oral iron administration. The hematological parameters improvement was more significant in children of GA and its subgroup with IDA compared with those of GB and its subgroup with IDA. Regarding children with ID, only changes in sTfR values were more significant among children with ID in GA and GB compared to GC children. Only changes in sTfR values were

more significant in those with ID in GA compared to children in GB. Failure of drug intervention on hematological parameters among treatment groups: (Tab. 10) showed that the correction of *H. pylori*-associated ID and IDA failed in all children of GC, only in 15% of children in GA and in 20% of those in GB. The *HP*-infected children receiving anti-*HP* therapy with and without iron supplementation had significantly less frequent treatment failure compared with those without anti-*HP* therapy in correcting *HP*-associated ID or IDA

Table 10: Treatment failure among treatment groups

Parameters	GA (n=20)	GB (n=20)	GC (n=20)	χ^2	P-value
Treatment success (%)	17 (85%)	16 (80%)	0 (00%)		
Treatment failure (%)	3 (15%)	4 (20%)	20 (100%)	36.770	0.0001*

Discussion

H. pylori infection and IDA are prevalent in disadvantaged populations' worldwide (Yuan *et al,* 2010). Infection with HP has been linked to IDA, a risk factor of diminished cognitive development. Thus, HP infection might be associated with lower cognitive function at early school age (Muhsen *et al***,** 2011). The benefit of HP eradiation for IDA has been extensively studied, but data are still equivocal (Yuan *et al***,** 2010). Because many populations in developing countries worldwide have high prevalence of ID/IDA and HP infection, and because ID/IDA have substantial health effects, continuing research work in this area is still indicated (Gessner *et al,* 2006).

In this study, seroprevalence of HP infection was 45%. Since patients were enrolled from a population evaluated at a pediatric gastroenterology clinic for dyspeptic complaints, it is possible that the prevalence of HP infection is higher than in the general population in Egypt. However, this prevalence is still within the range reported in previous pediatric studies from Egypt **(**Nasser *et al,* 1996; Naficy *et al,* 2000) and from many areas of the developing world **(**Klein *et al***,** 1991; Sack *et al,* 1994). However, this prevalence is higher than that reported in other pediatric studies from industrialized countries **(**Pounder *et al,* 1995; Leandro *et al,* 2005; Sullivan *et al,* 1994). Such differences might be a reflection of variations in environmental and genetic factors that determine the susceptibility to HP infection (Sullivan *et al,* 1994) as well as great variations between communities in the incidence of HP infection during childhood **(**Pounder *et al,* 1995).

Increased frequency of IDA (44.4%) in *H. pylori*-infected patients in the present study is supported by similar findings in the literature including several seroepidemiologic studies (Milman, *et al*, 1998; Parkinson *et al*, 2000; Choe *et al*, 2001, 2003; Seo, *et al*, 2002) and a meta-analysis study (Xin-Hua *et al*, 2010) on the association between HP infection and IDA that supported an association between HP infection and decreased iron stores and IDA mostly in older children, adolescent, and adults. These data suggested prevention or treatment of HP infection as important to reduce the IDA burden worldwide. However, in contrast to these studies, few epidemiologic studies (Choi, 2003; Ali *et al,* 2011; Collett *et al*, 1999; Vendt *et al*, 2011) failed to find an association between HP infection and IDA in children and adults. These discrepancies may be related to differences in the age of the study population, onset of HP infection or duration of HP–related gastritis (Vendt *et al,* 2011). The discrepancies in different studies may be also related to differences in methodological issues where relationships between HP infection and ID/IDA may depend on the phase of infection measured, with serologic tests reflecting established HP infection associated with ID/IDA, and urea breath test and stool antigen results reflecting an earlier stage of infection that is not associated with ID/IDA (DiGirolamo *et al,* 2007).

In the present work, no significant differences were observed in the mean values of hematologic variables and iron parameters between subjects with and without HP infection. In keeping with our results, several authors (Collett *et al.* 1999; Choi 2003, 2006) found that there were no significant differences in Hb levels and serum ferritin levels between seropositive and seronegative groups. In contrast, others reported that serum ferritin concentrations were significantly lower in HP-positive patients than in HP-negative subjects (Milman *et al*, 1998; Parkinson *et al*, 2000). On the other hand, the mean values of serum sTfR concentrations in the present work were significantly higher in HP-positive than in HP-negative children. Elevated sTfR concentrations are usually encountered in ID or the conditions associated with erythroid hyperplasia (Choi and Pia 2003). In this study, the finding of no significant differences in reticulocytes counts and Hb levels between HP-positive and HP-negative groups confirms that the increase in serum sTfR concentrations seen in HP-positive children, is attributable to ID rather than erythroid hyperplasia. Thus, subclinical ID showed a higher occurrence in *H. pylori*-positive subjects. This result agreed with Choi, (2006).

In the present work, the mean values of serum sTfR concentrations in patients with both HP infection and IDA were significantly higher than that of the patients negative for HP with IDA concomitantly although the mean values of iron parameters and hematologic variables were not significant between the two groups. This finding agreed with Choi, (2006) who reported that the discrepancies between sTfR and ferritin concentrations among HP-infected children may be derived from the acute phase response of ferritin in relation to HP infection. Serum ferritin and transferrin saturation (TS) may be influenced by the presence of inflammation (Guyatt *et al*, 1992). It has been suggested that *H. pylori* subverts the human iron regulatory mechanism in a manner that is beneficial to *H. pylori*, but deleterious to the host, by inducing the up-regulation of hepcidin and/or down-regulation of ferroportin (Beutler, 2007). In response to inflammation and some infections, hepcidin binds to ferrportin and causes its phosphorylation, internalisation and degradation (Abboud, *et al*, 2000). This results in reduced iron export from enterocytes and macrophages resulting in decreased serum iron (i.e. restricted iron supply) and elevation of serum ferritin levels in such situations (Ganz *et al*, 2006). When ID exists, the sTfR concentration in serum rises even before the Hb concentration is significantly depressed. The sTfR concentration can therefore reflect the degree of tissue iron supply (functional iron status), while ferritin reflects the iron storage status **(**Cook *et al.* 1993; Annibale *et al*, 1999; Choi, 2005).

The only indicator of iron-deficient erythropoiesis is the compensatory elevation of sTfR concentration (Baynes *et al*, 1996) and the presence of such condition can be disclosed by measurement of sTfR concentrations (Suominen *et al,* 1998). In harmony with these data, the present work showed that 40% of the non-anemic HP-positive children and 32.4% of non–anemic HP-negative subjects were observed to have high sTfR levels consistent with the reported values of sTfR for ID (Vendt *et al*, 2011). This finding indicated that measuring serum sTfR concentrations is better than measuring serum iron or ferritin for reliable and early detection of subclinical ID for evaluating iron status in non-anemic subjects included.

On the basis of these results, it was assumed that serum sTfR concentration reflects functional body iron status more accurately than serum iron and ferritin levels in the patients with HP infection as it is not affected by the acute-phase response and allows for early detection of subclinical iron deficits that show a higher occurrence in *HP* -positive subjects in this study.

In the present study, the different treatment approaches for HP-associated ID and

IDA in the three treatment groups indicate a greater impact of the anti-*HP* therapy either combined with iron supplementations or alone than iron therapy on indices of ID and IDA status. Also, they indicate that the combined anti-*HP* triple therapy with iron supplementations is more effective than anti-*HP* therapy alone for the resolution of HP-associated ID and IDA and restoration of the normal iron status of children with such condition. Thus, treatment of HP infection combined with iron was associated with more rapid response to oral iron therapy as compared with the use of anti-HP therapy or iron therapy alone. Such treatment might led to enhanced iron absorption even in those subjects who did not receive oral iron therapy as a result eradication of *H. pylori* infection (Choe et al, 1999).

In the present work, although there was a significant difference in improvement of iron status between anti-HP therapy and iron compared with iron therapy alone, we observed a similar effect with anti-HP therapy alone. Therefore, the improvement of iron status in children who received the combined therapy can be attributed to the effect of anti-HP therapy rather than iron therapy. Our results indicated not only a significantly greater effect of anti-HP therapy compared to iron therapy in improving iron status in children with HP-associated ID or IDA, but also indicated that iron-therapy therapy alone produced no effect in improving iron status on day 90 compared to baseline values. The resolving of iron deficiency observed in this study and prior ones (Choe *et al*, 1999**,** 2000, 2001; Konno *et al*, 2000; Hacihanefioglu *et al*, 2004; Chen *et al,* 2007; Yuan *et al,* 2010; UmaKiran *et al* 2011) during the process of treatment of HP infection using anti-HP triple therapy either alone or combined with iron supplementations supports the proposal that HP infection is associated with ID and IDA in children, and that complete recovery of ID and IDA can be achieved by treatment of HP infection. These results, therefore, could be assumed to support a causal relationship between HP infection and ID and IDA in population of these studies.

In the present study, we found that HP-infected children receiving anti-HP therapy with and without iron supplementation had significantly less frequent treatment failure compared with those with no anti- *HP* therapy in correcting *HP* -associated ID or IDA. These findings indicate that failure of resolution of *HP* -associated ID and IDA in children receiving oral iron alone is clearly explained by absence of anti-HP therapy for this group. The failure of resolution of ID and IDA in groups of children who received anti- *HP* therapy could be explained by the assumption that HP infection might not be eradicated in these children and persistent infection prevented complete resolution of *HP* -associated ID and IDA in those children. Failure of resolution of ID and IDA in that receiving anti- *HP* therapy alone could not be explained by absence of oral iron therapy for this group because children who received anti- *HP* therapy plus iron therapy had a similar rate of treatment failure. In the present work, it was impossible to know the number of children who remained *HP*-positive and those who became negative at day 90 in respect to iron status because diagnosis of *HP* infection was based on positive serum IgG antibodies to *HP* by ELISA and such evidence may exist for several months in those patients who were treated and cured of their HP infection (Khanna *et al*, 1998).

These results agreed with Choe *et al*. (1999, 2000) and Kostaki *et al*. (2003) who reported resolution of IDA with resolution of HP infection, even in the absence of iron supplementation. Besides, the results agreed with a meta-analysis study of 16 randomized controlled trials comparing anti-*HP* therapy plus oral iron to oral iron alone for patients with *HP* -associated IDA. The authors of this meta-analysis study concluded that eradication of *HP* can improve Hb level and serum ferritin levels and suggested that treatment of *HP* infection could be effective in

improving anemia and iron status in IDA patients infected by *H. pylori*, particularly in patients with moderate or severe anemia (Yuan *et al*, 2010).

The significant positive effect of treatment of *HP* infection on correction of HP-associated ID and IDA observed in and other studies explained by reversal of the negative effect of *HP* infection on oral iron absorption (Annibale *et al,* 1999) as a result of correction of the impaired physiological mechanisms that are necessary for the absorption of alimentary iron in the duodenal mucosa in patients with *HP* gastritis and IDA (Chen *et al*, 2007). Infection with *HP* may lead to reduced acid secretion and decreased level of ascorbic acid (a potent enhancer of non-heme iron absorption) in gastric juice as a result of *HP* -associated gastritis and the treatment of HP gastritis and the return of acid secretion and the increasing gastric juice ascorbic acid levels can lead to better absorption of dietary iron in those who were treated even if they did not receive iron supplementation (Ruiz *et al,* 1994; Choe *et al,* 1999). Treatment of *HP* infection could prevent the occult gastrointestinal bleeding and the competition with the host for dietary iron by *HP*.

Besides, failure of reversal of the negative effect of *HP* infection on oral iron absorption in patients with *HP*-associated ID and IDA who were treated with oral iron alone, there were several proposed explanations for why patients with *HP* infection did not respond to oral iron until the infection is eradicated. A possible explanation for failure to respond to oral iron might be due to sequestration of iron by the microorganism itself (Barabino, 2002). Secondly, it has been suggested that disturbance of the hepcidin/ ferroportin iron regulatory mechanism induced by *HP* infection is the reason for the failure of patients with HP infection to respond to oral iron. This disturbance results from the up-regulation of hepcidin and/or down-regulation of ferroportin by the production of hepcidin mimetics that prevent response to oral iron and manipulates the host's iron homeostasis to ensure its survival even as upregulation of hepcidin appears to do in patients with acute inflammation ((Pellicano *et al*, 2004; Beutler, 2007). In agreement with this hypothesis, Lee *et al*. (2010) found that serum prohepcidin levels decreased significantly in the *HP* -infected IDA patients after combined *HP* eradication and oral iron therapy.

Contrary to the present data, Sarker *et al*. (2008) observed a significantly greater effect of iron therapy alone compared to anti-*HP* therapy in improving iron status in children with *HP* -associated ID or IDA. They observed that anti-HP therapy produced no effect in improving iron status on day 90 compared to placebo and failed to observe any additional impact of the combined anti- *HP* plus iron therapy over iron therapy alone. They found that *HP* -infected children receiving iron had significantly less frequent treatment failure compared with those with no iron in correcting ID or IDA. They added that *HP* infection is neither a cause of IDA/ID nor a reason for treatment failure of iron supplementation in young Bangladeshi children. Likewise, (Gessner *et al,* 2006) found that in a high-prevalence population, treatment and resolution of *HP* infection did not improve isolated ID or mild anemia up to 14 months after treatment initiation. These discrepancies on the effect of the anti-*HP* therapy either alone or in combination with iron supplementation on the resolution of *HP* -associated ID and IDA in different studies may be related to small sample sizes, lack of controls, and other methodological issues including the use of validated tests to confirm active *HP* infection that are among factors that limit the interpretation and ability to generalize the relevance of the results of these studies. Moreover, none of the population-based studies had a relatively large cohort of children, and none of them used validated test(s) for the determination of active HP infection (Sarker *et al*, 2008).

In the present work, serum level of sTfR in children with *HP* -associated ID or IDA decreased significantly to normal from baseline to day 90 during the process of treatment of HP infection using anti- *HP* triple therapy either combined with iron supplementations or alone indicating the resolution of HP-associated ID & IDA and restoration of their normal iron status. In contrast, higher levels of sTfR persisted in children with *HP*-associated ID and IDA receiving oral iron therapy alone indicating failure of resolution of *HP*-associated ID and IDA with iron supplementation alone. The data indicated that serum level of sTfR could be used as a specific indicator for assessing efficacy of anti- *HP* triple therapy either alone or combined with iron supplementations on the functional iron status of children with *HP* -associated ID and IDA.

Conclusions

Serum sTfR level proved to a better parameter for assessment of iron status in H. pylori-infected children than serum iron or ferritin which may be increased as the result of an acute-phase reaction to *H. pylori* infection. Treatment of *H. pylori*-associated iron deficiency (ID) and iron deficiency anemia (IDA) using the anti- *HP* triple therapy either combined with iron supplementations or alone is more effective than oral iron therapy alone for resolution of *HP* -associated ID or IDA and the restoration of the functional pool of iron status as assessed by serum level of sTfR in children with such conditions. Moreover, the combined anti-H pylori triple therapy with iron supplementations is more effective than anti- *HP* triple therapy alone for achieving this aim. In addition, iron therapy alone in is not effective in such cases. Further large-scale and multi-centers studies with long-term observations should further evaluate these conclusions.

References

Abboud, S, Haile, DJ, 2000: A novel mammalian iron-regulated protein involved in intracellular iron metabolism. J. Biol. Chem. 275:19906-12.

Ali, Z, Shariat, M, Yazdi, ZO, *et al,* 2011: Relationship between *Helicobacter pylori* infection and serum ferritin level in primary school children of Tehran-Iran**.** JPMA 61:658-62.

Annibale, B, Marignani, M, Monarca, B, *et al,* 1999: Reversal of iron deficiency anemia after *Helicobacter pylori* eradication in patients with asymptomatic gastritis. Ann. Int. Med. 131:668-72.

Ashorn, M, 2004: Acid and iron-disturbances related to Helicobacter pylori infection. Pediatr Gastroenterol. Nutr. 38:137-9.

Barabino, A, 2002: *Helicobacter pylori*-related iron deficiency anemia: a review. Helicobacter 7:71-5.

Barabino, A, Dufour, C, Marino, CE, *et al,* 1999: Unexplained refractory iron-deficiency anemia associated with *Helicobacter pylori* gastric infection in children; further clinical evidence. J. Pediatr. Gastroenterol. Nutr. 28:116-9.

Baynes, RD, 1996: Refining the assessment of body iron status. Am. J. Clin. Nutr. 64:793-4.

Beutler, E, 2007: Commentary: Hepcidin mimetics from microorganisms? a possible explanation for the effect of Helicobacter pylori on iron homeostasis. Blood Cells Mol. Dis. 38:54-9.

Bini, EJ, 2001: *Helicobacter pylori* and iron deficiency anemia: guilty as charged? Am. J. Med. 111:495-7.

Chen, LH, Luo, HS, 2007: Effects of *H pylori* therapy on erythrocytic and iron parameters in iron deficiency anemia patients with *H pylori*-positive chronic gastristis. Wld. J. Gastroenterol. 13:5380-83.

Choe, YH, Kim, SK, Hong, YC, 2003: The relationship between *Helicobacter pylori* infection and iron deficiency: Seroprevalence study in 937 pubescent children. Arch. Dis. Child. 88:178-82.

Choe, YH, Kim, SK, Hong, YC, 2000: *Helicobacter pylori* infection with iron deficiency anemia and subnormal growth at puberty. Arch. Dis. Child. 82:136-40.

Choe, YH, Kim, SK, Jung, MK, Hong, YC, 2001: *Helicobacter pylori*-associated iron-deficiency anemia in adolescent female athletes. J. Pediatr. 139:100-4.

Choe, YH, Kim, SK, Son, BK, Hong, YC, 1999: Randomized placebo-controlled trial of Helicobacter pylori eradication for iron-deficiency anemia in preadolescent children and adolescents. Helicobacter 4:135-9.

Choi, JW, 2003: Does *Helicobacter pylori* infection relate to iron deficiency anemia in prepubescent children under 12 years of age? Acta. Pediatr. 92:970-2.

Choi, JW, 2005: Brief communication: sensitivity, specificity, and predictive value of serum soluble transferrin receptor at different stages of iron deficiency. Ann. Clin. Lab. Sci. 35:435-39.

Choi, JW, Pai, SH, 2003: Associations between serum transferrin receptor concentrations and erythropoietic activities according to body iron status. Ann. Clin. Lab. Sci. 33:279-82.

Choi, JW, 2006: Serum-soluble transferrin receptor concentrations in *Helicobacter pylori*-associated iron-deficiency anemia. Ann. Hematol. 85:735-7.

Ciacci, C, Sabbatini, F, Cavallaro, R, *et al,* 2004: *Helicobacter pylori* impairs iron absorption in infected individuals. Dig. Liver Dis. 36:455-60.

Collett, JA, Burt, MJ, Frampton, CM, *et al,* 1999: Seroprevalence of *Helicobacter pylori* in the adult population of Christchurch: Risk factors and relationship to dyspeptic symptoms and iron studies. N. Z. Med. J. 112:292-5.

Cook, JD, Skikne, BS, Baynes, RD, 1993: Serum transferrin receptor. Ann. Rev. Med. 44: 63-74.

Dennison, HA, 1999: Limitations of ferritin as a marker of anemia in end stage renal disease. ANNAJ 26:409-14

DiGirolamo, AM, Perry, GS, *et al,* 2007: *Helicobacter pylori*, anemia, and iron deficiency: relationships explored among Alaska native children. Pediatr. Infect. Dis. J. 26:927-34.

Ganz, T, 2006: Hepcidin and its role in regulating systemic iron metabolism. Am. Soc. Hemat. Educ. Program. 35:507-12.

Gessner B D, Baggett H C *et al,* 2006: A controlled, household-randomized, open-label trial of the effect that treatment of *Helicobacter pylori* infection has on iron deficiency in children in Rural Alaska. J Infect Dis. 193:537-46.

Guyatt, GH, *et al,* 1992: Laboratory diagnosis of iron-deficiency anemia: an overview. J. Gen. Int. Med. 7:145-53.

Hacihanefioglu, A, Edebali, F, Celebi, A, *et al,* 2004: Improvement of complete blood count in patients with iron deficiency anemia and *Helicobacter pylori* infection after the eradication of Helicobacter pylori. Hepatogastroenterol. 51: 313-5.

Khanna, B, Cutler, A, Israel, NR, *et al,* 1998: Use caution with serologic testing for *Helicobacter pylori* infection in children. J. Infect. Dis.178:460-8.

Klein, PD, Graham, DY, *et al*, 1991: Water source as risk factor for *Helicobacter pylori* infection in Peruvian children. Lancet 337:1503.

Koike, T, Ohara, S, Sekine, H, Iijima, K, *et al*, 2001: *Helicobacter pylori* infection prevents erosive reflux esophagitis by decreasing gastric acid secretion. Gut 49:330-4.

Konno, M, Muraoka, S, Takahashi, M, Imai, T, 2000: Iron-deficiency anemia associated with *Helicobacter pylori* gastritis. J. Pediatr. Gastroenterol. Nutr. 31:52-56.

Kostaki, M, Fessatou, S, Karpathios, T, 2003: Refractory iron-deficiency anemia due to silent *Helicobacter pylori* gastritis in children. Eur J Pediatr 162:177-9.

Kurekci, AE, Atay, AA, Sarici, SU, *et al,* 2005: Is there a relationship between childhood Helicobacter pylori infection and iron deficiency anemia? J. Trop. Pediatr. 51:166-9.

Leandro Liberato SV; HernÃ¡ndez Galindo M; *et al,* 2005: *Helicobacter pylori* infection in the child population in Spain: prevalence, related factors and influence on growth. An Pediatr (Barc)., 63:489.

Lee, SY, Song, EY. *et al,* 2010: Serum prohepcidin levels in Helicobacter pylori infected patients with iron deficiency anemia. Korean J. Int. Med. 25:195-200.

Milman, N, Rosenstock, S, Andersen, L, *et al*, 1998: Serum ferritin, hemoglobin, and *Helicobacter pylori* infection: A seroepidemiologic survey comprising 2794 Danish adults. Gastroenterol. 115: \268-74.

Muhsen, K, Ornoy, A, Akawi, A, Alpert, G, Cohen, D, 2011: An association between Helicobacter pylori infection and cognitive function in children at early school age: a community-based study. BMC Pediatr. 11:43. 26-8.

Naficy, AB, Frenck, R, Abu-Elyazeed, Y, *et al,* 2000: Seroepidemiology of *Helicobacter pylori* infection in a population of Egyptian children. Int. J. Epidemiol. 29:928-32.

Nasser, M, El-Tahan, M, 1996: Incidence of *Helicobacter pylori* in children with recurrent abdominal pain. Gaz. Egypt. Ped. Ass. 44:10-2.

Parkinson, AJ, Gold, BD, Bulkow, L, *et al,* 2000: High prevalence of Helicobacter pylori in the Alaska native population and association

with low serum ferritin levels in young adults. Clin. Diag. Lab. Immunol. 7:885-8.

Pellicano R, Rizzetto M, 2004: Is hepcidin the bridge linking Helicobacter pylori and anemia of chronic infection? A research proposal. Panminerva Med. 46:165-9.

Pounder RE and Ng D. 1995: The prevalence of *Helicobacter pylori* infection in different countries. Aliment. Pharmacol. Ther. 9, 2:S33-9**.**

Ragab, L, Ibrahim, HA, Eid, AS; Kotb, T, *et al*, 2002: Suitability of soluble transferrin receptor for the clinical diagnosis of different types of anemia in children. East. Mediterr. Hlth. J. 8:298-307.

Ruiz, B, Rood, JC, *et al,* 1994: Vitamin C concentrations in gastric juice before and after anti-*Helicobacter pylori* treatment. Am. J. Gastroenterol. 89:5339.

Sack, RB, Gyr, K, **1994:** *Helicobacter pylori* infections in the developing world. J. Diarrh. Dis. Res. 12:144-5.

Santos, IS, Boccio, J, Davidson, L, 2009: *Helicobacter pylori* is not associated with anemia in Latin America: results from Argentina, Brazil, Bolivia, Cuba, Mexico and Venezuela. Pub. Hlth. Nurt, 12:1862.

Sarker, SA, Mahmud, H, *et al,* 2008: Causal relationship of Helicobacter pylori with iron-deficiency anemia or failure of iron supplementation in children. Gastroenterol. 135:1534-42.

Seo, JK, Koj, S, Choik, D, 2001: Serum ferritin and Helicobacter pylori infection in children: A seroepidemiologic study in Korea. J. Gastroenterol. Hepatol. 17:754-7.

Seo, JK, Koj, S, Choik, D, 2002: Serum ferritin and *Helicobacter pylori* infection in children: A seroepidemiologic study in Korea. J. Gastroenterol. Hepatol. 17:754-9.

Siebert S, Williams BD, et al, **2003:** Single value of serum transferrin receptor is not diagnostic for the absence of iron stores in anemic patients with rheumatoid arthritis. Clin Lab Haematol 25:155–60.

Speeckaert MM; Speeckaert R; Delanghe JR, 2010: Biological and clinical aspects of soluble transferrin receptor. Crit. Rev. Clin. Lab. Sci. 47:213-28.

Sullivan PB; Thomas JE; and Wight, DG, 1994: *Helicobacter pylori*: genetic and environmental influences. Ann. Intern. Med., 120: 982.

Suominen P, Punnonen K, et al. 1998: Serum transferrin receptor and transferrin receptor-ferritin index identify healthy subjects with subclinical iron deficits. Blood 92:2934–9.

Tian, W, Lin, XM, 2004: Effects of iron supplementation on human serum level of transferrin receptor. Zhonghua Yu Fang Yi Xue Za Zhi. 38:324-7.

UmaKiran A, Suneeta K, Kumar CS. **2011:** Impact of *Helicobacter pylori* on iron deficiency anemia in school children of age 5-12 years. Int. J. Biol. Med. Res. 2:1144-8.

Vendt, N, Kool, P, Teesalu, K, *et al,* 2011: Iron deficiency and Helicobacter pylori infection in children. Acta Paediatr. 100:1239-43.

Wang, YP, Shao, J, Zhuang, XL, 2011: Value of soluble transferrin receptor in the diagnosis of iron deficiency in children. Zhongguo Dang Dai Er Ke Za Zhi. 13:535-8.

WHO, CDCPTC, 2004: Assessing the iron status of populations: Report of a Joint WHO / CDC, Technical Consultation on the Assessment of Iron Status at the Population Level. Geneva, Switzerland.

Xin-Hua, Qu, Xiao-Lu, Huang, *et al,* 2010: Does *Helicobacter pylori* infection play a role in iron deficiency anemia? A meta-analysis. Wld. J. Gastroenterol. 16:886-96.

Yuan W, Li Yumin, Yang Kehu, *et al,* 2010: Iron deficiency anemia in Helicobacter pylori infection: A meta-analysis of randomized controlled trials. Scand. J. Gastroenterol. 45:665-76.

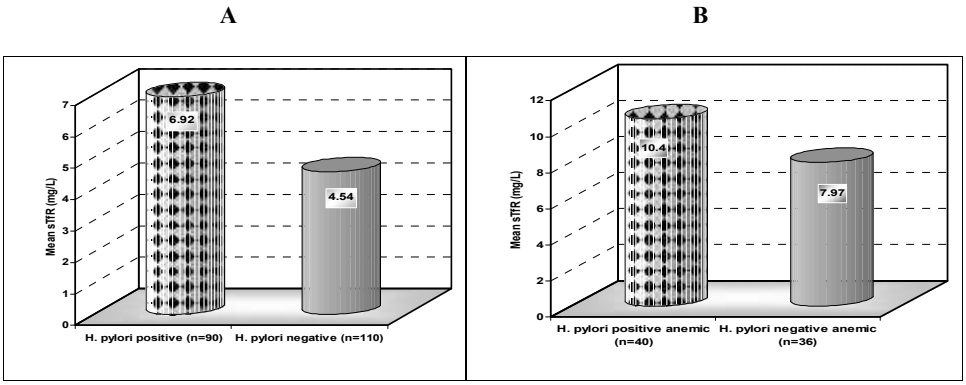

Fig. 1: Serum levels of serum soluble transferrin receptor (sTfR) among *H. pylori*-positive and *H. pylori*-negative groups (A) as well as among anemic *H. pylori*-positive and anemic *H. pylori*-negative children (B).

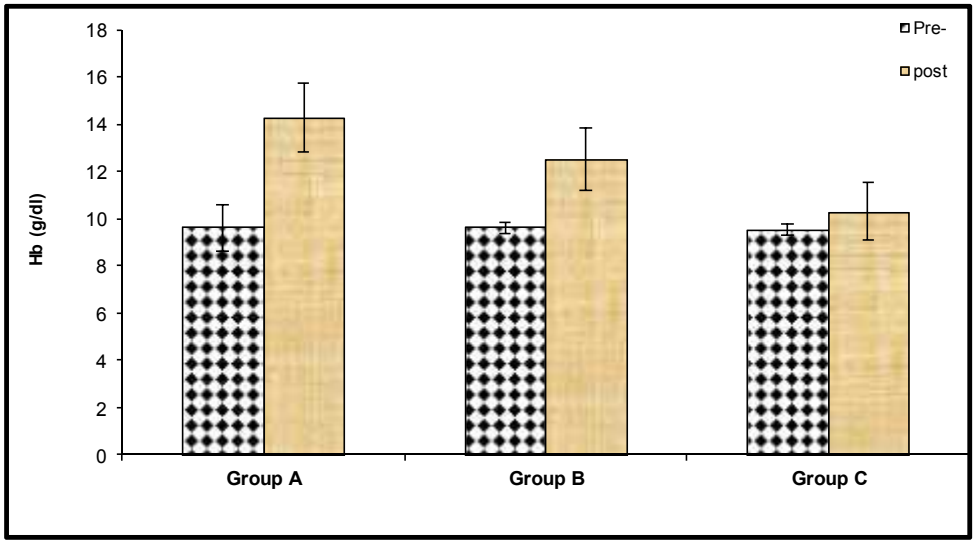

Fig. 2: Hemoglobin (Hb) level before and after treatment among treatment groups

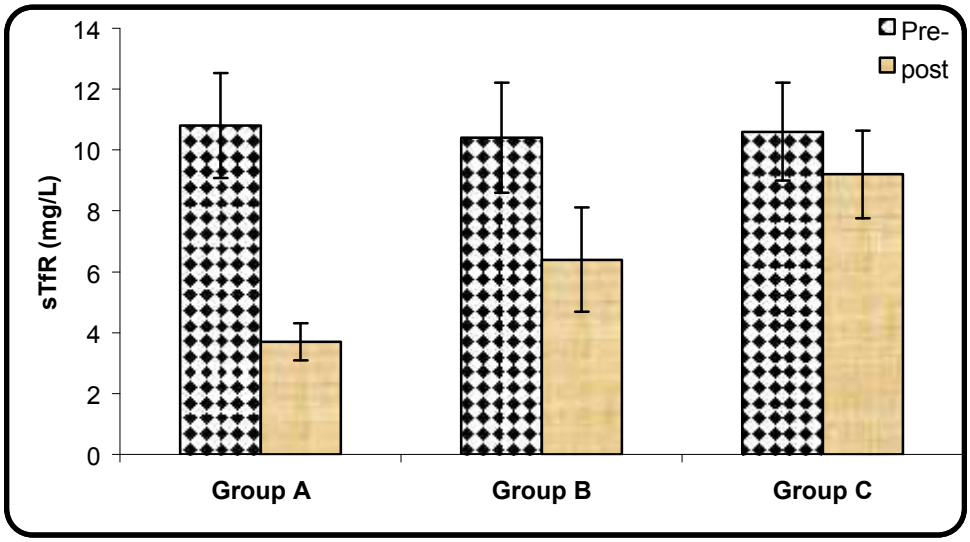

Fig. 3: Serum level of serum soluble transferrin receptor (sTfR) before and after treatment among groups