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RESEARCH ARTICLE

FREQUENCY OF *H .PYLORI* INFECTION IN MALNOURISHED CHILDREN ADMITTED TO NUTRITIONAL REHABILITATION CENTER

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ABSTRACT

A Case-control study was carried out to determine the frequency of *Helicobacter Pylori* (*H. pylori*) infection by *H. pylori* stool Ag test in malnourished children and it's relation to some selected variables. Sixty seven malnourished infants and children who have been admitted to nutritional rehabilitation center (NRC) in Basra General Hospital were regarded as cases and one hundred thirty nine healthy children who have visited primary health center, were regarded as control, their age ranged from 2 – 36 months over the period from the first of February till the end of September 2012. A special questionnaire was designed for the purpose of the study, information included: age, sex, presenting symptoms, past history, feeding history, and history of treatment with antibiotics. Measurements of weight and length by standard procedure done for all infants and children recruited in the study. Anthropometric data (weight and length) are applied to appropriate charts according to CDC/WHO charts. The study revealed a significantly higher percentage of positive *H. pylori* stool Ag in malnourished patients than control group (35.8%, 10.8%) respectively, $p < 0.0001$. In addition higher frequency of positive *H. pylori* stool Ag was found in patients with severe malnutrition than moderate malnutrition (54.2%, 45.8%) respectively but statistically not significant result $p > 0.05$. Regarding the sex of studied children although females have higher percentage of positive *H. pylori* stool Ag in both malnourished and healthy children (66.7%, 60%) respectively, but the difference statistically in not significant $p>0.05$. Positive *H. pylori* stool were found in higher frequency in malnourished patients older than 12 months (54.2%) compared to infants (45.8%) but in the control group there is a higher frequency of positive *H. pylori* stool in infants younger than 12 months (60%) compare to children older than 12 months (40%) and statistically not significant $p > 0.05$. Malnourished and control group who were not breast fed have higher frequency of positive *H. pylori* stool (70.8%, 73.3%) respectively than those with history of breast feeding (29.2%, 26.7%) respectively and statistically not significant $p > 0.05$. But absence of breast feeding is significantly associated with *H. pylori* infection in malnourished patients and control $p < 0.05$. Gastrointestinal symptoms were common presenting symptoms in malnourished patients 67.2%, with significant association with positive *H. pylori* stool Ag $p > 0.05$.as well as more than (56%) of malnourished patients with history of recurrent diarrhea have positive *H. pylori* stool Ag. Diarrhea is significantly associated with *H. pylori* infection in malnourished children. So detection of *H. pylori* infection by simple *H. pylori* stool Ag test allows early diagnosis and treatment to counteract its effect on growth of infants and children.

INTRODUCTION

Helicobacter pylori (*H. pylori*) previously named *Campylobacter pyloridis*, is a Gram-negative, microaerophilic bacterium found in the stomach. It was identified in 1982 by Barry Marshall and Robin Warren, who found that it was present in patients with chronic gastritis and gastric ulcers, conditions that were not previously believed to have a microbial cause and linked to the development of duodenal ulcers and stomach cancer. (Blaser 2006) Children differ from adults with respect to *H. pylori* infection in terms of the prevalence of the infection, the complication rate, the near-absence of gastric malignancies, age-specific problems with diagnostic tests and drugs, and a higher rate of antibiotic resistance. Compared with adults, peptic ulcer disease is found less often in infected children undergoing upper endoscopy. (Koletzko *et al.,* 2011) Children present an ideal model for studying the interaction between *H. pylori* and the gastric mucosa because a pediatric-age child is free from the common causes of secondary gastro intestinal diseases (drugs, smoking and alcohol). (Ertem 2011) An important consequence of chronic *H. pylori* gastritis and gastric atrophy is low gastric acid output. Low gastric acid secretion results in an impaired "gastric barrier," which is associated with increased

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susceptibility to enteric infections, a major public health concern linked to diarrhea, malnutrition, and growth failure in children in the developing world. (Sarker *et al.,* 2004) The mechanisms for *H. pylori* infection to cause growth retardation, as follows: infection causes peptic symptoms, and dyspeptic symptoms causes malnutrition; when the infection exists for a long time some cytokines affecting growth are released and a chronic, low-degree gastric inflammation persists; *H. pylori* is frequent among families with low socioeconomic level (already have malnutrition and chronic infections). (Tafiar *et al.,* 2006)

Subjects and Methods

A Case-control study has been carried out on infants and children admitted to nutrition rehabilitation center (NRC) in Basra General Hospital were assessed for *H. pylori* infection by stool Ag test over the period from 1st of February 2012 to the end of September 2012. A total of 67 malnourished patients were included, their ages ranged from 2-36 months; 28 males and 39 females. One hundred thirty nine healthy children were randomly selected from children visiting primary health care center for routine checkup and vaccination, their ages range from 2 -36 months. Children with family history of peptic ulcer, or those receiving treatment as antibiotics and other drugs as H2 blockers and proton pump inhibitors in the last 6 weeks were excluded from the study. (Gulcan *et al.,* 2005) A special Questionnaire was designed for the purpose of the study including presenting symptoms as diarrhea and its duration whether acute or chronic, vomiting, poor weight gain, fever and shortness of breath. Past history of recurrent diarrhea and previous hospitalization. Drug history of antibiotics used in the last 6 weeks. Feeding history; breast feeding, bottle feeding, or mixed and family history of gastrointestinal disease as peptic ulcer was taken. An informed consent was obtained from the parents for recruitment in the study.

All infants and children were underwent physical examination to assess their nutritional status and anthropometric measurement; weight and length were assessed and applied to appropriate charts Weight-for-height, weight-for-age and height-for-age (Z score) were estimated according to CDC/WHO normalized references (http://www.WHO.int/ nutgrowthdb/about/introduction/en/index5.html.Chapter Four References37) and accordingly classified as : >-1 SD normal -1 SD, mild -2 SD moderate and severe < -3 SD (wasting, underweight and stunting) respectively. Stool samples from patients and control children were tested for *H. pylori* stool antigen, the result were compared between malnourished patients and control group regarding their ages, sex, feeding history in addition nutritional status, presenting symptoms and past history of malnourished children. Data were analyzed using SPSS software Version 18.

RESULTS

A total of 67 malnourished patients were included in the study, their ages ranged from 2-36 months (mean age was 14.4±2); and 139 infants and children as control group (mean age 13.2±2)

Table-1shows that 61.2% of malnourished patients were younger than12 months, 28(41.8%) were males and 39(58.2%) were females. There is no statistically significant difference regarding feeding pattern between malnourished children and control group ($p > 0.05$).

Nutritional status of hospitalized children

Nutritional status of malnourished cases were assessed as wasting, stunting, and underweight according to weight/length, length/age, and weight/age respectively as shown in Table 2.

Table 1. Distribution of cases and control according to age, sex and feeding pattern

Variables		Cases		Control		p-value
		No.	%	No.	%	
Sex	Males	28	41.8	57	41	0.915
	Females	39	58.2	82	59	
Age	2-6	21	31.3	37	26.6	0.771
Months	>6-12	20	29.9	43	30.9	
	>12-36	26	38.8	59	42.5	
Feeding pattern						
breast feeding		26	38.8	58	41.7	0.895
Bottle feeding		23	34.3	44	31.7	
Mixed feeding		18	26.9	37	26.6	
Total		67	100	139	100	

Table 2. Types and severity of nutritional status of hospitalized children

Z-score	Wasting		Stunting		Underweight	
	No.	%	No.	%	No.	%
-2 to -3 SD Moderate (38)	41	61.2	17	25.4	42	62.7
<-3 SD Severe (29)	11	16.4	12	17.9	25	37.3
Total (67)	52	77.6	29	43.3	67	100

All admitted children to nutritional rehabilitation ward were underweight. Out of 67 malnourished patients, 52(77.6%) were wasted and 29(43.3%) were stunted. Moderate wasting and stunting were more frequent among admitted children (61.2%), (25.4%) respectively; while severe wasting was recorded only in 11(16.4%). Depending on either weight/height or weight/age, 38(56.7%) of patients have moderate malnutrition and 29(43.3%) have severe malnutrition.

Clinical presentation and past medical illness

Presenting symptoms and past history of hospitalized patients were shown in Table 3, about 67% of malnourished patients presented with gastrointestinal symptoms as diarrhea, vomiting or both. Only 16.4% presented with poor weight gain and 10.4% presented with pneumonia. From 67 malnourished patients, 37.3% had history of recurrent diarrhea and 46.3% had history of previous hospitalization.

Table 3. Distribution of malnourished infants and children according to their clinical presentation and past medical illness

Presenting symptoms	No.	%
Diarrhea and vomiting	19	28.4
Diarrhea	12	17.9
Vomiting	9	13.4
Chronic diarrhea	5	7.5
Poor weight gain	11	16.4
pneumonia	7	10.4
Fever	4	6
Total	67	100
Past medical illness		
Recurrent diarrhea	25	37.3
Previous hospitalization	31	46.3

H. pylori stool Ag results

Patients and control group were tested for *H. pylori* stool Ag and the results presented in Table 4-1. Higher frequency of positive *H. pylori* stool Ag in malnourished cases 24 (35.8%) than control group 15 (10.8%); with statistically significant result ($p < 0.0001$). *H. pylori* stool Ag result according to nutritional status

Table 4.1. Results of *H. pylori* stool Ag in malnourished patients and control group

Hps Ag	Malnourished patients		Cases		
	No.	%	No.	%	p-value
Positive	24	35.8	15	10.8	< 0.0001
Negative	43	64.2	124	89.2	
Total	67	100	139	100	

Breast feeding history					
Yes	7	29.2	4	26.7	0.698
No	17	*70.8	11	**73.3	
Total	24	100	15	100	

H. pylori stool Ag result according to age, sex and feeding history

Table 4-2 there was no statistically significant difference in the frequency of positive *H. pylori* stool Ag between malnourished patients and control group of both sexes and different age group. Malnourished patients older than 12 months have significantly higher frequency of positive *H. pylori* stool Ag ($p < 0.05$). There was no statistically significant difference between cases and control group regarding feeding pattern, ($p > 0.05$). The frequency of *H. pylori* infection is significantly higher among children in both groups who were not fed breast milk ($p > 0.05$).

Table 4.2. Distribution of *H. pylori* stool Ag results according to age, sex and breast feeding history

Variables		Positive *Hps* Ag				p-value
		Cases		Control		
		No.	%	No.	%	
Sex	Male	8	33.3	6	40	0.329
	Female	16	66.7	9	60	
Ages	2-6	6	25	5	33.3	0.133
Months	>6-12	5	20.8	4	26.7	
	>12-36	13	*54.2	6	40	

For each group P=0.002 **p<0.013

H. pylori stool Ag result according to nutritional status

Most cases (54.2%) of positive *H. pylori* stool Ag had severe malnutrition (statistically significant result). Table 4-3

Table 4.3 Relation of nutritional status with result of H. pylori stool Ag

Variables	Positive *Hps* Ag		Negative *Hps* Ag		p-value
	No.	%	No.	%	
Severe malnutrition (29)	13	54.2	16	37.2	
Moderate malnutrition (38)	11	45.8	27	62.6	0.015
Total (67)	24	100	43	100	

H. pylori stool Ag result according to clinical presentation and past medical illness

Table 4-4 shows higher frequency of positive *H. pylori* stool Ag result in malnourished cases presenting with diarrhea and vomiting or both (75%) with statistically significant difference $p < 0.05$. Malnourished patients with history of recurrent diarrhea have 50% positive *H. pylori* stool Ag result and 41.9% of cases with previous hospitalization.

Table 4.4. *H. pylori* stool Ag results according to presenting symptoms and past medical illness

Variables		Positive *Hps* Ag		Negative *Hps* Ag	
Presenting symptoms	Total	No.	%	No.	%
Diarrhea and vomiting	19	8	42.1	11	57.9
Diarrhea	12	5	41.7	7	58.3
Vomiting	9	3	33.3	6	66.7
Chronic diarrhea	5	2	40	3	60
Poor weight gain	11	3	27.3	8	72.7
pneumonia	7	2	28.6	5	71.4
Fever	4	1	25	3	75
Total	67	24	35.8	43	64.2
Past medical illness					
Recurrent diarrhea	25	14	56	11	44
previous hospitalization	31	13	41.9	18	58.1

P= 0.03

Logistic regression analysis

The whole variables included in the study were subjected to logistic regression analysis to adjust the possible confounders to know the variables that are associated with *H. pylori* infection.

Table 4-5 shows that age, sex, history of breast feeding, and severity of malnutrition are not associated with result of *H. pylori* stool Ag positivity; presenting symptoms especially gastro-intestinal symptoms are independent risk factor associated with *H. pylori* stool Ag positivity.

Table 4.5. Logistic regression of selected variables with positive *Hp*s Ag result

Variables	OR	p-value	95% CI	
			Upper	Lower
Age	0.551	0.155	0.264	1.146
Sex	0.528	0.366	0.161	1.736
Breast feeding	0.546	0.144	0.168	1.779
malnutrition	2.650	0.143	0.818	8.584
Presenting symptoms	3.438	0.044	1.080	10.950

DISCUSION

In developing countries, *H.pylori* is an infection acquired early in childhood causing chronic diarrhea and malnutrition. (Tafiar *et al.,* 2006) All malnourished patients admitted to NRC were assessed for *H. pylori* infection by *H. pylori* stool Ag (*Hp*SA). *Hp*SA is non invasive test with high sensitivity and specificity for detection of *H.pylori* infection as proved by many studies as in study in Tehran (100%, 83.4%) (Falsafi *et al.,* 2005) and in Istanbul (98%, 100%) (Gulcan *et al.,* 2005) respectively. Higher frequency of malnourished females admitted to NRC (58.2%) because probably female numbers more than males in the society. This result is similar to study carried out by Firas et alt in Basra, (Fadhil and Issa 2011) in contrast to a study done by Sunguya *et al*. (2006) in Tanzania which shows admitted malnourished males more than females. (Sunguya *et al.,* 2006) Regarding age of malnourished patients: more than 60% of patients were younger than 12months. This result was similar to a study carried in Babylon by Muder *et al.* (Noor *et al.,* 2009) this may be caused by absence of breast feeding, early weaning and in proper food preparation. Moderately malnourished children admitted to nutritional rehabilitation ward were more than severe malnourished patients because number of moderate malnourished children in the society is more than severe malnutrition. This result is similar to study done in Basra by Firas *et al.* (2011)

Malnourished patients with absence of breast feeding were more than with breast feeding. Same result was obtained by Abushray in Karbala (Abushray 2009) but in contrast to a study carried out in Basra by Saleem which shows that breast feeding is more common feeding pattern in children younger than 2 years, (Saleem 2006) This may be explained by that; availability of artificial milk and poor education of mothers about benefit of breast feeding. Approximately 2/3 of malnourished patients presented with gastrointestinal symptoms as diarrhea, vomiting and chronic diarrhea. More than 50% of malnourished patients presented with diarrhea. The relationship between diarrhea and malnutrition is bidirectional; diarrhea leads to malnutrition while malnutrition aggravates the course of diarrhea. Many factors contribute to the detrimental effect of diarrhea on nutritional status. These include reduced intake (due to anorexia, vomiting), mal-digestion, malabsorption, increase nutrient losses, and the effects of inflammatory response. (Nel *et al.,* 2010) Malnutrition increase risk of diarrhea due to many factors includes alteration of villus and crypt architecture, alter intestinal barrier function, and compromise innate immune barrier (Guerrant *et al.,* 2008). Females show higher percentage of positive *Hp*sAg, although not significantly different from males. The cause is unknown. This finding was similar to study carried out in Nairobi and west Iran by (Langat *et al*., 2006; Soltani *et al.,* 2013) and in contrast to a study done by Elin et alin Uganda which shows high prevalence of *H. pylori* infection in males. (Hestivik *et al.,* 2010) Malnutrition is risk factor for infection. Both acquired immunity (lymphocyte function) as well as innate host defense mechanisms (macrophages and granulocytes) is affected in severely malnourished patients. (Schaible and Kaufmann 2007) Malnourished children have higher frequency of *H.pylori* infection (35.8%) than control group (10.8%).Same result was reported in a study by Sullivan et al in Gambia which find higher prevalence of *H.pylori* infection in malnourished children. (Sullivan *et al.,* 2012) But in contrast to a study in Guatemala by Quinonez *et al*. (1999) which shows no significant association between *H.pylori* infection and malnutrition. (Sarker *et al*., 1997) Higher frequency of positive *Hp*sAg in malnourished infants older than 12 months, the possible explanation is that may be related to the gastric mucosal damage caused by initial *H. pylori* infection which then lead to facilitated and sustained infection with *H. pylori*. (Sarker *et al.,* 1997) Same result was obtained by *Elin et al.* in Uganda (Hestivik *et al.,* 2010) but in contrast to a study carried out in Egypt by abdollah *et al*. which reveals high frequency of H. pylori infection in young infants. (Tafiar *et al.,* 2006)

H. pylori infection predisposes children to the development of malnutrition and growth failure. The mechanism of this effect may include transient loss of gastric acid barrier during vulnerable periods as during the introduction of weaning food (Sarker *et al.,* 1997). In current study severely malnourished patients have higher frequency of *H. pylori* infection; similar results obtain in study carried out by Thomas et al in Gambian. (Sarker *et al.,* 1997) In this study absence of breast feeding enhance infection with *H. pylori*, this is possibly explained by absence protective effect of breast feeding against *H. pylori* infection. The possible mechanisms enrolled in this Protection may be due to the lactoferrin in human milk which binds to *H. pylori* liposaccharide inactivating the microorganism (Thomas *et al.,* 2004). Same result obtained from study carried out in Japan by Okada *et al.* (2001) but other studies failed to find such protective role in Brazil by Rodrigues *et al.* (2006) and in Tabriz by Mandana (Rafeey *et al.,* 2010).

Because *H.pylori* infection is accompanied with hypochlorhydria which facilitates acquisition of other enteric pathogens due to removal of the gastric acid barrier which then results in diarrheal disease and malnutrition (Windle *et al.,* 2007), so this study reveal higher percentage of positive

*Hps*Agin malnourished patients with diarrhea (58.3%). Same result concluded by Douglas et al in Peru (Rodrigues *et al.,* 2006), and differs from a study carried out in Cuba by Ruiz *et al*. which show no association between H. pylori infection and diarrhea. (Alvarez *et al.,* 2005)

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