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The significance of *Helicobacter pylori* Infection as a cause of recurrent abdominal pain in children.

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Abstract

Background: Recurrent abdominal pain (RAP) is a frequent gastrointestinal complaint in pediatrics. The roles of *Helicobacter pylori* (*H. pylori*) as a cause for these complaints remain controversial. *Helicobacter pylori* infection is a worldwide infection that is commonly acquired during childhood.

Aim of study: To detect the association between recurrent abdominal pain and *Helicobacter pylori* infection in children between (3-13) years. Patients and methods A hospital base case control study conducted in Alzahraa teaching hospital for maternity and children between first of November 2014 to 28th of February 2015.Thirty three children ranging between (3-13) years old with mean age ± SD (7.94 ± 2.51) years complaining from recurrent abdominal pain were studied. Patients were classified into three groups according to the age: group A (3patients) whom their age (3-5) years, constituent of group B (25 patients) whom their age ranged (5-10) years, and group C (5 patients) whom their age ranged (10-13) years. Control group consist of 35 healthy children with mean age ± SD (6.03 ± 3.79) years. Complete blood count, blood film, screen for celiac disease, general stool examination, urinalysis, erythrocyte sedimentation rate, ultrasound of abdomen, and screen for *Helicobacter pylori* in blood and stool were done to all patients. Screening for *Helicobacter pylori* screen in the blood and stool was done for control group.

Results: The present study demonstrated that, out of 33 samples of RAP there were 11 positive (33.33%) and 22 were negative for *H. pylori* (66.67%). while regarding control group, current study demonstrated that out of 35 cases there were 4 cases positive for *H. pylori* infection, with a statistically significant difference between patients and control group regarding to *H. pylori* infection (P=0.029). Moreover, current study demonstrated no a significant difference between the percentage of *H. pylori* infection when compared among different age groups (p=1.000). We found strongly significant correlation (p<0.001) between *H. pylori* infection and family history of recurrent abdominal pain.

Conclusion: We conclude that *H. pylori* represent an important cause of abdominal pain in children and must be included in RAP work-up.

Keywords: Recurrent abdominal pain (RAP), *Helicobacter pylori*.

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Introduction

Recurrent Abdominal Pain (RAP) in pediatrics is defined as three episodes of abdominal pain (at least), during a period of three months and it should be severe enough to affect their daily activities [1].

Prevalence of RAP in school children ranges between (10-20%) [2]. typically the pain is nonspecific although most children describe colicky, periumbilical discomfort, the child is healthy in between these episodes and physical examination is normal [3] .Early studies showed that in only 7% of cases there is an organic cause [4]. Many conditions may cause such pain, such as constipation, abdominal migraine, gastritis and peptic ulcer associated with *H. pylori* and the irritable bowel syndrome [5].

H. pylori is a negative gram stained rod that produces urease, catalase, and oxidase, which might play a role in the pathogenesis of peptic ulcer disease. It is likely transmitted by feco-oral road [6]. The organism considers as class one carcinogenic [7]. *H. pylori* is one of the most common bacterial pathogens in human and affect 50% of the world's population [8].

In pediatrics, infection with *H. pylori* can present as abdominal pain, vomiting and, less commonly, refractory iron deficiency anemia or failure to thrive. Chronic infection with *H. pylori* can put the patient in a high risk of having peptic ulcer and gastric malignancies. The relative risk of gastric carcinoma increases about 2.3-8.7 times more in *H. pylori* infected person when compared to uninfected one [7].

For diagnosis of *H. pylori* there are a lot of investigations. The selection of suitable one could be depended on availability that tests, presence of well-equipped laboratories, the patient's clinical status and probability of positive and negative tests on different clinical conditions. Diagnostic tests can be classified into invasive (endoscopy) and noninvasive tests [9].

Endoscopy and histology are the gold standard in diagnosis of *H. pylori* infection. However, many factors may adversely affect the accuracy of histopathology such as the size and location of biopsies, stain used, use of proton pump inhibitor (PPI), use of antibiotics and subjective influence of examining pathologist [10].

Rapid urease test (RUT) is a widely applied invasive investigation for detection of *H. pylori* infection because it is cheap, fast, easy applicable, highly specific and widely available. The *H. pylori* urease enzyme convert the urea test reagent to ammonia, causing rise in the pH level and change the color of the pH monitor [11].

Culturing of *H. pylori* has almost 100% specificity, but the sensitivity of culture range between 85%-95%. The *H. pylori* is very delicate so that its cultivation in vitro requires special transport medium, growth medium and optimum incubation environment. The commonly used media include Pylori agar, Skirrow agar, Columbia blood agar, Brucella agar, Brain heart infusion or Trypticase soy agar, supplemented with sheep or horse blood [12].

Polymerase Chain Reaction (PCR) provides high sensitivity and specificity, more than 95%. The advantages of PCR, including less bacterial colony count in specimen may yield positive result, rapid results and no need for sophisticated transportation, enable the physician make a precise and quick management plan [13].

Urea Breath Test (UBT) is a reliable investigation with many advantages, such as easy, noninvasive and safe but it is no so accurate in pediatric patients. The urease enzyme of *H. pylori* hydrolyze the 13C or 14C-labeled urea ingested by the patient is to labeled CO_2 in stomach, after that it will be absorbed to blood stream than expelled out of the body by expiration where it can be measured. Despite that UBT can be adversely affected by many factors such as patient, bacteria and the test itself, the UBT have 95% sensitivity and specificity when conducted under standard steps [14].

Stool antigen tests (SATs) are noninvasive diagnostic modules for *H. pylori* infection. There are two types of SATs, enzyme immunoassay (EIA) and Immune Chromatography (ICA). It is cheap, widely available and used for both primary diagnoses as well as for the assessment of eradication therapy. ICA-based tests do not need particular equipment so it is widely used developing countries [15].

A lot of serological investigations used in H pylori infection workup. They are based on the detection of anti-*H. pylori* IgG antibody. It is highly reliable in detection of *H. pylori* infection in children. The other advantage of serological test is that the result of Antibody-based tests is not affected by ulcer bleeding, gastric atrophy as well as the use of PPI or antibiotics, which cause false negative results in other invasive or noninvasive tests [16].

Aims of Study

To detect the association of *H. pylori* infection in children (3-13) years with recurrent abdominal pain.

Patients and Methods

A hospital based Case control study was conducted on 33 patients at Al Zhraa teaching hospital for maternity and children for 4 months duration from first of November 2014 to the end of February 2015. Their age ranged from 3 to 13 years with mean age ± SD (7.94 ± 2.51) years. They were complaining from at least three episodes of abdominal pain during three months period and sever enough to affect their activity (Figure 1).

Those 33 patients were divided into three age groups: Group A (3-5) years old consist of 3 patients, group B age ranged (5-10) years old consist of 25 patients and group C (10-13) years old consist of 5 patients. They were studied for relationship between *H. pylori* infection and RAP, and compared with control group which consist of 35 healthy children with mean age ± SD (6.03+3.79) years, even without family history of RAP.

Detailed history and clinical examination were done for all 33 patients which include:

(A) Age, gender, residence, water supply, duration of abdominal pain, associated symptoms like vomiting and diarrhea, family history of RAP in first degree relative, and if abdominal pain affect the daily activity of the child.

(B) The following investigation; complete blood count (CBC), blood film, urinalysis, stool analysis, ultrasound of abdomen and celiac screen were done to all patients.

(C) Screen of *H. pylori* in blood and stool were done to both patient and control groups.

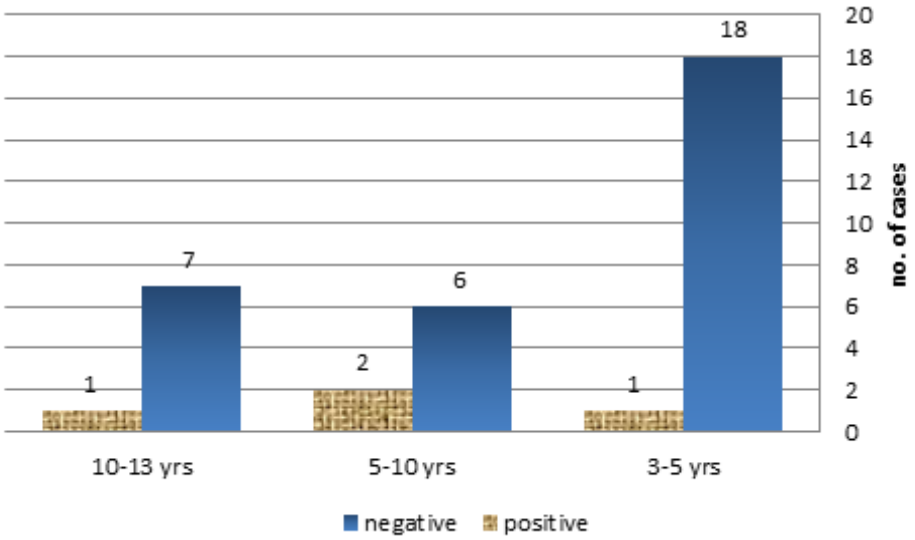

Figure 1. *Distribution of H. Pylori infection according to patients age*

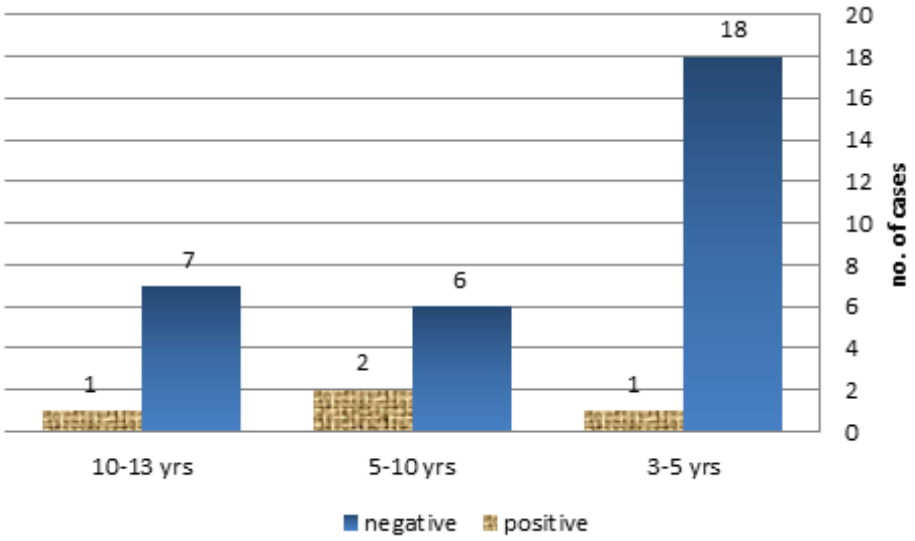

Figure 2. *Distribution of H. pylori infection according to control group*

Serology

ABON-Blopharm company one step *H. pylori* test device which is a rapid chromatographic immunoassay for qualitative detection of antibodies to H .pylori in serum was used according to manufacture instructions. The sensitivity of this test is 89.9-98.9 and specificity is 66.9-83.4.

Helicobacter pylori stool assay (HPSA)

The detection of *H. pylori* in stool done by using one step *H. pylori*Ag (Dia spot – Company). The sensitivity and specificity of this test are 94.5%-100%, 95.1%-100%, respectively.

All the patients guard was informed about the nature of the study and verbal consent was taken according to policy of ethical committee in our research center (Figure 2).

Statistical Analysis

Data were collected by excel from Microsoft office 2010 and analyzed by SPSS version 20 from IBM. Number, percent and mean+SD were used to express the numeric variables. Chi-square test was used to study association between numerical variables. P-value was considered significant when it was less than or equal to 0.05.

Results

Thirty three samples from patients with RAP were collected when they attended Al-Zahraa teaching hospital, at the same time about 35 samples from apparently healthy children were collected as a control. Mean age for both patients and control were (7.94 ± 2.51, 6.03 ± 3.79), respectively. Moreover when these samples were distributed according to (Residency, source of water supply, gender and family history of RAP) as shown in Table 1-3.

Discussion

Since, current study demonstrated that there were 11 out of 33patients with RAP were found to be positive for *H. pylori* in the stool, and 22 were negative (33.33%, 66.67% respectively; P=0.029). Thus, current result

Table 1. *Socio-demographic distribution of patients and control*

Sociodemographic Variable		Control n (%)	Patient n (%)	P-value
Residency	Urban	24 (68.6)	31 (94)	0.15
	Rural	11 (31.4)	2 (6)	
Water supply	Bottle	18 (51.4)	15 (45.5)	0.62
	Tap	17 (48.6)	18 (54.5)	
gender	Male	14 (40)	12 (36.4)	0.75
	Female	21 (60)	21 (63.6)	
Family history of RAP	Positive	0 (0)	9 (27.3)	0.0009
	Negative	35 (100)	24 (72.7)	

Table 2. *Show number and percentage of positive cases for H. pylori in control group and patients*

Characteristic		Control n (%)	Cases n (%)	P-value
H. pylori stool	Negative	31 (88.6)	22 (66.7)	0.029
	Positive	4 (11.4)	11 (33.3)	
H. pylori serum	Negative	33 (94.3)	24 (72.7)	0.016
	Positive	2 (5.7)	9 (27.3)	
Total		35 (100)	33 (100)	-

Table 3. *Relationship between H. pylori infection and certain sociodemographic parameters*

Socio-Demographic Parameters		Negative H.P n (%)	Positive H.P n (%)	P-value
Residency	Urban	21 (67.7)	10 (32.3)	1
	Rural	1 (50)	1 (50)	
Gender	Male	10 (83.3)	2 (16.7)	0.25
	Female	12 (57.1)	9 (42.9)	
Water supply	Pipe	11 (61.1)	7 (38.9	0.46
	Bottle	11 (73.3)	4 (26.7)	
Family history of RAP	Negative	22 (91.7)	2 (8.3)	0
	Positive	0 (0)	9 (100)	
Total		22 (66.7)	11 (33.3)	-

open the way to find out other possible causes for RAP, in most cases the causes can be identified-organic causes [17,18]. But differ from other studies which mention the non-organic causes for RAP were the commonest one [1]. Moreover a study done by Malfertheiner et al. [19] they found that RAP is not an indication for *H. pylori* in children.

However children should be tested for *H. pylori* after exclusion of other causes of symptoms [15]. However, there is a doubt about the association between recurrent abdominal pain (RAP) and *H. pylori* [20,21]. Some research support these association and however; there is evidence against this association because studies were done to fallow the resolution of abdominal pain eradication *H. pylori* infection in patient with RAP, show that bacterial eradication and healing of gastric inflammation did not lead to symptomatic relief of recurrent abdominal pain in children [22,23].

Several studies demonstrate that the incidence of *H. pylori* infection is more common in patients less than 6 years old [24-26]. And this percentage was decreased with increasing age of children in reverses correlation pattern [26]. But this is not the situation in our study when positive and negative cases for *H. pylori* were analyzed against patient age groups (3-5 years old, 5-10 years old and 10-13 years old), we found the rate or percentage of *H. pylori* infection among three groups about to be similar (32%, 33.3% and 40%, respectively). Thus, no significant differences between them. This difference could be belonging to small sample size.

Regarding for residency (urban vs. rural), gender (male vs. female) and nature of water supply (tap vs. bottle), current study showed no any significant effects for these factors on the chance of infection with *H. pylori* (P=1.00, 0.250, 0.458, respectively), so this result came in agreement and support previous study done by Shaker et al. [24] who found similar results. Other study also found that sex was not affecting characteristic for *H. pylori* infection [27,28].

We have found a significant correlation between Family history of RAP and infection with *H. pylori* (P<0.001). Same correlation was found in Sonny et al. [29]. This is because the mode of *H. pylori* transmission is fecal-oral. Thus, their first degree relative will be at high risk of infection.

Moreover, regarding to some clinical manifestation (vomiting, and diarrhea). The present study did not found any significant correlation between these parameters and *H. pylori* infection (P=0.292, P=0.452, respectively). However, this result came in agreement or supported by a previously conducted studies which demonstrated a RAP with or without vomiting as a common manifestation of *H. pylori* infection in children [30]. Moreover, another study done by Mohammed et al. [31] show that, abdominal pain with or without diarrhea or vomiting was the most important complaint that has significant association with *H. pylori* infection.

Conclusion

We conclude that *H. pylori* infection represent an important cause of recurrent abdominal pain in children and must be included to RAP workup.

Recommendations

1. We recommend using more advanced and sensitive methods for diagnosis of *H. pylori* such as PCR.

2. Conducting similar study based on large number of patients.

3. The eradication therapy should be started to all asymptomatic persons with positive *H. pylori* result.

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