

# Upper Gastrointestinal Endoscopy and Histopathology Appearance in Indonesian Children with Recurrent Epigastric Pain

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## ABSTRACT

**Background:** Recurrent Epigastric Pain (REP) is a clinical symptom frequently found in children. Data of the correlation between duration of illness, frequency of illness, associated symptoms of REP and the abnormality of endoscopic and histopathologic appearance are still limited, especially in Indonesia. The role of *Helicobacter pylori* (*H. pylori*) infection in causing organic abnormalities of the gastrointestinal tract (GIT) is also still controversial.

**Aim:** To know the endoscopic and histopathologic appearance and the prevalence of *Helicobacter pylori* infection, 169 children with REP was performed for endoscopic and histopathologic examination in Department of Pediatric, Cipto Mangunkusumo hospital.

**Result:** Endoscopic and histopathologic abnormalities were found significantly in children who suffered from REP more than 9 months and more than 6 times during 3 months of period.

**Conclusion:** Endoscopic and histopathologic examinations should be considered in children with REP.

**Keywords:** recurrent abdominal pain, epigastric pain, *Helicobacter pylori*, endoscopy and histopathology

## INTRODUCTION

Recurrent abdominal pain (RAP) is a clinical symptoms frequently found in children causes school absence and daily activities disturbance. Approximately 30% school-aged children has ever had RAP, and 70% of them had psychogenic causes.<sup>1,2</sup> Recurrent epigastric pain (REP) is one of several indication to perform endoscopic examination.<sup>3,4</sup> Mucosal biopsy of the gastrointestinal tract (GIT) is also important since normal endoscopic examination could result in abnormal histopathology.<sup>3</sup>

The correlation between duration of illness, frequency of illness, and symptoms with endoscopic and histopathologic appearance in children with recurrent epigastric pain (REP) has not been vastly studied yet. This study was designed to (1) find out the prevalence of endoscopic and histopathologic abnormalities in children with REP, (2) describe the varieties of endoscopic and histopathologic

abnormalities in REP patients, and (3) find out the correlation between duration and frequency of illness with the result of endoscopic and histopathologic examination.

## METHODS

One hundred and sixty nine children with REP who performed endoscopic and histopathologic examination were enrolled the study. Biopsy was performed in esophagus, antrum, corpus, and duodenum. The materials were examined for pathology anatomy with hematoxylin eosin and giemsa stain. Data including duration and frequency of pain, endoscopic and histopathologic appearance were analyzed using SPSS 11.0 program. Recurrent epigastric pain was defined as three or more bouts of epigastric pain which severe enough to interfere with normal activities, occurring over a period of not less than 3 months during the year preceding the examination. A chi-square test was used to compare recurrent epigastric pain with or without endoscopic and histopathologic abnormalities. Fisher's test was used on appropriate data. The calculation of cut off point used Receiver Operation Curve (ROC) graphic.

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**RESULTS**

The majority of subjects (78.1%) was 5-10 years old children, both in the male and the female group. The median age was 8 years and 9 months old (range 5-18 year). There were 83 boys and 86 girls. The difference in the distribution of boy and girl among the age groups was not comparable.

Normal endoscopic examination were mostly found in the esophagus (65.7%) and the least in the stomach (25.4%). Hyperemic mucosal was found in esophagus (32.5%), stomach (42.6%), and duodenum (23.7%). Erosion was mostly found in stomach (30.1%) and ulcer was found in duodenum (4.8%) and stomach (1.6%) respectively. Nodule only found in duodenum (0.04%). Abnormal histopathology examination was described as gastritis in 100 children (59.2%), esophagitis in 70 children (41.3%), and duodenitis in 55 children (32.6%). Peptic ulcers was found in 8 children (4.6%) (table 1).

**Table 1. Histopathologic appearance of GIT**

Histopathologic appearance	Total (N)	%
Normal	21	12.4
Gastritis	42	24.9
Esophagitis	47	27.8
Gastroduodenitis	31	18.5
Esophagogastroduodenitis	19	11.2
Esophagogastroduodenitis + peptic ulcer	4	2.3
Gastritis + peptic ulcer	4	2.3
Duodenitis	1	0.6
Total	169	100

Endoscopic abnormalities were found more in patient having the symptoms for more than 9 months compared to those who had it for 9 months or less ( $p = 0.010$ ) (table 2). The cut-off point of 9 months was established by ROC (Receiver Operation Curve) graphic.

**Table 2. Correlation between duration of illness and upper GIT endoscopic appearance**

Duration of illness (month)	Upper GIT endoscopic appearance		Total (N)
	Abnormal (N)	Normal (N)	
≤ 9	40	17	57
> 9	97	15	112
Total	137	32	169

$X^2 = 6.645$ ;  $df = 1$ ;  $p = 0.010$

Histopathologic abnormalities were significantly more frequent among patients suffered more than 6 attacks in 3 months compared with 6 attacks or less ( $p = 0.000$ ) (table 3).

**Table 3. Correlation between frequency of illness and upper GIT histopathologic appearance**

Frequency of illness (in 3 months)	Upper GIT histopathologic appearance		Total (N)
	Abnormal (N)	Normal (N)	
≤ 6	63	18	81
> 6	85	3	88
Total	148	21	169

$X^2 = 13.178$   $df = 1$   $p = 0.000$

**Associated Symptoms and Endoscopic/Histopathologic Abnormalities**

There were 84 children (49.7%) suffered from REP with associated symptoms (such as nausea, vomiting, or fullness), whereas those without any were 85 children (50.3%). There was significant correlation between associated symptoms and endoscopic/histopathologic abnormalities in the esophagus ( $p = 0.004$ ) and stomach ( $p = 0.014$ ), but no significant correlation in the duodenum ( $p = 0.238$ ).

**Helicobacter pylori Infection and Recurrent Epigastric Pain**

Based on histopathological examination, *Helicobacter pylori* was found in 48 children (28.4%) and 27% of them were 7 years-old. *Helicobacter pylori* significantly more frequent in children who had REP for more than 9 months compared to children who had it for 9 months or less (table 4), and also in children who had more than 6 attacks compared to children who had it 6 attacks or less in 3 months (table 5).

**Table 4. Correlation between H. pylori infection and duration of illness**

Duration of illness (month)	Histopathology of H. pylori		Total (N)
	Positive (N)	Negative (N)	
≤ 9	8	49	57
> 9	40	72	112
Total	48	121	169

$X^2 = 8.731$   $df = 1$   $p = 0.003$

**Table 5. Correlation between H. pylori infection and frequency of illness**

Frequency of illness (in 3 months)	Histopathology of H. pylori		Total (N)
	Positive (N)	Negative (N)	
≤ 6	15	66	81
> 6	33	55	88
Total	48	121	169

$X^2 = 7.473$   $df = 1$   $p = 0.006$

*Helicobacter pylori* was found more frequent in esophagogastroduodenitis and gastroduodenitis respectively. Seven of 8 patients with ulcer result in *H. pylori*. There was significant correlation between *H. pylori* and the abnormalities of upper GIT histopathology (table 6).

**Table 6. Correlation between H. pylori and upper GIT Histopathologic abnormalities**

H. pylori	Upper GIT histopathologic appearance		Total (N)
	Abnormal (N)	Normal (N)	
Positive	48	0	48
Negative	100	21	121
Total	148	21	169

Fisher's test  $p = 0.002$

## DISCUSSION

This study found 352 children who fulfilled the Apley's criteria for recurrent abdominal pain, however only 169 enrolled the study. The other 183 patients did not meet the inclusion criteria due to the location of pain was not at epigastric area, lack of data of endoscopic/histopathologic examination, and or the parents refused to sign the informed consent for endoscopic procedure.

Our study found an equal number of boys (49.1%) and girls (50.9%). A similar distribution also shown in 65 India's children (age 3-1 years) with recurrent abdominal pain (50.7% boys and 49.3% girls).<sup>5</sup> Our study found that until the age of 9 year the distribution of both sexes are almost equal, however at the age of 9-12 years, girls are more dominant than boys. Study from Apley's also showed an equal distribution between boys and girls until the age of 9 year and a domination of girls was seen at the age of 9-12 years (1.5 : 1 ratio).<sup>2</sup> The majority of subjects were between the age of 5 and 10 years. There is a tendency of declining number of cases with the increasing of age. The most frequent age was 6 year-olds (11 boys and 23 girls with ratio 2:4). There was no significant difference between boys and girls distribution between age groups.

Eighty five subjects (50.3%) had no associated symptoms, and while the rest 84 (49.7%) had, mostly were nausea and or vomiting (43.2%). Strickler et al, found nausea in 72 children (44%) and vomiting in 56 (37.4%).<sup>6</sup> Das et al, reported a symptom resembling nausea and vomiting in 35 children (55%) and nausea in 12 children (20%).<sup>5</sup> Literatures supported that RAP were frequently associated with these symptoms.<sup>7,8</sup>

The most frequent abnormalities of endoscopic appearance in esophagus was hyperemia (30,%). In the gaster were hyperemia (43.2%) and erosion (30.2%). In the duodenum were hyperemia (23.7%). Ulcer was found in duodenum (7%) and gaster (1.2%). Nodules only found in duodenum (4.7%). Ashorn et al reported endoscopic abnormalities in 51.5% of recurrent abdominal pain cases.<sup>3</sup> Quak et al, found organic abnormalities in 83.1% of 183 children and endoscopic abnormalities in 77 children (42.8%).<sup>9</sup> These findings were in contrary with Apley's who found only 10% organic abnormality in recurrent abdominal pain among school-aged children. This difference might be due to the application of the criteria that we used for epigastric pain. Other factors that could influence this condition is the increasing of endoscopic and histopathologic examination in the management of children with recurrent abdominal pain during the last decade. Normal endoscopic appearance was seen in 42 cases, but 35.7% of them showed histopathologic abnormalities. It seems that normal endoscopic

appearance does not ensure a normal histopathologic feature, so histopathologic examination is a necessity in children with REP.

The prevalence of abnormal endoscopic appearance in esophagus, gaster, and duodenum increases after 9 months of illness. This suggests that organic abnormality as a cause of REP increases with the duration illness (Table 2). Ashorn et al, reported a mean duration of illness of 21 months (3-72 months) in recurrent abdominal pain with organic causes, whereas 17 months in non-organic causes, however there was no significant difference between those groups.<sup>3</sup> In our study showed that duration of illness of more than 9 months indicated endoscopic abnormalities.

Histopathologic abnormalities was found in 87.6% of cases, mostly was gastritis (83.4%) (table 1). Roma et al, found a similar data (85.4%),<sup>10</sup> whereas Ashorn et al reported a lower result (58.5%)<sup>3</sup> and Das et al, found gastritis in 69% of cases.<sup>5</sup> These findings suggest that chronic gastritis is an organic abnormality that should be bore in mind in dealing with children who suffered from REP.

Histopathologic abnormalities in the esophagus, gaster and duodenum were significantly correlated with frequency of illness more than 6 times in 3 months. Endoscopic abnormalities in the esophagus and especially the gaster were found significantly more frequency in REP with associated symptoms compared to REP without associated symptoms, whereas in the duodenum there was no significant difference ( $p = 0.046$ ,  $p = 0.014$ ,  $p = 0.238$ , respectively). Ashorn et al, reported no correlation between associated symptoms and endoscopic abnormalities, whether in the esophagus, gaster, or duodenum. He also reported that there was no specific symptom to differentiate organic or non-organic cause in recurrent abdominal pain.<sup>3</sup> Our study showed that associated symptoms act as an indicator of abnormalities in the esophagus and gaster, but not in the duodenum.

The prevalence of *H. pylori* infection (histopathologically) in REP was 28.4%, higher than the result of the studies by Ashorn et al, 22% in Finland,<sup>3</sup> and Raymond et al, 18.1% in Paris,<sup>11</sup> but lower than Hendelberg et al, 54% in Israel,<sup>12</sup> Das et al, 66% in India,<sup>5</sup> and Giacomo et al, 60% in Italy.<sup>13</sup> A metaanalysis by Macartur et al, reported that the prevalence of *H. pylori* infection in children with REP ranged 0-82% (median 22%).<sup>14</sup> It suggests that the prevalence of *H. pylori* infection still high, in accordance with literatures which said that *H. pylori* infection was more frequently found in developing countries than developed countries.<sup>7,8</sup>

*H. pylori* infection was found in 87.5% (7/8)

children with ulcer (6 in duodenum and 1 in gaster), whereas 48% (48/100) in children with gastritis. It seems that duodenal ulcer tends to indicate an *H. pylori* infection rather than chronic gastritis in REP children.

A significant difference between REP with and without *H. pylori* infection was occurred among children who suffered the illness for more than 9 months ( $p = 0.003$ ). Ashorn et al, reported that recurrent abdominal pain with *H. pylori* generally had longer duration of illness compared to those without the infection, although it was statistically insignificant. In their study showed that mean duration of illness of recurrent abdominal pain caused by *H. pylori* was 26.1 months and not significantly different with recurrent abdominal pain without *H. pylori*.<sup>3</sup> Our study showed that frequency of illness of 6 times in 3 months indicated a presence of *H. pylori* infection.

## CONCLUSION

Recurrent epigastric pain should be considered as a symptom that indicate an organic causes. There were a significant correlation between endoscopic abnormalities and histopathologic abnormalities. Nine months duration of illness, 6 times/3 months frequency of illness, and associated symptoms is the indication of performing endoscopic examination in children with REP.

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