



Use of Alarm Symptoms to Discriminate Abdominal Pain Related to Organic GI Diseases from Functional Gastrointestinal Disorders

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Received 25 July 2019; Received in revised form 29 July 2020
Accepted 14 September 2020; Available online 28 March 2022

ABSTRACT

Recurrent abdominal pain (RAP) is one of the most commonly encountered problems in children and is usually attributable to functional gastrointestinal disorders (FGIDs) rather than organic disease. Although alarm symptoms help to discriminate organic disease from FGIDs, further investigation might still be helpful. The aim of this study was to determine the role of alarm symptoms in this discrimination, at Thammasat University Hospital between 2010 and 2016. The medical records of 71 patients with RAP were retrospectively reviewed. Clinical diagnoses of FGIDs were based on the Rome III criteria. Information was collected on demographic data, clinical characteristics (alarm symptoms), laboratory test results, esophagogastroduodenoscopy (EGD) results and radiography. Descriptive statistical analysis was performed. A total of 71 patients were included in the study. The patients' mean age was 9 years (range: 2-15 years), and the majority was composed of females (61.43%). FGIDs (61.97%) were more common causes of RAP than organic GI diseases. The alarm symptoms of FGIDs and organic GI diseases were found in 27 percent and 100 percent of the patients, respectively. The most commonly encountered alarm symptoms in organic causes were nocturnal pain (51.85%), followed by weight loss (40.74%) and then GI blood loss (37%). The significant alarm symptoms for discriminating between FGIDs and organic GI diseases were nocturnal pain, weight loss, gastrointestinal blood loss and anemia ($p < 0.05$).

Keywords: Alarm symptoms; Functional gastrointestinal disorders; Pediatric; Recurrent abdominal pain; Rome III

1. Introduction

Recurrent abdominal pain (RAP) is the second most frequently encountered problem after headaches in children and adolescents [1]. Internationally, the incidence of chronic abdominal pain is 9-15 percent [2-4], with greater prevalence in the 4- to 6-year age group and early adolescents [5-6] and with greater prevalence among females than males, at a ratio of 19:14. For the most part, the causes of RAP in children have been attributed to functional GI disorders (FGIDs) at 8-27 percent and organic causes [2, 7-9]. Although no data is available on the incidence of organic caused presentations of RAP in Thailand, Prapan Arnbruang et al. conducted a study by performing upper gastrointestinal endoscopies to determine the causes of RAP, finding gastroduodenitis at a rather high rate at 27.4 percent, *Helicobacter pylori* (*H. Pylori*) gastritis at 17.7 percent and esophagitis at 6.5 percent [10]. Although most RAP in children is attributed to FGIDs, organic causes might also be present.

Therefore, in discriminating between functional causes and organic causes, pediatricians need to properly assess children with abdominal pain by relying on questions about medical history, physical examinations and surveying for alarm symptoms that indicate organic causes of the disease [11]. According to a study by Motamed F. et al. in Iran in 2012, children with RAP in the organic causes group had significantly higher incidences of fever, abdominal pain not in the umbilical area, nighttime awakening due to abdominal pain, weight loss, delayed growth, abdominal tenderness during physical examination and elevated ESR levels [12]. The aforementioned symptoms are found significantly more frequently in the organic causes group than in the functional GI disorder causes group without organic causes. Regardless, no research has been conducted indicating the significance of any alarm symptoms that would contribute to distinguishing children with chronic abdominal pain in the functional GI disorder

causes group from those in the organic causes group. The objective of this study was to determine the correlations between conditions and alarm symptoms based on the diagnostic criteria of Rome III to properly identify children with RAP caused by FGIDs rather than organic disease.

2. Materials and Methods

Data was collected retrospectively from the medical records of pediatric patients aged 4-18 years with RAP for more than or equal to two months [11] who had been diagnosed with the following abdominal pain-related functional gastrointestinal disorders: functional dyspepsia, irritable bowel syndrome (IBS), abdominal migraine, functional abdominal pain (FAP) and functional abdominal pain syndrome (FAPs) with organic causes such as peptic ulcer disease, *H. pylori* gastritis, eosinophilic esophagitis/gastritis, gastroesophageal reflux disease (GERD) and inflammatory bowel disease. Diagnosis of FGIDs was based on criteria of Rome III. Blood chemistry, stool examination, stool occult blood, ambulatory pH monitoring and 24-hour multichannel intraluminal impedance pH testing and gastroduodenoscopy/colonoscopy data were selected case by case depending on the organic disease suspected. Alarm symptoms were recorded as the following: a family history of inflammatory bowel disease, celiac disease, or peptic ulcer disease, persistent right upper or right lower quadrant pain, dysphagia, persistent vomiting, gastrointestinal blood loss such as melena, hematochezia and positive stool occult blood, nocturnal diarrhea, arthritis, perirectal disease, weight loss $\geq 5\%$ of their body weight within a 3-month period, deceleration of linear growth and unexplained fever.

2.1 Exclusion criteria

Patients presenting with cholestatic jaundice, hepatosplenomegaly or symptoms indicating hepatobiliary disease admitted to

Thammasat University Hospital in 2006-2016. The patients were sought in the hospital's computer system by using international classification of disease code, as well as reviewing the patients' medical records in order to affirm diagnosis before data collection.

2.2 Statistical analysis

All statistical analyses were conducted using STATA version 15.1. Categorical variables were calculated as frequencies (%) and continuous variables were summarized as mean \pm SD. A two-tailed Student's *t*-test was used for comparisons of continuous variables with normal distribution, and the Mann-Whitney *U* test was used for continuous variables with non-normal distribution. Chi-square was used to compare categorical variables between groups.

3. Results

According to the findings, all of the patients had visited the hospital with RAP for more than two months. In all, 18 patients with recurrent abdominal pain due to constipation were eliminated, for a total sample of 91 patients for the study. Of these, the medical records for two patients were missing. Table 1 shows the final diagnosis after follow-up on treatment for at least six months. Based on the findings, 44 of the patients were found to have FGIDs (61.9%) and 38 percent were found to belong to the organic causes group. Both groups had a mean age of 9 ± 2.67 years and most were female (73%). *H. pylori* induced gastritis and ulcers were most frequently found in the organic causes group at 29.63 percent. The other causes were duodenal ulcers not caused by *H. pylori* and GERD at 22.22 percent and 18.52 percent, respectively. As for the group with FGIDs diagnosed with Rome III criteria, irritable bowel syndrome (IBS) was found at 43.18 percent, functional dyspepsia at 36.36 percent and FAP at 13.64 percent.

3.1 Alarm symptoms

According to the findings of the present study, in 71 pediatric patients with RAP, one or more alarm symptoms were present at a rate of 21.45 percent; alarm symptoms were present in 14 patients in the functional causes group (32.5%) and in 27 patients in the organic causes group (100%). The alarm symptoms most frequently found in the organic causes group were nocturnal pain at 51.85 percent, weight loss at 40.74 percent and rectal blood at 37 percent. The symptoms found only in the organic causes group but not in the functional causes group, were referred pain, nocturnal diarrhea and rectal blood. The conditions and presenting symptoms found in the organic causes group which significantly differed when compared with the functional group ($p < 0.05$) were nocturnal pain, weight loss, gastrointestinal bleeding, and physical examination revealing anemia. In addition, there were no significant differences between the groups in patients with persistent right upper quadrant pain. In the organic causes group, Hb was below normal for age, at 11.32 ± 2.36 g/dL, and positive stool occult blood test results were found at 30.43%, with statistical significance.

In the functional causes group, the alarm symptoms found were nocturnal pain at 25 percent, persistent right upper quadrant pain at 20.45 percent and deceleration of linear growth at 11.63, while Hb was normal for age at 12.3 ± 1.07 g/dL. In the functional causes group, one subject tested positive for stool occult blood due to a diagnosed case of IBS-constipation. In the group diagnosed with functional dyspepsia, 10 of the 16 patients underwent upper gastrointestinal endoscopy due to the following alarm symptoms: nocturnal pain at 80 percent, delayed growth at 40 percent and physical examination revealing anemia at 20 percent. Furthermore, following the upper gastrointestinal endoscopies, the results of the tests were found to be normal.

Table 1. The demographic data of the children with recurrent abdominal pain with organic causes and functional causes.

	All (N=71)	Organic cause (n=27)	Functional cause (n=44)	p-value
Age (year)	9 ± 2.67 (2-15)	9.38 ± 3.21 (2-15)	8.78 ± 2.27 (4-14)	0.36
Gender: Male	27 (38.57)	12 (44.44)	15 (34.88)	0.458
Duration (month)	2-48	2-12	2-48	0.108
Comorbidities: Asthma, Allergic rhinitis		7/27	10/43	0.34

4. Discussion

In western countries, 14 reports from systematic literature reviews were found to survey the prevalence of abdominal pain in children aged 3-19 years in communities and schools. Approximately 0.3-19 percent of the children had chronic abdominal pain (median = 8.4), and more females had chronic abdominal pain than males at a ratio of 1.4:1. The age groups in which the prevalence of

abdominal pain was high included children aged 4-10 years and early adolescents at 8-10 years of age [13]. In addition, studies in pediatric gastrointestinal clinics or secondary and tertiary hospitals revealed a prevalence increase to 6-30 percent [14-15]. For patients in Thailand, Suporn Tripongkaruna et al. conducted a study in 104 children aged 4-15 years with chronic abdominal pain who received treatment at pediatric gastrointestinal clinics from 2006-2009 [16].

Table 2. The organic and functional causes of RAP.

Organic Causes	N (%) N= 27	Functional Causes	N (%) N=44
<i>H.pylori</i> Gastritis	6 (22.22)	Functional Dyspepsia	16 (36.36)
Duodenitis	4 (14.81)	IBS	19 (43.18)
NSAID-induced Gastritis	2 (7.41)	FAP	6 (13.64)
Duodenal Ulcer		FAPs	2 (4.55)
<i>H.pylori</i> negative	6 (22.22)		
<i>H.pylori</i> positive	2 (7.41)		
GERD	5 (18.52)	Abdominal migraine	1 (2.27)
Crohn's Disease	1 (3.7)		
Ulcerative Colitis	1 (3.7)		

Note: NSAIDs:Non-steroidal anti-inflammatory drug

The study found that 83 percent suffered from functional GI disorders with no organic illnesses and that 17 percent had organic illnesses. In the present study, the prevalence of chronic abdominal pain in children receiving examination at pediatric gastrointestinal clinics was 18.7 percent. This study found a fairly high prevalence when compared to previous studies. The high prevalence was caused by the fact that this study was conducted in pediatric gastrointestinal clinics in tertiary hospitals. As for the causes of RAP, FGIDs without

organic illness as diagnosed by Rome III criteria was a major cause for abdominal pain, occurring in 61.97 percent of the children, while organic causes contributed to abdominal pain in 38 percent of the children. However, the prevalence of organic causes did not differ from findings in previous studies, which ranged from 23 to over 80 percent [16-17]. In regards to the prevalence of abdominal pain caused by FGIDs without an organic illness in the present study, IBS was the most prevalent at 43.18 percent, followed by functional dyspepsia and FAP at

36.36 percent and 13.64 percent, respectively. When the aforementioned prevalence was compared to international studies, no differences were found. Internationally, IBS was the most prevalent at 22-51 percent, while the prevalence of functional dyspepsia ranged from 10 to 22 percent [14-15]. At the same time, a study conducted in Thailand by Suporn Tripongkaruna, using Rome III diagnostic criteria showed that FGIDs without an organic illness was the most prevalent at 31 percent. The findings indicated that the causes of abdominal pain without organic illness are the same, because nationality, age group and diagnostic criteria were the same and Rome III diagnostic criteria were used. Regardless, the prevalence of abdominal pain caused by organic illness was rather high when compared to previous studies, due to the fact that the majority of patients had been transferred for additional diagnosis. The etiology of the organic causes group found in the present study are as follows: *H. pylori* gastritis, duodenal ulcer and GERD.

In patients with recurrent abdominal pain, background interviews and detailed physical examinations, particularly for alarm symptoms, are essential in determining the cause of abdominal pain, whether by organic illness and functional GI disorders, or non-organic illness. In addition, detection of alarm symptoms is an important reason for attending physicians to conduct additional detailed examinations and testing [11, 18, 19]. A report from AAP and NASPGHAN in 2005 found that no studies reported pain frequency, severity, location or impact on daily living [20]. Furthermore, related patient background information such as occurrence of headaches, joint pain, anorexia, nausea, vomiting or changes in bowel movements are unable to identify abdominal pain caused by organic illness. In addition, a study on the red flags of 100 pediatric patients with abdominal pain in 2012 found abdominal pain occurring outside the umbilical area, nocturnal pain, weight loss and growth

disorders, while physical examinations of these patients found abdominal tenderness [12]. Interestingly, a history of nocturnal pain, weight loss and physical examination results in the present study showed that anemia occurred significantly more frequently in patients with abdominal pain caused by organic illness than in patients with abdominal pain caused by non-organic illness. Furthermore, laboratory investigations found the mean Hb value in patients with organic illness to be significantly lower than that of patients with non-organic illness, as well as positive stool blood occult results occurring in 30 percent of patients with organic illness (7 out of 23 patients tested). However, no differences were found in other symptoms such as site of pain and nocturnal diarrhea. In the present study, the presence of weight loss, anemia and positive stool occult blood test results indicated that additional examinations should be conducted to determine organic causes. Anemia and positive stool occult blood test results indicated mucosal inflammation.

The Rome III diagnostic criteria set is currently recommended as a guideline for diagnosis. Although it is not necessary to perform a thorough investigation to rule out all other illnesses, physicians should thoroughly interview and physically examine patients to detect potential alarm symptoms of organic illness. According to the findings of the present study, if significant weight loss is present, a physical examination should be conducted to rule out anemia and investigate a potential organic illness.

In addition, preliminary tests such as a complete blood count and stool occult blood test should be performed to check for anemia based on presenting symptoms in order to reveal the cause. Nevertheless, it might not be possible to classify and detect anemia by a laboratory test for organic and functional causes, because anemia might have other causes unrelated to GI blood loss and GI inflammation. Anemia might also be caused

by inadequate food intake, which can also cause iron deficiency.

5. Conclusion

In distinguishing the causes of recurrent abdominal pain between organic causes and functional GI disorder causes,

physicians need to rely on alarm symptoms, particularly presentations of weight loss, nocturnal pain, anemia and gastrointestinal blood loss. However, additional studies should be conducted to more accurately categorize both groups of illnesses based on alarm symptoms.

Table 3. The conditions and presenting symptoms of alarm symptoms in the organic and functional causes groups.

Symptom	Organic Cause n=27, (%)	Functional Cause n=44, (%)	p-value
Persistent right upper quadrant	7 (25.93)	9 (20.45)	0.771
Referred pain	2 (7.41)	0	0.141
Nocturnal pain	14 (51.85)	11 (25.00)	0.039
Bilious vomiting	3 (11.11)	1 (2.27)	0.151
gastrointestinal blood loss	10 (37.04)	0	<0.001
Nocturnal diarrhea	1 (3.7)	0	0.380
Fever	1 (3.7)	1 (2.27)	1.000
Linear deceleration of growth	2 (7.41)	5 (11.36)	0.701
Weight loss	11 (40.74)	1 (2.27)	<0.001
Family history	2 (7.41)	2 (4.55)	0.632
Anemia	8 (29.63)	2 (4.55)	0.005
Abdominal signs	4 (14.81)	5 (11.36)	0.723

Acknowledgements

This study was funded by the Faculty of Medicine, Thammasat University, Thailand.

References

- [1] Ellert U, Neuhauser H, Roth-Isigkeit A: Pain in children and adolescents in Germany: the prevalence and usage of medical services. Results of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). *Bundesgesundheitsblatt Gesundheits für Schung Gesundheitsschutz*.2007;50:711-7.
- [2] Apley J. editor. *The child with abdominal pains*. London: Blackwell, 1975.
- [3] Arnhold RG, Callas ER. Composition of a suburban pediatric office practice: an analysis of patient visits during one year. *Clin Pediatr*.1996; 5:722-7.
- [4] Hyams JS, Burke G, Davis PM, Rzepski B, Andrulonis PA. Abdominal pain and irritable bowel syndrome in adolescents: a community-based study. *J Pediatr*.1996;129:220-6.
- [5] Croffie JM, Fitzgerald JF, Chong SK. Recurrent abdominal pain in children-retrospective study of outcome in a group referred to a pediatric gastroenterology practice. *ClinPediatr (Phila)*2000;39:267-74.
- [6] Apley J, Naish N. Recurrent abdominal pains: a field survey of 1,000 school children. *Arch Dis Child*.1958; 33:165–70.
- [7] Chitkara DK, Rawat DJ, Talley NJ. The Epidemiology of Childhood Recurrent Abdominal Pain in Western Countries: A Systematic Review. *Am J Gastroenterol*.2005; 100:1868.

- [8] Ramchandani PG, Hotopf M, Sandhu B, Stein A. The epidemiology of recurrent abdominal pain from 2 to 6 years of age: Results of a large, population-based study. *Pediatrics*.2005;116:46.
- [9] Petersen S, Bergström E, Brulin C. High Prevalence of Tiredness and Pain in Young School Children. *Scand J Public Health*.2003;31:367-74.
- [10] Aanpreung P, Atisook K, Suwanagool P, Vajaradul C. Upper Gastrointestinal Endoscopy in Children with Recurrent Abdominal Pain. *J Med Assoc Thai*.1997; 80:22-5
- [11] Rasquin A, Lorenzo CD, Forbes D, Guiraldes E, Hyams JS, Staiano A, et al. Childhood functional gastrointestinal disorders:Child/adolescent. *Gastroenterology*. 2006;130:1527-37
- [12] Motamed F, Mohsenipour R, Seifirad S, Yusefi A, Farahmand F, Khodadad A, et al. Red Flags of Organic Recurrent Abdominal Pain in Children: Study on 100 Patients. *Iran J Pediatr*.2012; 22:457-62.
- [13] Chitkara DK, Rawat DJ, Talley NJ. Review.The epidemiology of childhood recurrent abdominal pain in Western countries: a systematic review. *Am J Gastroenterol*.2005;8:1868-75.
- [14] Helgeland H, Flagstad G, Grøtta J, Vandvik PO, Kristensen H, Markestad T. Diagnosing Pediatric Functional Abdominal Pain in Children (4-15 years old) According to the Rome III Criteria: Results from a Norwegian Prospective Study. *J Pediatr Gastroenterol Nutr*.2009;49:309-15.
- [15] Devanarayana NM, Rajindrajith S, De Silva HJ. Recurrent abdominal pain in children. *Indian Pediatr*. 2009;46:389-99.
- [16] Treepongkaruna S, Jitraruch S, Engkakul P, Phuapradit P. Chronic Abdominal Pain without Organic Causes: Symptom Subtypes Based on RomeIII Criteria. *Thai J Pediatr*. 2014;53:173-80.
- [17] Chitkara DK, Rawat DJ, Talley NJ. The Epidemiology of Childhood Recurrent Abdominal Pain in Western Countries: A Systematic Review. *Am J Gastroenterol*.2005;100:1868-75.
- [18] Gijsbers CF, Benninga MA, Schweizer JJ, Kneepkens CM, Vergouwe Y, Büller HA. Validation of the Rome III Criteria and Alarm Symptoms for Recurrent Abdominal Pain in Children. *J Pediatr Gastroenterol Nutr*. 2014;58:779-85.
- [19] Oberlander TF, Rappaport LA. Recurrent abdominal pain during childhood. *Pediatr Rev*. 1993;14:313-9.
- [20] Di Lorenzo C, Colletti RB, Lehmann HP, Boyle JT, Gerson WT, Hyams JS, et al.; AAP Subcommittee; NASPGHAN Committee on Chronic Abdominal Pain. Chronic Abdominal Pain in Children: a Technical Report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J. Pediatr Gastroenterol Nutr*.2005;40:249-61.