

The Role of Endoscopic, Histopathologic and Parasitic Findings in Diagnosis of Recurrent Abdominal Pain in Children

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Abstract: *Objective:* To evaluate the diagnostic role of gastrointestinal endoscopy and biopsy in children with recurrent abdominal pain (RAP). *Patients and methods:* Fifty children with RAP were included, their ages ranged from 3 to 15 years. All patients were subjected to detailed history, examinations, routine investigations, IgG for *H. pylori*, upper and lower endoscopy and biopsy. Antigliadin antibodies and indirect hemagglutination test for amebiasis. *RESULTS:* The endoscopic findings were abnormal in 34 cases. Erythematous mucosa, nodular mucosa then ulceration and oedema, were strongly associated with presence of histopathological findings with sensitivity 94.3%, specificity 93.3%, positive predictive value (PPV)=97.1% and negative predictive value (NPV) = 87.5%. *H. pylori* infection was diagnosed in 15 patients serum IgG for *H. Pylori* was positive in 11 patients with sensitivity 73.3%. Endoscopic findings were positive in 13 patients with *H. pylori* infections with sensitivity 86.7%, while histopathological findings were positive in all patients with *H. pylori* infections with specificity 100%, PPV=100% and NPV =94.6%. Parasitic infestations were diagnosed in 9 patients. Four patients for each GE reflux disease and gastroduodenitis .Two patients were diagnosed for each of celiac disease, ulcerative colitis, chronic non specific colitis, duodenal ulcer and infected juvenile polyp .No etiology identified in 8 patients. *Conclusions:* Pediatric gastrointestinal endoscopy is a valuable and informative diagnostic procedure even in young children and can be used safely with the use of intravenous sedation.

[Hosny M.A. El-Masry, Alaa-Eldin A. Hassan, Ahmed H. Abdel tawab, M. Abd Al Fatah, Nabila F. Amin, and Gehan M. Elosaily. **The Role of Endoscopic, Histopathologic and Parasitic Findings in Diagnosis of Recurrent Abdominal Pain in Children.** *J Am Sci* 2012;8(9):16-23]. (ISSN: 1545-1003). <http://www.jofamericanscience.org>. 3

Key words: Recurrent Abdominal Pain, Endoscopy, Histopathology *H. pylori* infections

1. Introduction

RAP is a common presentation to primary care pediatricians, emergency physicians, and pediatric gastroenterologists. It is estimated to affect 10% to nearly 25% of children ⁽¹⁻³⁾. RAP represents one of the most common complaints seen in general pediatric practices. A community based study identified 10% of children with this entity. With the advent of new technology and gastrointestinal endoscopies (upper and lower), more recent studies have described an increasing proportion of organic causes of RAP ⁽⁴⁻⁶⁾. The development of gastrointestinal endoscopic instruments has dramatically improved the understanding of the pathophysiological processes of RAP in different diseases of gastrointestinal tract and also provided opportunities for non-surgical treatment. Further more endoscopic examination provides the advantage of allowing direct visualization of the mucosa with the ability to obtain a tissue biopsy for histopathological examination ⁽⁷⁾.

The aim and work: to evaluate the children with clinically significant recurrent abdominal pain, and to determine its different etiologies.

2. Patients and Methods

Fifty children, 3-15 years old, (28 females and 22 males) present with three or more episodes of RAP

over a period of at least three months, severe enough to impair their normal activities. *Exclusion criteria:* congenital heart disease or bleeding tendency, active upper gastrointestinal bleeding, acute abdominal pain, diabetic children and children with RAP of non gastrointestinal etiology as hepatic, pancreatic, renal or non abdominal origin as respiratory, musculoskeletal or metabolic. All patients were subjected to detailed history& examinations, CBC, ESR, ALT, AST, s.IgG for *H. pylori*, urine and stool analysis. A diagnosis of pinworm is made by a "cellophane tape test." All patients were also subjected to both upper and lower endoscopy and biopsy. Antigliadin antibodies and indirect hemagglutination test for amebiasis, radiological investigations as plain X-ray, abdominal ultrasonography, barium swallow, barium meal and barium enema, were done only according to suspected diseases. A simplified description of the endoscopic examination was given for the child parents and a written consent was obtained ⁽⁸⁾. Patients GIT preparation & intravenous sedation was used through incremental doses of midazolam. Instruments used for upper endoscopy: Small diameter video oesophago-gastro duodenoscopy (Pentax EG, 1840). *Instruments used for colonoscopy:* videoscope (Pentax: EC-3440F). During endoscopy, biopsies were obtained from different lesions & If no lesion can be found

biopsies were obtained from normal gastric and colonic mucosa. Biopsy specimens were fixed and stained using haematoxylin and eosin. Suspected patients with *H. pylori* infection was diagnosed histopathologically and by *H. pylori* antigen detection test in the serum ⁽⁸⁾.

Statistical analysis of data: Statistics were done by computer using Epi-info. Software, Version 6.04. A word processing, data base and statistics program ⁽⁹⁾.

3. Results

Table (1): Percentage of children with positive endoscopic findings according to type of endoscopy.

Endoscopic findings	No of children	Percentage %
Upper endoscopic findings		
Normal upper endoscopic findings	22	44
<u>Abnormal upper endoscopic findings</u>	<u>28</u>	<u>56</u>
Erythema	13	26
Nodular mucosa	8	16
Erosion	3	6
Oedema	2	4
Ulceration	2	4
Total	50	100
Lower endoscopic findings		
Normal lower endoscopic findings	37	74
<u>Abnormal lower endoscopic findings</u>	<u>13</u>	<u>26</u>
Erythema	7	14
Polyp	2	4
Ulceration	2	4
Friability	1	2
Oxyuris worms	1	2
Total	50	100
Both upper and lower endoscopic findings		
Erythema in upper endoscopy and lower endoscopy	4	57.1
Nodularity in upper endoscopy and erythema in lower endoscopy	1	14.3
Oedema in upper endoscopy and ulceration in lower endoscopy	1	14.3
Erythema in upper endoscopy and oxyuris worm in lower endoscopy	1	14.3
Total	7	100

Table (2): Results of histopathological examinations of the studied children with recurrent abdominal pain.

Histopathological diagnosis	No of children	Percentage %
No specific pathologic lesion	15	30
<i>Helicobacter pylori</i> gastritis	15	30
Non <i>H.pylori</i> gastroduodenitis	4	8
Chronic oesophagitis	4	8
Ulceration of the duodenal mucosa with surrounding inflammation	2	4
Celiac disease	2	4
Ulcerative colitis	2	4
Amoebic colitis	2	4
Juvenile polyp with secondary bacterial infection	2	4
Chronic non specific colitis	2	4
Total	50	100%

Table (3): Final diagnosis of the studied children with recurrent abdominal pain in relation to age and sex .

Diagnosis	Age Mean age \pm SD	Sex				Total N=50	
		Male N=22		Female N=28		No	%
	No	%	No	%			
H.pylori infection	12.27 \pm 2.15	6	27.3	9	23.1	15	30
Parasitic infestation	10.55 \pm 2.51	4	18.2	5	17.9	9	18
GERD	3.75 \pm 0.96	2	9.1	2	7.1	4	8
Gastroduodenitis	10.25 \pm 1.71	1	4.5	3	10.7	4	8
Celiac disease	8.5 \pm 3.54	0	0	2	7.1	2	4
Duodenal ulcer	13 \pm 2.83	1	4.5	1	3.6	2	4
Infected juvenile polyp	9 \pm 1.41	2	9.1	0	0	2	4
Chronic non specific colitis	11.5 \pm 0.71	1	4.5	1	3.6	2	4
Ulcerative colitis	13 \pm 2.83	1	4.5	1	3.6	2	4
No etiology identified	10.38 \pm 2.56	4	18.2	4	14.3	8	16

GERD: Gastroesophageal reflux disease

Table (4): Sensitivity, specificity and predictive values for endoscopic examination in relation to histopathological findings and Serum IgG for H.pylori in studied cases.

	Histopathological findings		Total	Sensitivity	specificity	PPV	NPV
	+ve	-ve					
Endoscopic findings							
+ve	33	1	34	94.3%	93.3%	97.1%	87.5%
-ve	2	14	16				
Total	35	15	50				
Endoscopic findings (for H.pylori)							
+ve	13	0	13	86.7%	100%	100%	94.6%
-ve	2	35	37				
Total	15	35	50				
Serum IgG for H.pylori							
+ve	11	0	11	73.3%	100%	100%	94.6%
-ve	4	35	39				
Total	15	35	50				

PPV : Positive predictive value NPV : Negative predictive value +ve : Positive -ve : Negative

Table (5): Data of patients diagnosed as parasitic infestation (N=9).

Diagnosis	Number of patients		Age in years	Sex		Endoscopic finding		Histopathological findings	
	No	%		Male n=4	Female n=5	+ve	-ve	+ve	-ve
Single parasitic infestation									
Giardiasis	3	33.3	7-10-12	1	2	-	-ve finding	-	-ve finding
Ascariasis	1	11.1	9	-	1	-	-ve finding	-	-ve finding
Amoebiasis	1	11.1	10	1	-	Ulceration +oedema	-	Amoebic colitis	-
Entrobiasis	1	11.1	13	1	-	Oxyuris worms	-	-	-ve finding
Mixed parasitic infestation									
Giardiasis and amoebiasis	2	22.2	8-11	1	1	Erythema	-ve finding	Amoebic colitis	-ve finding
Amoebiasis and entrobiasis	1	11.1	15	-	1		-ve finding	-	-ve finding

Table (6): Differences between H.pylori cases, parasitic infestation and unidentified cases.

Variables		H.pylori cases (15)	Parasitic infestation (9)	No etiology detected (8)	P
Age (in years)		12.27±2.15	10.56±2.51	10.38±2.56	0.115
Sex	Male	6 (40%)	4 (44.4%)	4 (50%)	0.89
	Female	9 (60%)	5 (55.6%)	4 (50%)	
Upper endoscopic findings					
Erosions		1 (6.7)	0	0	0.557
Erythema		4 (26.7)	1 (11.1)	0	0.222
Nodular mucosa		8 (53.3)	0	0	0.002
Odema		0	1 (11.1)	0	0.267
No specific lesions		2 (13.3)	7 (77.8)	8 (100%)	0.001
Lower endoscopic findings					
Erythema		2 (13.3)	1 (11.1)	0	2.566
Oxyuris worms		0	1 (11.1)	0	0.267
Ulceration		0	1 (11.1)	0	0.267
No specific lesion		13 (86.7)	6 (66.7)	8 (100)	0.157
Stool analysis (+ve)		0	88.9	0	0.001
Serum IgG for H.pylori +ve		11 (73.3)	0	0	0.002
Histopathological diagnostic features					
H.pylori gastritis		15 (100)	0	0	0.001
Amoebic colitis		0	2 (22.2)	0	0.065
No specific lesions		0	7 (77.8)	8 (100)	0.002

p>0.05: non significant p<0.05: significant p<0.01: highly significant



Fig (1): Endoscopic picture revealed gastritis involving the gastric fundus.

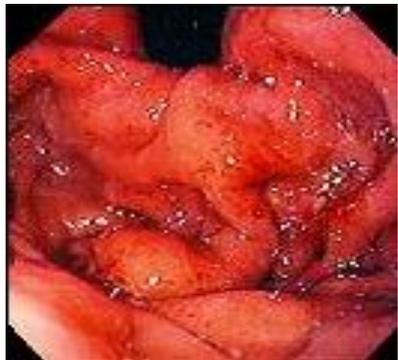


Fig (2): Endoscopic picture revealed duodenitis with erosions and tiny superficial ulcerations.



Fig (3): Endoscopic picture shows peduncles polyp in the colon of a child undergone colonoscopy for evaluation of recurrent abdominal pain and rectal bleeding.

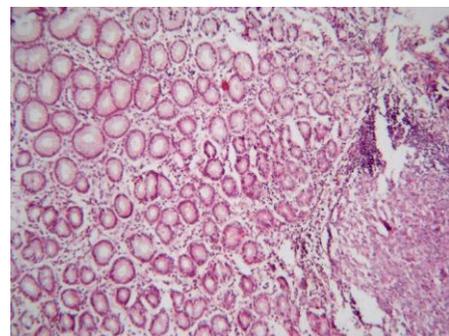


Fig (4):A photomicrograph showing infiltration by chronic inflammatory cells (nodular pattern) destructing the normal gastric mucosal glands (H&E x 200).

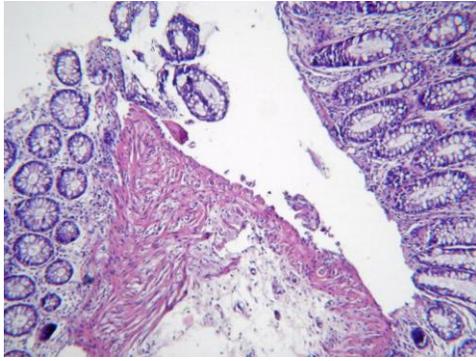


Fig (5): A photomicrograph showing infiltration of the gastric mucosa with chronic inflammatory cells (H&E x 100).

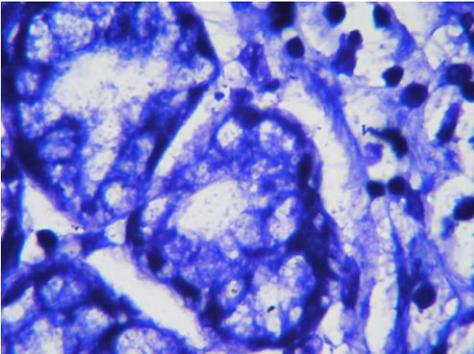
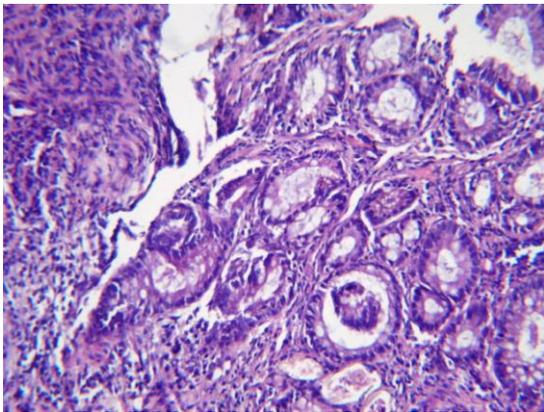


Fig (6): A photomicrograph showing positive H.pylori (violet bacilli) inside the superficial mucosal cells (Giemsa x 1000).



Fig(7): A photomicrograph showing heavy infiltrate by chronic inflammatory cells in between colonic glands with focal area of ulceration .

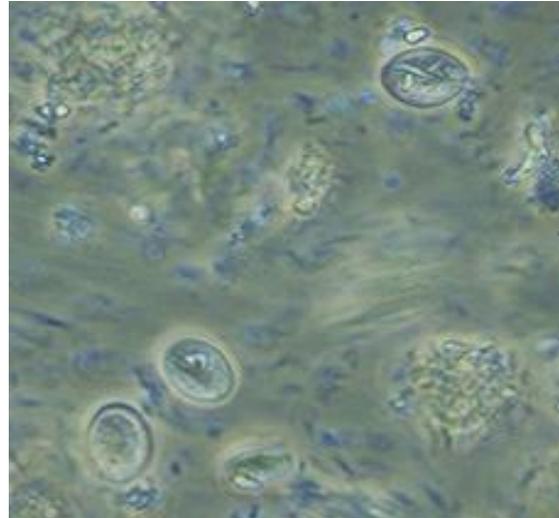
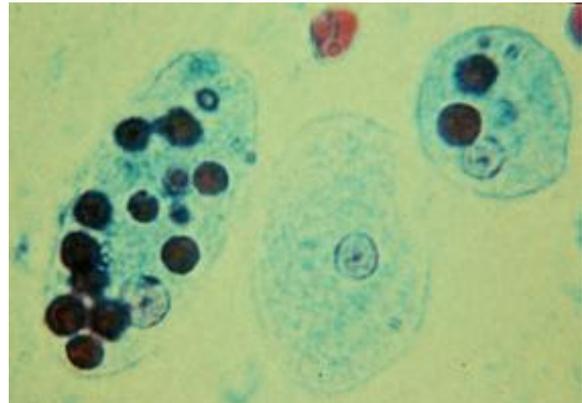


Fig.(8): In wet mounts, Giardia lamblia cysts show the typical ovoid ellipsoid shape measuring from 8-19 mm (range 11-14 mm)



Fig(9): Trophozoites of Entamoeba histolytica (Trichrome stain).



Fig(10): Oxyuris eggs by a cellophane tape test.

4. Discussion

Endoscopic findings were positive in 34 cases (68%) while 16 cases (32%) had completely normal finding upon endoscopic examination. These data are in agreement with Ukarapol *et al.*,⁽⁴⁾ however these data differ from the results of Christopher *et al.*,⁽¹⁰⁾ who found that 45 cases (88%) had normal finding upon endoscopic examination. In the current study patients with positive endoscopic findings (34 cases); 21 patients had upper endoscopic findings and normal colonoscopy, 6 patients had lower endoscopic findings and normal upper endoscopy and 7 cases had both upper and lower endoscopic findings. Gastritis was the most common histopathological findings, it was found in 19 cases (38%), 15 cases were *H.pylori* gastritis (30%) and 4 cases were non *H.pylori* gastritis (8%). These data are in agreement with Mangiaterra *et al.*,⁽¹¹⁾ and Ashorn *et al.*,⁽¹²⁾. The presence of an endoscopic findings in 68% of the patients was strongly associated with presence of histopathological finding in 70% of the patients, while absence of endoscopic findings (32% of cases) was also strongly associated with absence of histopathologic findings (30% of cases), with sensitivity 94.3%, specificity 93.3%, PPV and NPV were 97.1% and 87.5% respectively. These results were in agreement with Ukarapol *et al.*,⁽⁴⁾. Although our study evaluated a selected population of children and may not represent the true incidence in general population, we found an identified etiology in 42 children (84%) and no etiology in 8 children (16%). In the present study *H. pylori* infection was found to be the most common cause of RAP followed by parasitic infestation. This finding is in agreement with Ukarapol *et al.*,⁽⁴⁾, Fischer *et al.*,⁽¹³⁾, Ashorn *et al.*,⁽¹²⁾ and Roma *et al.*,⁽¹⁴⁾. However these results do not agree with Segal *et al.*,⁽¹⁵⁾. As Apley and Naish⁽¹⁶⁾ in their community based study found the incidence of RAP was 10.8% and the majority of cases were diagnosed as non organic. This and other studies described an association between RAP and emotional disturbances, including over-concern of illnesses in family member, and maternal anxiety disorders^(16,17). Croffie *et al.*,⁽¹⁸⁾ further confirmed that most children with RAP had a functional disorder and suggested that cost-effectiveness evaluation should be carefully considered. Also, Ukarapol *et al.*,⁽⁴⁾ reported that with the advent of pediatric endoscopy and motility studies, more studies have reported increase organic causes of RAP. In the present study, gastritis was found histopathologically in 100% of cases with *H.pylori* infection. This finding is in agreement with Carranza *et al.*,⁽¹⁹⁾. Endoscopic findings were positive in 13 patients among *H.pylori* infection patients with sensitivity 86.7%, while all of the cases diagnosed as *H.pylori* infection showed positive histopathologic findings, specificity 100%, PPV=100% and

NPV=94.6% (Table,4). These results were in agreement with the results of Wewer *et al.*,⁽²⁰⁾, however these results were high in incidence than the results of Carranza *et al.*⁽¹⁹⁾. S. IgG for *H.pylori* was positive in 11 cases (73%) of 15 cases and 4 cases were negative for IgG Sensitivity of IgG = 73.3%, specificity = 100%, PPV = 100% and NPV = 94.5% (Table,4). These results were in agreement with the result of study by Carranza *et al.*,⁽¹⁹⁾ in which the seroprevalence of s. IgG for *H.pylori* among 50 children complaining of RAP was 68%. In the present study parasitic infestation is the second common cause of RAP after *H.pylori* infection. These results were in agreement with the results by Silverman (21). Also, Ukarapol *et al.*,⁽⁴⁾, found in their study done on 38 cases, 17 cases (45%) had an identified organic cause and parasitic infestation was founded in 3 cases (17.6%) after *H.pylori* infection in 10 cases (28.9%). Giardiasis was the most common parasitic infestation in the present study. These results were in agreement with the results of Rita and Ravinderk⁽²²⁾ and Gora *et al.*,⁽²³⁾. The incidence of *H. pylori* and parasitic infestation in developing countries are higher because of overcrowdings, poor living condition and bad hygiene⁽²⁴⁾. In the present study, GERD was diagnosed in 4 cases (8%) two males and two females with mean age 3.75±0.96 years. These results were highly statistical significant because the children suffering from GERD were the youngest children ($p=0.0001$). GERD documented by presence of evidence of esophagi is on endoscopy and histopathology and by barium swallow. GERD was the third common cause of RAP in our study (8% of cases). This result was in agreement with the results of Ukarapol *et al.*,⁽⁴⁾. However El-Matary *et al.*⁽²⁵⁾ found that from 31 cases of organic etiology of RAP, 9 cases had GERD (29%). Croffie *et al.*,⁽¹⁸⁾ study on 356 patients, 149 (42%) were male, extensive evaluation yielded that non *H.pylori* gastritis and duodenitis in 16 patients (4.5%). Also Ukarapol *et al.*,⁽⁴⁾ found one case from 17 cases had organic etiology of RAP suffered from gastroduodenitis (6%). In the present study, duodenal ulcer was diagnosed in 2 cases (4%) one male and one female with mean age 13±2.83. These results were high statistical significant results as these children suffered from duodenal ulcer were the eldest children ($p=0.001$). Duodenal ulcer was diagnosed by endoscopic examination showed ulceration in the duodenal mucosa and by histopathology of duodenal biopsies. These results agree with the results of El-Matary *et al.*,⁽²⁵⁾ and Croffie *et al.*,⁽¹⁸⁾. In our study; celiac disease was diagnosed in 2 females cases (4%), endoscopic examination showed erythema, histopathologically: atrophy of intestinal villi. Antiglyadin antibodies were highly positive in the two cases. These results were in agreement to some extent with El-Matary *et al.*,⁽²⁵⁾ In

our study; ulcerative colitis was diagnosed in 2 cases (4%), one male and one female with mean age 13 ± 2.83 years. Endoscopic examination showed erythema and friability of colonic mucosa, with loss of normal vascular pattern. Histopathologically : oedema of the colonic mucosa, infiltration by acute and chronic inflammatory cells and crypt abscesses. In our study; chronic non specific colitis was diagnosed in 2 cases (4%) one male and one female, with mean age 11.5 ± 0.71 years. The endoscopic finding was erythema and superficial ulceration and histopathologically: showed infiltration of colonic mucosa by heavy chronic inflammatory cells. In our present study, rectosigmoid, juvenile polyps with secondary bacterial infection was diagnosed in two cases (4%) 2 male patients, their mean age 9 ± 1.41 years. Lower endoscopic finding showed multiple polyps with surrounding erythema in between. Histopathologically: polyp with secondary bacterial infection. In our study; juvenile polyps are common under the age of 10 years to be usually single, pedunculated and more prevalent in the rectosigmoid area of the colon, these findings in agreement with Poddar *et al.*,⁽²⁶⁾. In this study most of the juvenile polyps were small in size (<3 cm in diameter). In our study endoscopic findings were positive in 34 children and normal in 16 children while histopathological examination were positive in 35 children and normal in 15 children. This means that there is two patients had normal endoscopic finding but histopathological examination revealed gastritis. On the other hand one patient showed erythema and oxyuris worms by endocopy but histopathological examination was normal and no specific lesions. This poor correlation between endoscopic and histopathology finding has been also reported by Stordal *et al.*,⁽²⁷⁾ and Ukarapol *et al.*,⁽⁴⁾.

In our study 16 patients with normal endoscopic findings ,two of them were diagnosed as *H. pylori* infection by histopathology and positive s. IgG for *H.pylori* and 6 patients were diagnosed as parasitic infestation by stool analysis, No etiology was identified in 8 cases (16%) .These results were in agreement with the results of Alven⁽²⁸⁾ and Croffie *et al.*⁽¹⁸⁾.The cause of RAP in the 8 cases in which no etiology identified may be functional RAP .These findings are in agreement with Bufler *et al.*^(29,30)

Conclusions: Pediatric gastrointestinal endoscopy is a valuable and informative diagnostic procedure even in young children and can be used safely with the use of intravenous sedation. *Helicobacter pylori* infection is an important cause of RAP and gastritis in children. Parasitic infestation is the second most common cause of an organic RAP. Functional gastrointestinal disorders should be considered when most of the investigations are negative.

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