

# Recurrent abdominal pain in children: the utility of upper endoscopy and histopathology

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## ABSTRACT

**Introduction:** To study the utility of upper gastrointestinal endoscopy with biopsy in the evaluation of children with clinically-significant recurrent abdominal pain.

**Methods:** Over a three-month period, children with three or more episodes of upper abdominal pain that was severe enough to impair their normal activity and required medical attention were included in the study. After complete history, physical examination and basic investigations, upper gastrointestinal endoscopy with biopsy was performed in all patients.

**Results:** Thirty-eight children were enrolled. Their average age was 10.5 years and 21 were female. Organic causes were identified in 44.7 percent of the cases, with *Helicobacter pylori* gastritis being the most common diagnosis (28.9 percent). No specific dyspeptic symptom was significantly associated with either organic cause of recurrent abdominal pain or *Helicobacter pylori* infection. Antral nodularity was the only endoscopic finding significantly associated with *Helicobacter pylori* infection (sensitivity 63.4 percent, specificity 85.2 percent). All patients improved after specific therapy was instituted.

**Conclusion:** The organic causes of recurrent abdominal pain in children have been increasingly identified in our hospital, a tertiary care centre in Northern Thailand. One of the most common causes found in this study was *Helicobacter pylori* infection. Upper endoscopy was very helpful in identifying the underlying pathology.

**Keywords:** abdominal pain, children, endoscopy, *Helicobacter pylori*, recurrent abdominal pain

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## INTRODUCTION

Recurrent abdominal pain (RAP) represents one of the most common complaints seen in general paediatric

practice. A community-based study identified 10% of children with this entity<sup>(1)</sup>. Traditionally, 90% of cases of RAP have been considered functional disorders. However, with the advent of new technologies, more recent studies have described an increasing proportion of organic causes<sup>(2-7)</sup>. The most challenging task for the clinician seeing a child with RAP is to determine whether a specific organic cause may be present and what the most appropriate investigations to be undertaken should be<sup>(8)</sup>. The purpose of this study is to assess the utility of upper gastrointestinal endoscopy with biopsy in the evaluation of children with clinically-significant RAP.

## METHODS

This is a prospective descriptive study conducted from 2000 to 2002 at the Department of Paediatrics, Chiang Mai University Hospital. All children older than five years of age that were seen at our Paediatric Gastroenterology clinic with RAP as their presenting complaint were included. Clinically-significant RAP was defined as at least three episodes of upper abdominal pain during the three consecutive months preceding the study that was severe enough to affect their normal activities and required medical attention. Children who had received proton pump inhibitors, amoxicillin, metronidazole or clarithromycin within two weeks prior to the study were excluded. The study protocol was approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University. Written informed consent was obtained from all participating subjects.

Complete history that focused on dyspeptic symptoms and physical examination were performed by a single physician (NU). Peptic-like dyspepsia was diagnosed by the presence of two or more of the following: periodic pain, pain relieved by food, pain relieved by antacid, pain before meal or while hungry, nausea and/or vomiting, and night pain. Dysmotility-like dyspepsia was diagnosed by the presence of two or more of the following: abdominal bloating or distention, anorexia or weight loss, pain aggravated by food or milk, and pain relieved by

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belching. Finally, reflux-like dyspepsia was diagnosed if the child presented with either heartburn, chest pain or acid regurgitation. Complete blood count, urinalysis, stool examination, and erythrocyte sedimentation rate were done in all patients. If the clinical picture suggested hepatobiliary or pancreatic diseases, further investigations were undertaken as indicated.

Oesophagogastroduodenoscopy was performed in the surgical suite under general anaesthesia, using Olympus GIF N30 and XP20 endoscopes. Endoscopic abnormalities were classified as ulcer, mass, erosion, erythema, friability, nodularity, and oedema. Tissue biopsies were obtained from all abnormal lesions as well as representative sites of the gastrointestinal tract, including the oesophagus (one), gastric body (one), antrum (two; one for pathology and one for rapid urease test), and duodenum (one). Biopsy specimens were fixed in 10% formalin, embedded in a paraffin wax block, and sections were stained using haematoxylin and eosin. Gastritis was graded using the updated Sydney system<sup>(9)</sup>.

Warthin-Starry and polyclonal antibody stains for *Helicobacter pylori* infection were also done. One biopsy from the gastric antrum was tested for the presence of *Helicobacter pylori* using a rapid urease test (Pronto Dry, Medical Instrument Corp, Solothurn, Switzerland). *Helicobacter pylori* infection was diagnosed by a positive rapid urease test and the visualisation of characteristic spiral-shaped organisms on histopathology. Interpretation of tissue biopsies were blindly performed by a single pathologist (NL) who did not know the clinical history, endoscopic findings as well as the result of rapid urease test. Comparison of two discrete or continuous variables was performed using standard techniques such as the Fisher's exact test and the Mann-Whitney U test, respectively. P value less than 0.05 was considered significant for the two-tailed test.

## RESULTS

A total of 51 children were initially included into the study. Thirteen of them refused endoscopy. Therefore, the final study group consisted of 38 children. The average age was 10.5 years (S.D. 2.9 years) and 21 (55%) were female. Most children complained of peptic-like dyspepsia (20 cases), followed by reflux-like dyspepsia (11) and dysmotility-like dyspepsia (3). Fifteen patients had symptoms corresponding to more than one category of dyspepsia. Seventeen patients (45%) were diagnosed to have an organic aetiology for their RAP, while 21 had a non-organic cause. The most common organic cause of RAP was *Helicobacter pylori* infection (10 cases), followed by each one of

**Table I. Correlation between endoscopic abnormality and the aetiology of recurrent abdominal pain in children (p=0.006).**

	Organic causes of recurrent abdominal pain	Non-organic causes of recurrent abdominal pain
Endoscopic abnormality present	15	9
Endoscopic abnormality absent	2	12

*Helicobacter pylori* infection with giardiasis, *Capillaria philippinensis* infection, duodenitis, reflux oesophagitis, prolapse gastropathy, gastroparesis, and gastric carcinoma. The most common non-organic cause of RAP was functional abdominal pain (18). Children with organic RAP were significantly older than children with non-organic RAP (11.7 vs. 9.6 years, p=0.04). No category of dyspepsia syndrome was specifically associated with organic or non-organic causes of RAP.

The gastric antrum was the most common site of abnormal endoscopic findings (13 cases), followed by the duodenum (8), gastric body (6) and oesophagus (4). The most common findings were antral nodularity (7), duodenal ulcer (1), gastric ulcer and mass (1), and oesophageal ulcer (1). The presence of an endoscopic abnormality was strongly associated with an organic cause of RAP (p=0.006), with positive and negative predictive values of 62.5% and 85.7%, respectively (Table I). Twenty-four (63%) patients had histological abnormalities. Mild chronic non-specific inflammation in the duodenum was the most common finding (17), followed by chronic superficial gastritis (11) and chronic active gastritis (7). Parasitic infestations were documented in two cases (*Giardia intestinalis* and *Capillaria philippinensis*). Three cases had evidence of oesophagitis, with one case diagnosed as reflux oesophagitis. Corpus and antral gland atrophy were reported in two cases. One patient was diagnosed to have signet ring cell carcinoma of the stomach.

In the subgroup of patients with *Helicobacter pylori* infection, the most common endoscopic abnormalities were antral erythema (8 cases), antral nodularity (7), duodenal erythema (6) and duodenal ulcer (1). Antral nodularity was the only endoscopic finding significantly associated with *Helicobacter pylori* infection (positive predictive value 63.6%, negative predictive value 85.2%). The histopathological findings included chronic superficial gastritis (10 cases), chronic active gastritis (7), duodenitis (6) and corpus gland atrophy (1). All patients received treatment according to their specific diagnosis and none has shown recurrence of the RAP symptoms during the follow-up period. Children with *Helicobacter pylori* infection were treated with omeprazole, amoxicillin, and clarithromycin for 14 days.

The child with gastric adenocarcinoma could not be treated and died.

## DISCUSSION

The entity known as RAP in children was first described by Apley and Naish in 1958. The incidence found in their community-based study was 10.8% and the majority of cases were diagnosed as non-organic<sup>(1)</sup>. This and other studies described an association between RAP and emotional disturbances, including over-concern of illnesses in family members, neuroticism, and maternal anxiety disorder<sup>(1,10-12)</sup>. The postulated mechanism is that imitation of illnesses and inappropriate response to emotional stresses in children could lead to psychosomatic symptoms, such as abdominal pain<sup>(13)</sup>. Croffie et al further confirmed that most children with RAP had a functional disorder and suggested that cost-effectiveness evaluations should be carefully considered<sup>(14)</sup>. McGrath et al, on the other hand, found no difference between a group of children with RAP and a control group in terms of stressful events, extreme personality characteristics, and imitation of abdominal pain from the family members, thus contradicting the perception that the majority of RAP in children had a psychogenic origin<sup>(15)</sup>. Similarly, a study by Raymer et al failed to find an emotional disturbance that could significantly differentiate between organic and non-organic RAP<sup>(16)</sup>.

With the advent of paediatric endoscopy and motility studies, more studies have reported organic causes of RAP<sup>(2-7)</sup>. Hyams and Hyman identified certain clinical signs (such as night pain, weight loss, hematemesis, haematochezia, fever, arthritis, delayed puberty, and family history of inflammatory bowel diseases) that should alert the physician to a likely organic cause of RAP<sup>(17)</sup>. Although our study evaluated a select population of children referred to a tertiary centre and may not represent the true incidence in general population, we found that almost one-half of the cases with RAP (44.7%) had an organic cause. Similar to what has been reported by other authors, we could not identify a particular set of symptoms specifically associated with either organic RAP or *Helicobacter pylori* infection<sup>(18,19)</sup>.

*Helicobacter pylori* infection was the most common aetiology of RAP in our study (28.9%), followed by parasitic infestations and motility disorders (reflux oesophagitis and gastroparesis). The average age of children with an organic cause of RAP was higher than that in children with a non-organic cause. We believe this may be caused by the fact that the prevalence of *Helicobacter pylori* infection increases with age<sup>(20)</sup>. Some children had abnormal histopathological findings on biopsy specimens,

despite normal gross endoscopic findings. This poor correlation between endoscopic and histopathology findings has been previously reported<sup>(21)</sup>. However, the histological inflammation noted in patients with normal endoscopic findings was mild and rarely provided an additional specific diagnosis. Therefore, tissue biopsies may not be always necessary in patients with normal endoscopy (the negative predictive value of normal endoscopy was 85.7%).

As noted by previous studies, *Helicobacter pylori* infection in children was significantly associated with antral nodularity that histologically contained lymphoid follicles, and active gastritis (seen in 64% of our patients with *Helicobacter pylori* infection)<sup>(19,22)</sup>. Although *Helicobacter pylori* infection has been increasingly reported among children with RAP, empirical antibiotic treatment is not currently recommended<sup>(23)</sup>. Since *Helicobacter pylori* infection is so frequent in our population, we cannot establish with certainty whether this bacteria was the cause of RAP in our patients. Our observation that all our infected patients improved once antimicrobial therapy was administered suggests a possible link.

In conclusion, organic causes of RAP in children are increasingly identified in our hospital, a tertiary care centre in Northern Thailand. One of the most common causes in this study was *Helicobacter pylori* infection. Because of the frequency and type of organic causes of RAP, upper endoscopy proved to be very useful in the evaluation of our patients who presented with clinically-significant RAP. Although histopathology revealed mucosal inflammation in some patients with normal endoscopic findings, this inflammation was mild and non-specific. Consequently, from our experience in the evaluation of children with RAP, tissue biopsy may be of value only in those with abnormal endoscopic findings. After a diagnosis was established, specific treatment improved and cured the RAP symptoms in most of cases.

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– Prof Li Shu Chuen, National University of Singapore

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- 1) Overview of Pharmacoeconomics and Outcome Research by Paul Kind
- 2) Pharmacoeconomics: Uses in Practice and Research by Li Shu Chuen
- 3) Health Related Quality of Life: Uses in Practice and Research by Paul Kind

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**Fee** : **Morning Seminar** : SGD 50 (*Doctor & other healthcare professionals*),  
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