ORIGINAL ARTICLE

Psychiatric, somatic, and gastrointestinal disorders, and *Helicobacter pylori* infection in children with recurrent abdominal pain

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Aims: To examine the utility of the Rome II criteria in children with recurrent abdominal pain (RAP) and compare them to those who met Apley's criteria and those who met neither criteria.

Methods: Prospective study in general paediatric clinics in Komagane, Japan. Children with abdominal pain were classified into those who met Rome II criteria, those who met Apley's criteria, and those who met neither.

Results: A total of 182 children with RAP participated; 45 children met Rome II criteria, 55 met Apley's criteria, and 82 met neither. Children who met Rome II criteria had a significantly higher prevalence of psychiatric and somatic disorders compared to the group met neither (36% v 6%, 22% v 10%, respectively). The overall prevalence of *H pylori* was 7%; prevalence increased with age from 3% at age ≤ 10 to 10% for children >10 years. Children who met Rome II criteria had a significantly higher prevalence of *H pylori* infection than the reference group (18% v 4%). In a logistic regression model, all the study variables were included in the model specifying first the Rome II criteria group as the independent variable; psychiatric disorders, *H pylori* infection, and older age group were independent risk factors.

Conclusions: More than half the children suffering from recurrent abdominal pain met neither Apley's nor Rome II criteria. Children who meet Rome II criteria should be evaluated for psychiatric disorders and should be tested for *H pylori* infection. Despite the overall trend for a fall in the prevalence of *H pylori* infection among children in Japan, there are subpopulations of sick children where the prevalence of the infection is relatively high.

Recurrent abdominal pain (RAP) occurs in 10–15% of school age children and often interferes with school attendance and performance, peer relationships, participation in organisations and sports, and personal and family activities.^{1–5} Recent studies have also reported that children who suffer from RAP often exhibit anxiety, mild depression, withdrawal, and low self-esteem.^{6–8} Children with abdominal pain, especially those with recurrent abdominal pain (RAP), are frequent users of medical services because of multiple somatic complaints such as nausea and vomiting.⁹

A number of symptom based criteria have been proposed to help clinicians and researchers identify children with RAP. The original Apley's criteria were designed to identify RAP in community samples without medical assessment.¹ Von Baeyer and Walker modified Apley's criteria and suggested that the primary outcome should measure both amount of pain and the level of disability.¹⁰ The Rome I and Rome II diagnostic criteria^{11–13} recommended that evaluation of RAP should be based on medical assessment, and the patient's report of pain. The status of the existing literature was recently reviewed by the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition in a report concerning the diagnostic and therapeutic value of a medical and psychological history, diagnostic tests, and pharmacological and behavioural therapy associated with chronic abdominal pain in children.¹⁴ However, there is considerable heterogeneity in the presentation of RAP and its aetiology remains unclear. Importantly, many children presenting with abdominal pain do not meet either Apley's or Rome II criteria.

Our study evaluated the prevalence and applicability of the paediatric Rome II criteria and Apley's criteria within a group of children who sought medical attention for recurrent

abdominal pain at a general paediatric clinic. We compared children seeking medical attention for abdominal pain and classified them into three groups: those who met Apley's criteria; those who met Rome II criteria; and those that did not meet either criterion due to the short duration of having symptoms (less than three months). We also compared the three groups for the prevalence of psychiatric, somatic, and other gastrointestinal disorders.

METHODS

Study population

A prospective cross-sectional study was conducted among children seeking medical attention for abdominal pain from the paediatric outpatient practice of a general hospital, Showa Inan General Hospital, in Komagane, Japan. The study was conducted between 2001 and 2004. The inclusion criteria for enrolling children with abdominal pain were: (1) age 5–18 years; (2) referral by their physician because of abdominal pain that persisted for more than two weeks; (3) abdominal pain that was moderate to severe and interfered with some or all regular activities; (4) abdominal pain that may or may not be accompanied by upper gastrointestinal symptoms; and (5) willing to give informed consent by the parent/guardian. Exclusion criteria included history of alarm symptoms (gastrointestinal bleeding or acute abdomen), fever, frequent diarrhoea, gastro-oesophageal regurgitation, or regular use of non-steroidal anti-inflammatory drugs or acid suppression drugs. General laboratory tests, such as blood analysis, urinalysis, x ray examination, and ultrasonography, were conducted on each child. If one had any abnormal findings, he/she was excluded from the study. Eligible children whose parents agreed to participate gave written consent/assent.

Questionnaire

On agreement to participate in the study, a detailed questionnaire was administered to the parent and the child to obtain data regarding sociodemographic factors and general information regarding the abdominal pain symptoms that led to the doctor's visit. The questionnaire was completed by the one of the investigators. Questions elicited information concerning the location, frequency, duration, and nature of the abdominal pain. Dyspepsia was defined as pain or discomfort (fullness, early satiety, bloating, belching, queasiness, nausea, retching, or vomiting) centred in the upper abdomen.

The patients were then classified into three groups: those who met the Rome II criteria; those who met Apley's criteria but did not meet the Rome II criteria; and those who met neither the Rome II criteria nor Apley's criteria.

The definition of RAP using the Rome II criteria are: (1) persistent or recurrent pain or discomfort centred in the upper abdomen for at least 12 weeks, which need not be consecutive, within the preceding 12 months; (2) no evidence of alarm symptoms; and (3) no evidence that dyspepsia is exclusively relieved by defecation or associated with the onset of a change in stool frequency or stool form. Children who met Apley's criteria had at least three episodes of abdominal pain that occurred over a period of three months and which were severe enough to affect the activities of the child. Additional questions regarding lower gastrointestinal symptoms, (e.g. diarrhoea, constipation, irritable bowel syndrome-like symptoms, and whether they were post-enteritis) were obtained.

Patients were also questioned regarding the presence of orthostatic dysregulation (box 1),¹⁵ school absenteeism (more than two weeks), epilepsy, and past history of psychiatric disease (eating disorder, depression, anxiety, and neurosis). Somatic symptoms recorded included frequency of headache, chest pain, or limb pain.

Diagnosis of *Helicobacter pylori* infection

H. pylori infection was diagnosed by urea breath test (UBT), stool antigen test (HpSA), and serum IgG antibody (ELISA). *H. pylori* positivity was considered if the UBT and one of the other tests were positive. The ¹³C-UBT was performed as previously described,¹⁶ using a cut-off value of 3.5‰. The stool antigen test was performed using the HpSA enzyme linked immunosorbent assay (ELISA) (Premier Platinum HpSA).¹⁷ Anti-*H. pylori* IgG values were determined by ELISA using the GAP-IgG kit.¹⁸

Statistic analysis

Mantel-Haenszel χ^2 analyses was performed to measure the differences in the overall prevalence of the outcomes. Risk factors associated with Rome II criteria were analysed by the relative risk (RR) and 95% confidence intervals were calculated for all the study variables. Psychiatric and somatic disorders, presence of lower GI symptoms, and the family history of peptic ulcer disease were categorised into dichotomous variables (present or absent). The *H. pylori* variable was defined as positive or negative. Age was categorised into two groups: ≥ 10 or < 10 years. A Poisson regression model was applied. All p values calculated were two tailed; the alpha level of significance was set at 0.05. The data were analysed using the SAS program (SAS Institute, Cary, NC).

RESULTS

The study population consisted of 182 symptomatic children suffering from recurrent abdominal pain; 45 children met the Rome II criteria, 55 met Apley's criteria, and 82 did not meet Apley's or the Rome II criteria. The children were aged 5–18 years (mean 10.9 ± 3); 87 (48%) were boys. The Rome II

Box 1: Criteria for the diagnosis of orthostatic dysregulation

The determination of orthostatic dysregulation: the subject has one major and three minor symptoms, or two major and one minor symptoms, or three major symptoms and organic diseases are excluded

Major symptoms

- Dizziness or vertigo
- Nausea or sometimes fainting when standing
- Nausea when taking a bath or at an unpleasant sight or at bad news
- Palpitation or difficulty with a slight movement of the body
- Difficulty rising in the morning and continuing malaise during the morning

Minor symptoms

- Pallor
- Poor appetite
- Severe abdominal pain from time to time
- Lack of energy or easily fatigued
- Frequent headaches
- Motion sickness: unable to ride in a vehicle due to motion sickness
- Decrease in pulse pressure by 16 mm Hg or more when standing
- Decrease in systolic blood pressure by 21 mm Hg or more when standing
- Increase in pulse rate by over 21 beats per minute when standing
- More than 0.2 mV decrease in T waves in lead II and other changes in electrocardiograms performed while standing

criteria were fulfilled for only 25% of children suffering from recurrent abdominal pain.

We compared the three groups using the children who met neither Apley's nor the Rome II criteria as the reference group. Table 1 shows the relative risk for the study characteristics among children who met Rome II and Apley's criteria. Children who met Rome II criteria had a significantly higher prevalence of psychiatric and somatic disorders compared to the reference group (36% v 6% [RR = 5.8 (95% CI 2.1–24.3); $p = 0.001$], 22% v 10% [RR = 2.2 (95% CI 1.1–5.1); $p = 0.05$], respectively). No differences were observed for psychiatric or somatic disorders between the Apley's and the reference groups. Lower GI symptoms were more common among Rome II criteria children compared to the reference or Apley's groups; however, that difference was not statistically significant ($p = 0.24$). A family history of peptic ulcer disease was also less frequent among the children who met the Rome II criteria compared to the reference group. Children over the age of 10 years, and girls were disproportionally and significantly more common among children who met the Rome II criteria compared to the reference group (box 1).

The overall prevalence of *H. pylori* was 7%; prevalence increased with age from 3% at age ≤ 10 to 10% for children > 10 years (RR = 3.0, 95% CI 0.9–16.2, $p = 0.06$). Children who met the Rome II criteria had a significantly higher prevalence of *H. pylori* infection than the reference group (18% v 4%; RR = 4.9, 95% CI 1.2–22.7, $p = 0.002$).

Table 1 Crude odds ratios and 95% confidence intervals for characteristics of children meeting the Rome II criteria

Characteristics	Reference group† (n = 82) Total no. (%)	Apley's group (n = 55) Total no. (%) OR (95% CI)	Rome II criteria group (n = 45) Total no. (%) OR (95% CI)	p Value for trend
Psychiatric disorders	5 (6%)	4 (7%) 1.3 (0.3–4.7)	16 (36%) 5.8 (2.1–24.3)**	0.001
Somatic disorders	8 (10%)	6 (11%) 1.1 (0.4–3.5)	10 (22%) 2.2 (1.0–5.1)**	0.12
GI-like symptoms	12 (15%)	10 (18%) 1.3 (0.5–3.2)	12 (27%) 1.8 (0.9–5.2)	0.24
Family history of peptic ulcer	24 (29%)	20 (36%) 1.2 (0.6–2.7)	7 (16%) 0.5 (0.2–1.1)	0.06
<i>H pylori</i> infection	3 (4%)	1 (2%) 0.5 (0.1–4.8)	8 (18%) 4.9 (1.2–22.7)**	0.002
Female gender	35 (43%)	29 (53%) 1.2 (0.7–2.8)	31 (69%) 1.6 (1.3–6.0)**	0.03
Age group ≥10 years	34 (41%)	33 (60%) 1.4 (1.1–4.2)**	36 (80%) 2.1 (1.4–13.4)**	0.001

†Children met neither Apley's nor Rome II criteria.

**p<0.05.

OR, odds ratio; CI, confidence interval.

In a Poisson regression model, we included all the study variables in the model, specifying first the Rome II criteria group as the independent variable. Psychiatric disorders, *H pylori* infection, and age >10 years were found to be independent risk factors with relative risk of 4.1 (95% CI 2.0–12), 3.2 (95% CI 1.1–12.0), and 3.0 (95% CI 1.9–8.0), respectively. We then specified Apley's criteria as the independent variables, applying the same model; age >10 years emerged as a significant risk factor with a relative risk of 1.5 (95% CI 1.0–2.8).

DISCUSSION

Over the past several decades, a number of symptoms based criteria have been proposed to help clinicians and researchers identify children with RAP. The original Apley's criteria were designed to identify RAP in community samples without medical assessment.¹ Apley's definition of RAP required that pain be severe enough to affect activities for three months.¹ Subsequently, several authors added to Apley's definition to exclude children whose RAP was a manifestation of an organic disease.^{19–22} This additional criterion was included in the official classification of pain published by the International Association for the Study of Pain, where the diagnostic criteria for RAP are "paroxysmal abdominal pain that affects normal activities, persists for more than 3 months, and is without organic findings".²³ The Rome I and Rome II diagnostic criteria^{11–13} recommended that evaluation of RAP be based on medical assessment, the patient's report of pain, and psychological measures. However, it has recently been reported that the inter-rater reliability of the Rome II criteria was low among paediatric gastroenterologists, suggesting that more work is needed to define practical diagnostic criteria.²⁴

The Rome II criteria for functional dyspepsia were fulfilled in only 25%, Apley's criteria were fulfilled in 30%, and 45% failed to meet either criteria. Only 33 children (18%) met both Apley's and Rome II criteria. These findings are in contrast with a study from Italy, which showed that only 2% of children who sought medical attention from primary care physicians satisfied one of the criteria for the diagnosis of a functional gastrointestinal disorders (FGIDs).²⁵ However, in that study, it was reported that children who received a prospective diagnosis of FGIDs using the Rome criteria, 97.5% continued to satisfy the diagnostic criteria or were improved at follow up. We found that 60% of the children who met

Apley's criteria also met Rome II criteria; this is similar to the previously reported rate of 73% of children with RAP meeting Apley's criteria and Rome II criteria.²⁶ That slightly lower proportion might reflect difference in the study setting; our study was conducted in a primary care facility in a hospital setting, whereas the comparator was conducted in tertiary centres.

We also found that children who met Rome II criteria had a significantly higher prevalence of psychiatric disorders than the other two groups. These results, although not parallel, are similar to those of Campo *et al*, who reported that children with RAP were more likely to receive a diagnosis of psychiatric disorders, depressive symptoms, temperamental harm avoidance, and functional impairment than control subjects.²⁷ Somatic disorders were present in the three studied groups; however the prevalence was highest among children who met Rome II criteria. Somatic disorders have also previously been reported in association with recurrent abdominal pain,^{28–29} including the original report by Apley, which reported that children with abdominal pain suffered from headache more frequently than controls.¹

We found that among children meeting the Rome II criteria, gender played a significant role, with the prevalence of RAP being higher in girls; however, the difference disappeared after adjusting for the other variables. This finding is consistent with a previous community based study which evaluated IBS-type RAP and did not find a gender based difference among adolescents.⁵ Our finding that children ≥10 years of age were more prevalent among those who met both Apley's and Rome II criteria is consistent with the notion that older children can exhibit more sophisticated knowledge of illness than the younger children;³⁰ that is, they are better at reporting symptoms, or illness is more developed with increasing age.

The overall prevalence of *H pylori* infection was 7%. Although we found a low prevalence of *H pylori* among children with RAP, the prevalence was significantly higher among children who met Rome II criteria. The reason for this is unknown. It is of interest that those meeting the Rome II criteria also had a higher prevalence of psychiatric disorders; eating disorders have been associated with increased susceptibility to infection.³¹

In summary, our study showed that more than half the children from a community setting referred to a general hospital for evaluation of recurrent abdominal pain failed to

What is already known on this topic

- Recurrent abdominal pain (RAP) can be functional, organic, or a combination of both
- Not all children with RAP meet certain defining criteria; children who meet the Rome II criteria have a significantly higher prevalence of *H pylori* infection

What this study adds

- More than half the children suffering from recurrent abdominal pain meet neither Apley's nor Rome II criteria
- Children who meet Rome II criteria should be evaluated for psychiatric disorders and should be tested for *H pylori* infection

meet either Apley's or Rome II criteria. Psychiatric disease and *H pylori* infection were disproportionally represented among the children meeting the Rome II criteria, suggesting that these criteria are biased towards identifying such patients, and those patients who meet the Rome II criteria should be evaluated for *H pylori* and psychiatric disorders.

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REFERENCES

- 1 Apley J. *The child with abdominal pains*. London: Blackwell Scientific Publications, 1975.
- 2 Faull C, Nicol AR. Abdominal pain in six year-olds: an epidemiological study in a new town. *J Child Psychol Psychiatry* 1986;**27**:251–60.
- 3 Zuckerman B, Stevenson J, Bailey V. Stomach aches and headaches in a community sample of preschool children. *Pediatrics* 1987;**7**:677–82.
- 4 Boyle JT. Chronic abdominal pain. In: Walker WA, Durie PR, Hamilton JR, Walker-Smith JA, Watkins JB, eds. *Pediatric gastrointestinal disease*. Philadelphia, PA: BC Decker, 1991:45–54.
- 5 Hyams JS, Burke G, Davis PM, et al. Abdominal pain and irritable bowel syndrome in adolescents: a community-based study. *J Pediatr* 1996;**129**:220–6.
- 6 Walker LS, Garber J, Greene JW. Psychosocial correlates of recurrent childhood pain: a comparison of pediatric patients with recurrent abdominal pain, organic illness, and psychiatric disorders. *J Abnorm Psychol* 1993;**10**:248–58.
- 7 Walker LS, Garber J, Greene JW. Somatization symptoms in pediatric abdominal pain patients: relation to chronicity of abdominal pain and parent somatization. *J Abnorm Child Psychol* 1991;**19**:379–94.
- 8 Garber J, Zeman J, Walker LS. Recurrent abdominal pain in children: psychiatric diagnoses and parental psychopathology. *J Am Acad Child Adolesc Psychiatry* 1990;**29**:648–56.
- 9 Starfield B, Gross E, Wood M, et al. Psychosocial and psychosomatic diagnoses in primary care of children. *Pediatrics* 1980;**66**:159–67.
- 10 Von Baeyer CL, Walker LS. Children with recurrent abdominal pain: issues in the selection and description of research participants. *J Dev Behav Pediatr* 1999;**20**:307–13.
- 11 Drossman DA. The functional gastrointestinal disorders and the Rome II process. *Gut* 1999;**45**(suppl 2):II1–5.
- 12 Drossman DA. Presidential address: Gastrointestinal illness and the biopsychosocial model. *Psychosom Med* 1998;**60**:258–67.
- 13 Rasquin-Weber A, Hyman PE, Cucchiara S, et al. Childhood functional gastrointestinal disorders. *Gut* 1999;**45**(suppl 2):II60–8.
- 14 Di Lorenzo C, Colletti RB, Lehmann HP, et al. 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.
- 15 Okuni M. Orthostatic dysregulation in children with special reference to the standing electrocardiogram. *Jpn Circ J* 1962;**27**:200–4.
- 16 Kato S, Ozawa K, Konno M, et al. Diagnostic accuracy of ¹³C-urea breath test for childhood *Helicobacter pylori* infection: multi-center Japanese study. *Am J Gastroenterol* 2002;**97**:1668–73.
- 17 Kato S, Ozawa K, Okuda M, et al. Accuracy of the stool antigen test for the diagnosis of childhood *Helicobacter pylori* infection: a multicenter Japanese study. *Am J Gastroenterol* 2003;**98**:296–300.
- 18 Schembri MA, Lin SK, Lambert JR. Comparison of commercial diagnostic tests for *Helicobacter pylori* antibodies. *J Clin Microbiol* 1993;**31**:2621–4.
- 19 Hodges K, Kline JJ, Barbero G, et al. Depressive symptoms in children with recurrent abdominal pain and in their families. *J Pediatr* 1985;**107**:622–6.
- 20 Hodges K, Kline JJ, Barbero G, et al. Anxiety in children with recurrent abdominal pain and their parents. *Psychosomatics* 1985;**26**:859–66.
- 21 Hodges K, Kline JJ, Barbero G, et al. Life events occurring in families of children with recurrent abdominal pain. *J Psychosom Res* 1984;**28**:185–8.
- 22 Feuerstein M, Barr RG, Francoeur TE, et al. Potential biobehavioral mechanisms of recurrent abdominal pain in children. *Pain* 1982;**13**:287–98.
- 23 Merskey H. Visceral and other symptoms of trunk apart from spinal and radicular pain. In: Merskey H, Bogduk N, eds. *Classification of chronic pain syndrome and definitions of pain terms*, 2nd edn. Seattle, WA: IASP Press, 1994:159.
- 24 Miguel M, Di Lorenzo C. Inter-rater reliability of the Rome criteria in children. *Gastroenterology* 2004;**126**:M1658.
- 25 Miele E, Simeone D, Marino A, et al. Functional gastrointestinal disorders in children: an Italian prospective survey. *Pediatrics* 2004;**114**:73–8.
- 26 Walker LS, Lipani TA, Greene JW, et al. Recurrent abdominal pain: symptom subtypes based on the Rome II criteria for pediatric functional gastrointestinal disorders. *J Pediatr Gastroenterol Nutr* 2004;**38**:187–91.
- 27 Campo JV, Bridge J, Ehmann M, et al. Recurrent abdominal pain, anxiety, and depression in primary care. *Pediatrics* 2004;**113**:817–24.
- 28 Hyams JS, Burke G, Davis PM, et al. Abdominal pain and irritable bowel syndrome in adolescents: a community-based study. *J Pediatr* 1996;**129**:220–6.
- 29 Walker LS, Garber J, Greene JW. Psychosocial correlates of recurrent childhood pain: a comparison of pediatric patients with recurrent abdominal pain, organic illness, and psychiatric disorders. *J Abnorm Psychol* 1993;**102**:248–58.
- 30 Williams JM, Binnie LM. Children's concepts of illness: an intervention to improve knowledge. *Br J Health Psychol* 2002;**7**:129–47.
- 31 Birmingham CL, Hodgson DM, Fung J, et al. Reduced febrile response to bacterial infection in anorexia nervosa patients. *Int J Eat Disord* 2003;**34**:269–72.