

Helicobacter Pylori infection among children with recurrent abdominal pain using non invasive diagnostic tests.

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ABSTRACT

Helicobacter pylori (HP) is mainly acquired during childhood and causes one of the most widespread infection worldwide; it is recognized as a cause of gastritis and peptic ulcer and it has been classified as a group A carcinogen by world health organization (Sabbi T *et al*, 2011). The aim of our study is to find if there is a relation between recurrent abdominal pain (RAP) and the occurrence of HP infection, to evaluate for the prevalence of HP infection among children with RAP, relation of HP to age and sex of the patient, and to assess for the non invasive tests as an easy and reliable method for the diagnosis of HP infection in children and to evaluate for their sensitivity and specificity compared to each other. Two hundred forty eight child (248) aged 7-14 years with RAP, according to Apley's criteria (Apley J, 1958), enrolled into this study versus eighty (80) asymptomatic child (control) were tested for HP infection using the non invasive diagnostic methods, enzyme linked immunosorbent assay (ELISA) and 13(C) urea breath test (UBT).

Key words: HP : Helicobacter Pylori – RAP : Recurrent Abdominal Pain – ELISA : Enzyme Linked Immuno Sorbent Assay – 13 (C) UBT : 13 (C) Urea Breath Test – PCR : Polymerase chain Reaction

Introduction

Recurrent abdominal pain (RAP) is a common problem in childhood. Many factors i.e; organic changes in the gut, psychological, and environmental factors contribute to RAP in children (Biswal N *et al*, 2005). The role of HP as a cause of RAP and gastrointestinal symptoms is controversial, but in proven HP infection, some stated that RAP is the most common marker (Raymond *et al*, 2008). The incidence and prevalence rates of childhood HP infection vary greatly by nation, with infection rates of 8.9% to 72.8% reported in developing and developed countries respectively (Segal L *et al*, 2008). Diagnosis of HP infection is based on methods requiring gastric biopsies (invasive methods) performed using endoscopy (histology, culture, rapid urease test, PCR) or non invasive methods (serology, 13(C) UBT, stool antigen test) (Dekorwin JD *et al*, 2003). Endoscopy is a complicated procedure in children and diagnosis of infection can be based on non invasive tests (Pellicano R, 2000). Non invasive tests may provide a more rapid diagnosis, be less expensive, and offer similar accuracy in diagnosing HP infection (Hahn M *et al*, 2000). Serological tests are widely available and cheap and may be helpful in screening population infected with HP. The 13 (C) UBT is the most accurate method in patients irrespective of age (Dekorwin JD *et al*, 2003).

Patients and Methods:

This study is a prospective cohort study. It was conducted over a period of 2 years (Sept.2008 to Aug.2010) in both Gannas medical center, Al Kharj, KSA and Sohag university hospital, Sohag, Egypt. Two hundred forty eight (248) child with RAP (according to Apley's criteria) were enrolled into this study. Their ages ranged from 7-14 years, 144 were males and 104 were females. Eighty (80) asymptomatic child with the same age range were used as a control, 42 were males and 38 were females. Both symptomatic and asymptomatic (control) children were divided into two age groups, group 1 aged 7-10 years included 132 child, and group 2 aged 11-14 years included 116 child. Cases receiving antibiotics, bismuth, H2 antagonists, or proton pump inhibitors during the last 45 days were excluded. According to Apley's criteria, RAP is characterized by three or more episodes of abdominal pain that occurs over at least three months and are severe enough to interfere with activities. Clinically, these episodes are characterized by vague abdominal pain that may be dull or crampy, lasts for less than one hour, and is poorly localized or periumbilical. The pain frequently presents with nausea, vomiting, and other signs of autonomic arousal (Apley J, 1958). All of these children (symptomatic and control) were subjected to screening of HP infection using non invasive tests (ELISA test & 13 (C) UBT). IgG antibodies for HP infection were measured in patients sera using a commercially available ELISA, EUROIMMUN (Medizinische labordiagnostike, AG, Deutschland) with a cut off ratio ≥ 1.1 for positive cases. 13 (C) UBT was

done for all studied children using Heliprobe and Helicap (Kibion AB, Upsala, Sweden) with cut off > 50 index for positive cases.

Statistical Analysis

Statistical analysis was done using SPSS statistical analysis software. Chi square test was used for comparison between various groups. A p value of less than 0.05 was considered statistically significant.

Results:

In our study, we found a higher incidence of HP infection among patients suffering from RAP (total of 48 cases with HP infection diagnosed with both ELISA and 13 (C) UBT out of 248 patients with RAP) than in control group (7 cases positive for HP infection out of 80 asymptomatic child).

Chi square test shows a significant difference with p value of 0.02. (95% CI :1.05 to 1.4, with RR = 1.2). This is shown in table 1: -

Table 1: Relation of HP positivity and RAP in both cases and control group.

RAP	Patients	Controls	P value
Positive	48	7	0.02
Negative	200	73	

Out of 248 child with RAP who enrolled into this study, 43 child were positive for HP using the ELISA method, while 46 child were positive for HP using the 13 (C) UBT

Chi square test to compare between these 2 tests shows ELISA is as sensitive and specific as UBT in the diagnosis of HP infection as shown in table 2:-

Table 2: Comparison between the 2 noninvasive tests for detection of HP infection.

ELISA	P value	Sensitivity	Specificity	PPV	NPV
Negative	0.0001*	98%	95%	99%	89%
UBT					
Negative	200	2			
Positive	5	41			

We compared patients groups according to age and the positivity of HP infection in control and RAP group. We found no significant difference between the 2 groups as shown in table 3.

Table 3: HP infection according to age group in both patient and control groups

Age group	Patients	Control	P value
7-10 years (Positive/total)	20/132 = 15.2%	3/43 = 6.9%	0.3
11-14 years (Positive/total)	28/116 = 22.4%	4/37 = 10.8%	0.2

We also could not find any significance of the sex of the child in relation to positivity of the HP infection in both groups with a P value of 0.8 as shown in table 4.

Table 4: Relation of HP positivity to the sex of the child among patients and control group.

Child sex	Patients	Control	P value
Boys	26/48 = 54.2%	4/7 = 57.1%	0.8
Girls	22/48 = 45.8%	3/7 = 42.9%	

Discussion:

The relation between HP infection and RAP is still controversial. Some studies found no relation, while others found a significant relation between HP infection and RAP among school students (Telmesani AM, 2009).

In our study, a significant relation also was found, where Chi square test shows a significant difference with a P value of 0.02 between patient and control groups as explained in table (1). This is in agreement with Sedlackova *et al*, 2003, who found that the prevalence of HP infection was 33% among symptomatic versus 7.5% among controls. Others as Malaty *et al* 2006 found different results, where they found a higher prevalence among asymptomatic versus symptomatic children. Poddar *et al* 2007 found that most infected children remain asymptomatic throughout their childhood. Nurgalieva *et al* 2002 and others found that some factors can affect the change of prevalence of HP infection including age of the child, gender, history of breast feeding, educational level of the mother, number of siblings, family income, and sanitation including clean water and waste disposal. This may explain the variation in prevalence among different studies.

Definite diagnosis of HP infection may need invasive tests which may be inconvenient and carries some risks. Non invasive methods rather than endoscopy (as the later is a complicated procedure in children) can be used for diagnosis of HP infection (Pellicano R, 2000). In this study, we used both ELISA and 13 (C) UBT for

diagnosis of HP infection among the studied children. Chi square test used to compare between these 2 tests showed ELISA is as sensitive and specific as UBT in the diagnosis of HP infection. We intended to use two non invasive tests rather than one for more accurate results. Combination of various diagnostic methods gives more precise information on the presence of HP infection (Suarval *et al*, 2011). Screening for the serum IgG antibodies to HP is a practical method for diagnosing HP infection in children (Chong SK et, 1995). Rapid serology test is a simple and convenient way for diagnosing HP infection (Hung CT *et al*, 2002). The 13 (C) UBT is a reliable non invasive method for diagnosis of HP infection in children and adults (Yang HR *et al*, 2005). Based on the previous consideration, we used both serology and UBT for diagnosing our cases.

In our study, the increased incidence of positive cases among symptomatic group with the 13 (C) UBT rather than those with ELISA test may be explained as the 13 (C) UBT is more sensitive and accurate than ELISA test. UBT has the best sensitivity in all age groups (Megraud F *et al*, 2005). The 13 (C) UBT is the most accurate method irrespective of age (Dekorwin JD *et al*, 2003).

In our study, the incidence of HP infection among the symptomatic children increased with the advancement of age, where it was less in children aged 7-10 years (15.2%) than children aged 11-14 years (22.4%) as shown in table 3. This variation may be attributed to the increased chances of contact with infected people and acquisition of infection in the older ages. This is in agreement with Sasidharan S *et al*, 2011 who found that the prevalence of HP infection increases with age. Suraval *et al*, 2011 found in his research that HP infection in symptomatic children is minimal in children aged 7-8 years (36.84%) and reaches maximum levels in students aged 14 years (66.67%) while others found the prevalence of HP infection in children with RAP fell with age from 20% at age of \leq 5 years to 7% for children $>$ 10 years (Malaty HM *et al*, 2006).

In this study, the incidence of HP infection among the asymptomatic children is also increased with the advancement of age, where it was less in children aged 7-10 years (6.9%) than children aged 11-14 years (10.8%) as shown in table 3. Sykora J *et al* 2009 found a positive association with age among the asymptomatic children, while Sedlackova *et al* 2003 found that the prevalence tended to fall with age among asymptomatic children (11% in children below 6 years versus 6% in children over 10 years). Chi square test showed no significant difference regarding the age of the child between the patient and control groups (table 3).

In our study, there was no significant difference regarding the gender of the child and the prevalence of HP positive cases between the symptomatic and control groups. It was 54.2% in males, 45.8% in females among the symptomatic children compared to 57.1% in boys, 42.9% in girls among the controls (table 4). Sedlackova *et al* 2003 found that the prevalence was similar among boys and girls (32% versus 34.5% respectively). Also Olesatro *et al* 2011 found similar results among genders (34.5% in boys versus 28.4% in girls).

Conclusion:

In this study, we can conclude that, HP infection has a significant prevalence in the studied children with RAP compared to the control group. Both ELISA and 13 (C) UBT tests used for diagnosis of HP infection have a similar sensitivity and specificity. The incidence of HP infection increased with advancement of age in both the symptomatic and control groups. No significant difference regarding the relation of HP positivity to the sex of the child.

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