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RECURRENT ABDOMINAL PAIN;
THE FREQUENCY OF H. PYLORI INFECTION IN CHILDREN

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ABSTRACT... Objective: To assess the association between the Helicobacter Pylori (H.pylori) infection and recurrent abdominal pain (RAP) by documenting the frequency of Helicobacter pylori infection in children aged 5 to 15 years in our setup. **Design:** A comparative study. **Place and Duration of Study:** The study was conducted in pediatric unit Military Hospital Rawalpindi over one year period from 1st Apr 200 to 31st Mar 2002. **Subject and Methods:** We divided the patients into two groups; group A or the study group and the group B or the control group. In group A, a total of 87 Children aged 5 to 15 years presenting with RAP in which no underlying cause was found on initial assessment underwent upper gastrointestinal tract (GIT) endoscopic examination. In group B (control) we included 68 children in whom upper GIT endoscopy was done for any reason other than the RAP. In both the groups the gastroduodenal biopsy samples were sent for culture and histological examination for the diagnosis of H. pylori infection. The signs and symptoms of these patients were analyzed in detail. **Results:** In group A, out of 87 patients who were endoscoped there were 44 female and 43 male. 54(62%) were found positive and 33(38%) were found negative for H.pylori on histopathology and culture examination of biopsy samples. In the control group (B) the frequency of H.pylori infection was 35% (24 of 68) which was significantly lower than the study group (p-value .001). The frequency of H.pylori increased significantly with advancement in age (p-value .003) and lowering of the socioeconomic status (p-value.002). The commonest endoscopic finding was antral gastritis (31 of 87; 35.6%). Antral nodularity was observed in 8(26%) out of 36 cases of antral gastritis and in 23(74%) cases there was antral erythema without nodularity. The remaining endoscopic findings were pan-gastritis (14 of 87;16%), duodenal ulcer (10 of 87;11.5%), duodenitis (4 of 87;4.6%) and gastric ulcer (2 of 87;2.3%). The less frequent findings were gastric and duodenal erosions and esophagitis (about 1% each).Their was no abnormal finding in 22(25.3%) cases. Children predominantly (52%) had the symptoms characteristics of ulcer-like dyspepsia. Recurrent epigastric pain was significantly more common in the H.pylori positive than the H. pylori negative children (44 of 87 vs 16 of 33 [p-value .001]). There was no difference for other symptom characteristics when comparing infected with non-infected children. **Conclusion:** The frequency of H.pylori infection is high in children with recurrent abdominal pain and there is a high

degree of association between recurrent abdominal pain, endoscopic findings (chronic gastritis, duodenitis, gastric and duodenal ulcer) and the H. pylori infection.

Key words: Recurrent abdominal pain, Upper GI Endoscopy, Histopathology, Helicobacter Pylori infection

INTRODUCTION

Recurrent abdominal pain (RAP) is defined according to Apley's criteria as at least three discrete episodes of abdominal pain of sufficient severity to interrupt normal daily activities, occurring over a period of at least 03 months[1]. RAP is one of the most common complaints among children and affects about 10-15% of the children between the ages of 5 to 15 years[2].

In about 90 to 95% of these patients no underlying etiology is found and are labeled to have functional abdominal pain. However with the application of endoscopic, motility, imaging and other technological equipment, many unsuspected gastrointestinal disorders are being uncovered[3].

Helicobacter pylori infection is also being implicated as one of the organic cause of RAP[4]. Since its discovery by Warren and Marshal in 1983, H.pylori has emerged as an important pathogen in the gastric microbiology. The role of Helicobacter pylori in the colonization of the stomach in adults and children with chronic gastritis, peptic ulcer, MALT lymphoma and gastric carcinoma is now well documented[4,5]. An association between H.pylori infection and chronic antral gastritis in children was first reported by Czinn et al in 1986 and confirmed by other researchers[6,7]. Recently, a European pediatric consensus recommended a search for H pylori infection using upper GI endoscopy with biopsy in children suffering from upper-digestive symptoms suggestive of organic disease without any additional clear information on the nature of the symptoms[8]. The frequency of Helicobacter pylori infection in healthy children ranges from 10-60% depending upon the age and socioeconomic background[9,10]. However the relationship between the Helicobacter pylori infection, gastro duodenal disease and recurrent abdominal pain is not clear. The frequency of Helicobacter pylori infection in children with recurrent abdominal pain has been found inconsistent (Range 0% to 81%, median 22%) in different countries[7].

Many of the patients with RAP display certain patterns of complaints and a classification system of recurrent abdominal pain known as ROME II guidelines has been formulated. According to these guidelines there should be the abdominal pain for at least 12 wk, which need not be consecutive, in the preceding 12 months and it includes; functional dyspepsia, irritable bowel syndrome, functional abdominal pain, abdominal migraine and aerophagia. Functional dyspepsia is subdivided into; dysmotility like dyspepsia, ulcer-like dyspepsia, and unspecified dyspepsia[11].

The aim of the study was to assess the association between H. Pylori infection and RAP by finding the frequency of H. Pylori infection in children with RAP.

PATIENTS AND METHODS

A comparative study was conducted in pediatric unit Military Hospital Rawalpindi over one year period from 1st Apr 2001 to 31st Mar 2002. Sampling was done from all the social classes. Children were divided into two groups; group A or the study group and the group B or the control group. Children with a total family income of less than Rs 5000 per month were classified as those belonging to lower socioeconomic group, those with a total family income between Rs 5000 to 15000 per month as middle socioeconomic group and those with an over Rs 15000 per month as upper socioeconomic group. Children of both sexes aged 5 to 15 were enrolled. We divided the patients into three age groups, (1) 5 to 8 years, (2) more than 8 to 12 years and (3) more than 12 to 15 years. A detailed analysis of the signs and symptoms of the patients was done.

Children presenting with 03 or more discrete episodes of moderate to severe abdominal pain in epigastric or umbilical region in the last 03 months were included in the study group (A). Children in whom other important causes of recurrent abdominal pain were ruled out on history, physical examination and investigations including stool and urine analysis, abdominal ultrasound and other relevant investigations were selected for upper GI endoscopy.

We excluded the children < five years old on the assumption that they might be unable to describe their symptoms in detail, and the patients in whom history, physical examination, or investigations including stool and urine analysis, ultrasound abdomen and other relevant investigations were suggestive of some cause other than H.pylori infection. A standardized questionnaire was filled regarding the characteristics of their abdominal pain, frequency (days per week), diurnal variation, night time awakening, relationship of pain with food intake, nausea, vomiting, tenderness, school absence, any associated symptom like constipation and any intake of drugs (Aspirin, NSAIDS, steroids, antacids and antispasmodics) in the preceding one month.

In control group (group B) we included all the children of similar age and socioeconomic age group who underwent upper GIT endoscopy for various indications other than the chronic abdominal pain. The major indications in this group were chronic diarrhea and malab-sorption, short stature and failure to thrive, portal hypertension and GI bleeding.

All enrolled patients were assessed for fitness regarding general anesthesia. The child along with parents was explained about the procedure and written consent was obtained from the parents. The patients were ensured to be empty stomach for at least six hours before endoscopy. An attempt was made to carry out all the procedure without sedation in all the co-operative children. General anesthesia and sedation were used only in the younger and non-cooperative children. Intravenous ketamine was used for general anesthesia by the anesthetist and i/v midazolam or diazepam was used for sedation. Pediatric size Olympus CLV-40 fiber optic endoscope was used. A complete endoscopic examination of esophagus, stomach and duodenum was carried out. Multiple antral biopsies from at least three sites were obtained. The biopsy samples were also taken from any other site in the stomach and duodenum showing signs of inflammation or ulcer. The biopsy samples were labeled with reference number; formalin fixed and sent for culture and histological examination. The biopsy samples were stained with Haematoxylin & Eosin and Giemsa stains for the histological examination. Infected children were defined as those who showed positive H pylori cultures and positive histological findings (Sydney classification) from their biopsy specimen.

RESULTS

From 1st Apr 2001 to 31st Mar 2002, 87 patients in study group A (range: 5-15 years; mean age: 10.02;SD:4.0;44 females and 43 male) presenting with the complaints of recurrent abdominal pain with no identifiable underlying cause on initial assessment underwent upper GIT endoscopy. Out of 87 patients, 54(62%) patients (range 5-15; mean: 11.02; SD: 3.67; female 29 and male 25) were found positive and 33(38%) (Range 5-15; mean: 8.09; SD: 3.81; female 15 and male 18) were found negative for H.pylori on histopathology of biopsy samples (Table I).

Table-I. Epidemiological Data (Study Group A)

	Total	H. Pylori +	H. Pylori -
No. of Patients	87	54	33
Age (Years)			
Range	5-15	5-15	5-15
Mean	10.02	11.02	8.09
SD (Standard deviation)	04	3.67	3.81
Sex			
Female	44	29	15
Male	43	25	18

In control group (group B) endoscopy was performed on 68 children. H.pylori was detected in 24(35%) children. The frequency of H. pylori infection was significantly lower (p-value .001) in the control group (Table II & III).

In our study the prevalence of H. pylori was found to increase significantly with increase in age (Table IV) and lowering of the socioeconomic status (Table V). There was no significant difference (p-value.3) in prevalence of H. pylori infection between male and female patients.

Analysis of symptoms revealed that the complaint suggestive of ulcer-like dyspepsia (central abdominal pain in the upper abdomen or epigastric pain and pain during meals) were significantly more common in the children positive for H.pylori infection [44 of 54 vs 16 of 33 (p-value .001)]. There was no difference for most of the other symptom characteristics when comparing infected with non-infected children. These characteristics included histories of nausea, vomiting, diffuse or para-umbilical abdominal pain, night awakening with pain, altered bowel habits, heartburn, halitosis, and upper abdomen fullness, early satiety, and bloating, belching, flatulence, regurgitation of food, abdominal distention, hematemesis, epigastric tenderness and weight loss (Table VI). In majority of patients more than one symptom was present.

Table-II. Group B (Control Group)

Indications (n = 68)	H. Pylori Positive	H. Pylori Negative
Chronic diarrhoea/mal-absorption (n = 36)	-	-
failure to thrive and short stature (n = 14)	-	-
GIT Bleeding (n = 06)	24(35%)	44(65%)
Portal Hypertension (n = 10)	-	-
Unexplained Anemia (n = 2)	-	-

Table-III. Comparison between the study group and the control group

Group	Cases					
	Total	H. pylori positive	H.pylori square values	Pearson Chi-square value	DF	P-Value
Group A (Study Group)	87	54(62%)	33(38%)	10.945	1	.001
Group B (Control Group)	68	24(35%)	44(65%)			

Table-IV. Frequency of H. Pylori infection according to age (Group A)

Age Group (years)	Total Cases (87)	H. Pylori			Pearson Chi-square value	DF	P-Value
		- (n = 33)	+ (n = 54)	%			
5-8	17	12	5	29.4%	11.682	02	.033
>8-12	24	10	14	58.3%			
>12-15	46	11	35	76%			

On endoscopy, the commonest finding was antral gastritis (31 of 87; 35.6%). Antral nodularity was observed in 8(26%) out of 36 cases of antral gastritis and in 23(74%) cases there was antral erythema without

nodularity. The remaining endoscopic findings were pan-gastritis (14 of 87;16%), duodenal ulcer (10 of 87;11.5%), duodenitis (4 of 87; 4.6%) and gastric ulcer (2 of 87;2.3%). The less frequent findings were gastric and duodenal erosions and esophagitis (about 1% each). Their was no abnormal finding in 22(25.3%) cases (Table VII).

Table-V. Frequency of H. Pylori infection according to socio-economic status (Group A)

Socioeconomic Group	Total Cases (87)	H. Pylori			Pearson Chi-square value	DF	P-Value
		- (n = 33)	+ (n = 54)	%			
Upper	15	11	04	26.7%	12.735	02	.002
Middle	34	14	15	44%			
Lower	38	08	35	92%			

Table-VI. Analysis of symptoms of patients (Group A)

Symptoms	Patients		P-Value
	H. Pylori + (n = 54)	H. Pylori + (n = 33)	
Pain Epigastrium	44	16	.001
Para-Umbilical pain	26	15	.49
Diffuse abdominal pain	04	05	.37
Associated Symptoms			
Heart Burn	21	11	.387
Recurrent vomiting	07	05	.50
Altered bowel habits	26	20	.18
Boating, Flatulence	07	08	.14
Halitosis	07	06	.35
Night awakening with pain	13	04	.13

Out of 87 patients, who were endoscoped, Helicobacter pylori was found in 54(62%) cases on histopathology. Thirty-one cases were diagnosed to have antral gastritis on endoscopy and H. pylori was positive in 26 biopsy samples on histopathological examination (84%). Nodular gastritis was found only in H pylori infected children. H. pylori was detected in 9 out of 14(56.2%) cases of pan-gastritis. On endoscopy duodenal ulcer was diagnosed in 10 cases and H.pylori infection was found in the 9 biopsy samples (90%). There were 4 cases of duodenitis. H.pylori was found in 3(80%) of these cases on histopathology. Gastric ulcer was diagnosed in two cases and H.pylori was present in 01(50%) case. H. pylori was not found in any case with endoscopic diagnosis of gastric and duodenal erosions, esophagitis and gastro-esophageal reflux.

In 22 cases, no mucosal abnormality was found on endoscopy. However on histological examination H.pylori was detected in 6 cases (27%). Co-relation of H.pylori in

different endoscopic findings is given in (Table VIII).

Table-VII. Endoscopic Findings (Group A)		
Findings	**Cases**	
	No.	**% Age**
Antral gastritis	31	35.6%
Normal	22	25.3%
Pan-gastritis	14	16%
Duodenal ulcer	10	11.5%
Duodenitis	04	4.6%
Gastric ulcer	02	2.3%
Duodenal erosions	01	1.14%
Gasteric erosions	01	1.14%
Esophagitis	01	1.14%
Gastro-esophageal reflux	01	1.14%
Total	87	100%

Table-VIII. Co-relation H.pylori infection with endoscopic findings (Group A)			
Endoscopic findings	**Total cases (n=87)**	**H. pylori positive cases**	
		No. (N=54)	**%age**
Duodenal ulcer	10	09	90%
Antral gastritis	31	26	84%
Pan-gastritis	14	09	56%
Duodenitis	04	03	80%
Gastric ulcer	02	01	50%
Normal	22	06	27%
Gastric erosions	01	-	-
Duodenal erosions	01	-	-
Esophagitis	01	-	-
Gastroesophageal reflux	01	-	-

DISCUSSION

The goal of the study was to assess the association between H.pylori infection and recurrent abdominal pain in children by documenting the frequency of H.pylori in these children. To find the answer we performed upper GI endoscopy on children presenting with recurrent abdominal pain selected according to the selection criteria.

We used upper G I endoscopy and histopathology of the biopsy samples to diagnosis the H.pylori infection. The pediatric consensus groups in North America and Europe have termed the endoscopy and biopsy as the optimal and only acceptable diagnostic test in children with persistent and undiagnosed abdominal pain[5]. The sensitivity and specificity of histology is 90% and 100% respectively[12].

The serology has been reported to be 84 to 93% sensitive and 58 to 60% specific as compared to histopathological examination. Serology is not recommended for the diagnosis of H.pylori infection in children[13].

The urea breath test is not an appropriate alternative to upper endoscopy for initial diagnosis of H.pylori infection in children. A positive UBT only indicates the presence or absence of H.pylori but does not confirm or exclude the presence or absence of H.pylori disease. Similarly a negative test cannot rule out alternative diagnosis[14,15].

Multiple (≥ 3) biopsies from gastric and duodenal mucosa were obtained because H.pylori colonization may be patchy. In addition two antral biopsies, one each from the lesser and greater curvatures were taken because these two sites have been reported to show almost 100% sensitivity for diagnosis of H.pylori infection[16,17]. Biopsy samples were taken even from normal looking mucosa because the macroscopic appearance in infected persons ranges from a completely normal mucosa to ulceration[18]. A study conducted at Karachi reported that the frequency of H.pylori colonization was 96% in apparently normal looking upper G I tract[12]. The normal mucosa in symptomatic children may represent an early stage of infection or resolution of gastritis[16]. In our study there were 22 patients who appeared normal on

endoscopy but H.pylori infection was found in 6(27%) cases on histological examination.

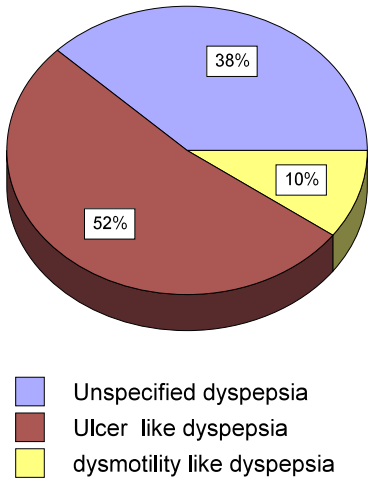
There is strong and consistent evidence that H.pylori infection is associated with gastroduodenal disease (antral gastritis and duodenal ulcer) in children[7]. We found a high degree of association between Helicobacter pylori infection and duodenal ulcer (90%), antral gastritis (84%), chronic (pan) gastritis (56%), duodenitis (80%), and gastric ulcer (50%) in this study as well (Table VIII).

The frequency of H.pylori infection in our study was 62% in the children presenting with RAP and under going upper GIT endoscopy. Several studies indicate that H.pylori infection plays a role in recurrent abdominal pain in children and adolescents. The prevalence of H.pylori infection in these children has been reported to be variable; USA 0% to 22%, UK 24%, Australia 32%, Israel 54%, French 63%, Ireland 67%, Finland 88%, and Spain 91% [7,19]. The prevalence of H.pylori infection in adults in Pakistan has been found to be 77% to 93% in different studies [20,21]. Butt A K et al, reported a 100% prevalence of H.pylori infection by using dental plaque CLO test and cytology as diagnostic test in a study conducted at Lahore[22].

The infection rate is higher in low socioeconomic group because of overcrowding, non-availability of safe drinking water, open toilets in the house and improper sewage disposal system. The prevalence of H.pylori infection increases with age both in developed and developing countries[8,23]. In our study the prevalence of H.pylori was found to increase significantly with increase in age and lowering of the socioeconomic status. H.pylori has been isolated from stool, saliva and dental plaques of the infected persons[14,22,24,25]. In Peru, Gambia and Bangladesh children were found to get infected within first few (as early as three) months of life. Kerr J R et al observed a high rate of H.pylori infection in infants who died as SIDS in a retrospective study done in UK[26].It has been reported that there is no statistically significant sex predilection for H.pylori infection[7]. This phenomenon was observed in our study as well.

The analysis of the symptoms of H.pylori positive children according to ROME II criteria in our study showed that these children predominantly (52%) had the symptoms characteristics of ulcer-like dyspepsia (Fig I).

Fig-1. Analysis of symptoms according to rome II criteria



A number of studies have proved that dyspepsia is the most frequent symptom present in H.pylori positive patients[21].Higher age related prevalence of H.pylori infection in patients with N U D have been documented[12,27]. Studies have shown that most of the children with RAP respond to HP eradication therapy by becoming free of abdominal pain after the eradication therapy[28].

It is now recognized that organic cause and gastrointestinal mucosal pathology is more common than previously thought in children with RAP[3]. In this study we found a high percentage of H.pylori infection (62%) and gastroduodenal disease (74.7%) in children undergoing upper GIT endoscopy and suffering from recurrent abdominal pain. We also observed a high degree of association between the symptoms, endoscopic findings (chronic gastritis, duodenitis, gastric and duodenal ulcer) and H.pylori infection (Table VIII). The fact is that if H.pylori infection was not looked for, these cases of

recurrent abdominal pain might have been labeled as functional abdominal pain.

CONCLUSION

Recurrent abdominal pain is a common and challenging problem both for the parents and the physician. Organic causes especially gastroduodenal diseases are more common than previously considered. The frequency of Helicobacter pylori infection in children presenting with recurrent abdominal pain is high. Our study provides strong evidence of a high degree of association between Helicobacter pylori infection and chronic gastritis, gastric and duodenal ulcer and recurrent abdominal pain especially in children with ulcer-like dyspepsia symptoms. Moreover the children acquire H.pylori infection at very early age and the prevalence increases with increasing age and lowering of socioeconomic status. The H.pylori infection should be looked for in the children presenting with recurrent abdominal pain.

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