

Recurrent Abdominal Pain in Children

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Context: Recurrent abdominal pain is one of the commonest gastrointestinal complaints in children, affecting approximately 10% of school aged children and adolescents. There is no consensus with regards to etiology, investigation and management of this common problem. This review addresses some of the issues related to epidemiology, etiology, management and prognosis of recurrent abdominal pain.

Evidence acquisition: We reviewed current literature on this broad subject, specially concentrating on epidemiology, etiology and, basic and advanced management strategies, from 1958 to date, using PubMed, Embase, Cochrane database and cross references.

Results: The majority of the affected children have functional gastrointestinal diseases. The exact cause of pain remains obscure. New evidence suggests that emotional stress, visceral hypersensitivity and gastrointestinal motility disorders may play a vital part in its origin. Pharmacological treatments are commonly used in an effort to manage symptoms, despite the lack of data supporting their efficacy.

Conclusions: Most children with recurrent abdominal pain have functional gastrointestinal diseases and a detailed history, examination and basic stool, urine and hematological investigations are sufficient to exclude organic pathology in them. Despite the magnitude of the problem, knowledge on the effective management options is poor.

Key words: *Abdominal pain, Adolescent, Children, Emotional stress, Functional gastrointestinal disorder, Helicobacter pylori, Gastrointestinal motility, Visceral hypersensitivity.*

Abdominal pain is perhaps the most common painful health problem in school-aged children. J Apley, a British pediatrician, studied abdominal pain among children extensively and observed that approximately 10% of school aged children get recurrent episodes of abdominal pain. He named this symptom complex as recurrent abdominal pain (RAP) syndrome and defined it as “at least three episodes of abdominal pain, severe enough to affect their activities over a period longer than three months”(1). His findings formed the main guidelines for the practising pediatricians and researchers dealing with this problem. Even though, the term chronic is used when referring to RAP, each episode of pain is distinct and separated by periods of well-being.

EPIDEMIOLOGY

RAP is reported in 10-12% of school aged children in developed countries(1,2). Epidemiological studies in Asia have reported similar prevalence. Boey and his colleagues studied RAP among school children in Malaysia and found a prevalence of 10.2% (urban 8.2-9.6%, rural 12.4%)(3,4). Similarly, Rasul and Khan reported RAP in 11.5% of Bangladesh school children(5). Prevalence of RAP in Sri Lanka is 10.5% (6). In the majority of studies, girls are more affected than boys(1,3-6).

CLINICAL PROFILE

It is generally agreed that the complaint of pain made by children with RAP is genuine, and not simply social modelling, imitation of parental pain, or a

means to avoid an unwanted experience (*e.g.* school phobia). The commonest presentation is periumbilical pain associated with autonomic and functional symptoms like nausea, vomiting, pallor and other painful conditions like headache and limb pains(1,5,6). Thus, on initial presentation, RAP may mimic any acute abdominal disorder, and may prompt extensive evaluation and unnecessary invasive investigation.

Often there is a family history of RAP among first-degree relatives(1,2,4-6). Similar associations have been found in functional bowel disorders causing abdominal pain, like irritable bowel syndrome(7). This may be due to genetic or environment vulnerability and further studies are needed to detect a definite genetic predisposition.

ETIOLOGY

The origin of abdominal pain is complex and does not lend itself to a single model of causation. Apley and Naish suggested that organic pathology cannot be identified in 90% of children suffering from this problem(1). During the last half century, new diagnostic methods have broadened the investigation of these children, and have contributed to improved knowledge of the pathophysiology of RAP. In some of the subsequent studies, the percentage of children with organic RAP was found to be higher than initially reported by Apley(8-11). The majority of these studies were carried out in secondary and

tertiary care hospitals where patients were highly selected and it was therefore more likely that an organic pathology was found(8-11). In some of these studies, the percentage of organic RAP was found to be as high as 82%(11). A recent epidemiological study in Sri Lanka has reported organic diseases in 23.6% of affected children(12).

Organic diseases causing RAP

Numerous organic disorders lead to abdominal pain; in most, the pathophysiology is related to infection (*e.g.* urinary tract infection), inflammation (*e.g.* Crohn's disease) or distension or obstruction of a hollow viscous (*e.g.* obstructive uropathy). **Table I** demonstrates common causes for RAP among children(13,14). Several etiological studies in India have recognised intestinal parasitic infections, including giardiasis, as the leading cause for RAP(8,9,11), while in Sri Lanka, commonest organic aetiology is constipation(12). In many developed countries, the common organic causes include chronic constipation and gastroesophageal reflux disease(10).

Few studies have demonstrated a contributory role of lactose malabsorption in the symptoms of RAP(15). In contrast to this, a large number of subsequent studies have neither demonstrated an association between RAP and lactose malabsorption nor a significant improvement in symptoms following lactose free diet(16,17). Lactase

TABLE I CAUSES OF RECURRENT ABDOMINAL PAIN

<i>Gastrointestinal</i>		<i>Urinary tract</i>
Chronic constipation	Hepatitis	Urinary tract infection
Inflammatory bowel disease	Gall bladder calculi	Urinary calculi
Parasitic infection (<i>e.g.</i> ameba, giardia)	Chronic appendicitis	Pelvi-ureteric junction obstruction
Dietary intolerance (<i>e.g.</i> lactose)	Chronic pancreatitis	
Gastro-esophageal reflux disease	Functional dyspepsia	<i>Gynecological</i>
<i>Helicobacter pylori</i> infection	Irritable bowel syndrome	Ovarian cyst
Celiac disease	Functional abdominal pain/syndrome	Endometriosis
Peptic ulcer	Abdominal migraine	Pelvic inflammatory disease
Gastritis	Aerophagia	<i>Miscellaneous</i>
		Abdominal epilepsy
		Physical, emotional and sexual abuse

deficiency is reported to be very high (70%) in Asian children with RAP but no causal association was found between the two conditions(17). Therefore, the diagnostic value of investigating Asian children with RAP for lactase deficiency is doubtful. The role of *Helicobacter pylori* in the aetiology of childhood RAP is controversial. Many researchers have shown an association between *Helicobacter pylori* infection and RAP(18-20), while several others contradict this finding(12,21-24).

Identifying organic abnormalities by comprehensive investigations does not necessarily mean that the explanation for the symptoms is found. It is also important to realize that the organic and non organic causes for RAP can co-exist in some patients.

Functional gastrointestinal disorders causing RAP

Until a decade ago 'functional gastrointestinal disorder' was a label used for the conditions with uncertain etiology, and was a diagnosis of exclusion. When Rome criteria were defined to diagnose functional gastrointestinal disorders (FGID), it became an important positive diagnosis. According to Rome II criteria, abdominal pain related conditions in children were classified into five categories; functional dyspepsia, irritable bowel syndrome, abdominal migraine, aerophagia and functional abdominal pain(25). Validation of pediatric Rome II criteria was done by Caplan, *et al.*(26). They found that more than half the patients classified as having functional problems met at least one pediatric Rome II criteria for FGID. Another study by Saps and Di Lorenzo reported low interobserver reliability (45-47%) for Rome II criteria among pediatric gastroenterologists and fellows(27).

Even though functional bowel diseases are considered as a cause of RAP in children(14), so far very few studies have been done to detect their prevalence among affected children(12,28,29). Walker, *et al.*(28) found that 73% of patients with RAP fulfilled Rome II criteria for FGID, and most of them had irritable bowel syndrome (44.9%). Using the same criteria, Schurman, *et al.*(29) found FGID in 84-89% of RAP children attending a tertiary care center. In this study, functional dyspepsia was the

commonest diagnosis (35-47%). Similarly, another study in Sri Lanka has reported FGID in 79% patients with functional RAP. Of them, 31% had functional abdominal pain(12). Unfortunately, 11-27% of the children with non-organic RAP could not be classified under any one of the FGID using Rome II criteria(12,28,29).

To overcome drawbacks in Rome II criteria, they were revised and modified in 2006, and Rome III criteria were developed(30). **Table II** summarizes the Rome III criteria for pediatric FGID. Validity and reliability of Rome III criteria in diagnosing pediatric FGID have yet to be studied. Using Rome III criteria, a recent study in Sri Lanka has reported FGID in 93% of patients with non-organic RAP. Of them, 45.2% had functional abdominal pain(12). Therefore, it is important to consider FGID in the differential diagnosis of RAP early in the evaluation.

Classification of non-organic RAP into the appropriate functional bowel disorder helps to let the child and the parents know that the symptoms they are feeling are real but not dangerous or life threatening, and also helps to direct the treatment appropriately. Once the diagnosis is made, a simple explanation of the condition and reassurance is usually enough to alleviate anxiety in the child and the family.

RAP and emotional stress

Many previous researchers have demonstrated a significant association between exposure to stressful life events and RAP(1,5,6,31). Patients can sometimes date the onset of pain to a specific stressful event, such as change in school, birth of a sibling or separation of parents. Boey and his colleagues have shown a significant association between recurrent abdominal pain and lower family income(3,4). Even though sibling rivalry is regarded as a predisposing factor for RAP, according to available data, family size, birth order and being an only child are not associated with RAP(2-4,6). Some case-control studies have shown higher levels of anxiety and depression in patients with RAP than in healthy children(32). In contrast to this, some other studies have failed to demonstrate significant differences in psychological distress between

TABLE II ROME III DIAGNOSTIC CRITERIA FOR PEDIATRIC FUNCTIONAL BOWEL DISORDERS*H2a. Diagnostic criteria* for functional dyspepsia*

Must include all of the following:

1. Persistent of recurrent pain or discomfort centered in the upper abdomen (above the umbilicus).
2. Not relieved by defecation or associated with the onset of a change in stool frequency or stool form (i.e., not irritable bowel syndrome).
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2b. Diagnostic criteria for irritable bowel syndrome*

Must include all of the following:

1. Abdominal discomfort (an uncomfortable sensation not described as pain) or pain associated with 2 or more of the following at least 25% of the time:
 - (a) Improved with defecation
 - (b) Onset associated with a change in frequency of stool; and
 - (c) Onset associated with a change in from (appearance) of stool.
2. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2c. Diagnostic criteria† for abdominal migraine

Must include all of the following:

1. Paroxysmal episodes of intense acute periumbilical pain that lasts for 1 hours or more.
2. Intervening periods of usual health lasting weeks to months.
3. the pain interferes with normal activities.
4. The pain is associated with 2 or more of the following: anorexia, nausea, vomiting, headache, photophobia, pallor.
5. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2d. Diagnostic criteria for childhood functional abdominal pain*

Must include all of the following:

1. Episodic or continuous abdominal pain.
2. insufficient criteria for other functional gastrointestinal disorders.
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms.

H2d1. Diagnostic criteria for childhood functional abdominal pain syndrome*

Must include childhood functional abdominal pain at least 25% of the time and 1 or more of the following:

1. Some loss of daily functioning
2. Additional somatic symptoms such as headache, limb pain, or difficulty in sleeping

H1c. Diagnostic criteria for aerophagia*

Must include at least 2 of the following:

1. Air swallowing.
2. Abdominal distension due to intraluminal air.
3. Repetitive belching and/or increased flatus.

* Criteria fulfilled at least once per week for at least 2 months before diagnosis; † Criteria fulfilled 2 or more times in the preceding 12 months.

children with functional RAP (non organic RAP) and those with demonstrable organic cause for their pain(12,33).

RAP and gastrointestinal motility

Even though altered gastrointestinal motility is considered as underlying cause for RAP, to date only

few studies were done to detect this association. A study done in 1988 reported abnormalities in migrating motor complexes (fasting contractions) in the affected children(34). More recent studies have reported impaired gastric myoelectrical activity, hypomotility of proximal and distal stomach and delayed gastric emptying in children with functional RAP(35,36). The exact cause of abnormal gastrointestinal motility is not clear. High levels of emotional stress and abnormalities in autonomic nervous system which regulate gastrointestinal motility probably contribute to this. Stress related changes have been reported in patients with FGID(37). Some studies have reported disturbances in the autonomic nervous system in children with RAP(38), while others contradict this(39).

RAP and visceral hypersensitivity

The most current theory on origin of pain in these patients is based on the “visceral hypersensitivity or hyperalgesia”. This means that the intensity of the signals from the gastrointestinal system, which travel by nerves to the brain, is exaggerated. This may occur following illnesses that cause inflammation in the intestine (*e.g.* viral gastroenteritis), or after psychologically traumatic events that “sensitize” the brain to stimuli. Previous studies in children with RAP and FGID have demonstrated visceral hyperalgesia of the gastrointestinal tract(40). In these children, the site of hyperalgesia varies with predominant symptom. For example; patients with irritable bowel syndrome shows predominantly rectal hypersensitivity while in those with RAP it is mainly in the stomach(40).

MANAGEMENT

RAP should not require an exhaustive series of diagnostic tests to rule out organic causes of pain. Excessive testing may increase parental anxiety and put the child through unnecessary stress. On the other hand, uncertainty about the diagnosis and the recurrent nature of the problem also tend to corrode the trust between clinician and the parents. Therefore, it is crucial from both child-parent’s end and the clinician’s end to come to a reasonable clinical diagnosis at initial consultation. A thorough analysis of the complain and the other components of the history, meticulous examination and ordering a judicious set of investigations will not only give a good insight to the clinician but also reassure the child and parents that their concerns are seriously taken in to consideration.

There are no studies that have evaluated the nature, location, severity and duration of the pain to differentiate between organic and functional disorders. However it had been noted that children with RAP are more likely than children without RAP to have headache, joint pain, anorexia, vomiting, nausea, excessive gas and altered bowel habits, although there is insufficient evidence to state that they can discriminate between functional and organic disorders(12). Similarly, no studies have critically evaluated the value of physical signs in identifying organic diseases in patients with RAP. The ‘red flag’ signs have long been used by clinicians to guide themselves to identify children who need further investigations and the salient ones on history and examination are noted in **Table III**(13,14).

TABLE III “RED FLAGS” IN HISTORY AND EXAMINATION OF RECURRENT ABDOMINAL PAIN

<i>“Red flags” on history</i>	<i>“Red flags” on physical examination</i>
Localized pain away from the umbilicus	Loss of weight or growth retardation
Pain awakening the child at night	Organomegaly
Pain associated with changes in bowel habits, dysuria, rash, arthritis	Localized abdominal tenderness, particularly away from the umbilicus
Occult bleeding	Joint swelling, tenderness or heat
Repeated vomiting, especially bilious	Pallor, rash, hernias of the abdominal wall
Constitutional symptoms like recurrent fever, loss of appetite, lethargy	

TABLE IV INVESTIGATIONS IN RECURRENT ABDOMINAL PAIN*Basic investigations (1st line investigations)*

Full blood count
 Erythrocyte sedimentation rate/C-reactive protein
 Urine analysis
 Urine culture
 Stool for ova, cysts and parasites

Second line investigations

Plain X-ray abdomen
 Liver function tests
 Renal function tests
 Abdominal ultrasound
 Breath hydrogen test for lactose intolerance
 Tests for *Helicobacter pylori*
 Barium follow through
 Esophageal manometry and pH-metry
 Upper and lower gastrointestinal endoscopy
 Intravenous urogram/micturition cystourethrogram

Only basic urine, stool and blood examinations are recommended to exclude organic causes in the diagnosis of RAP (**Table IV**)(13,14). Ultrasound scanning, extensive radiographic evaluation and invasive investigations like endoscopy in these children are rarely diagnostic or cost-effective(41,42). It is also important to realize that the presence of an abnormal test result alone does not pinpoint to a diagnosis unless it is clinically relevant.

The recommendation for treating children with non-organic RAP includes support and empathy for the family, with reassurance that no serious disease is present. The guidelines outlined by Rappaport and Leichtner in 1993 are still valid in the management of these children (**Box**)(43). With this approach, approximately 30% to 60% of children have resolution of their pain(44,45). However, the remainder continue to exhibit symptoms and go on to be adults with abdominal pain, anxiety, or other somatic disorders(46). Pharmacological treatments are commonly used in an effort to manage symptoms despite the lack of data supporting their efficacy. In fact, there are few randomized controlled medication trials in children with RAP, and conclusive evidence on the efficacy of any single treatment is lacking.

Pharmacological management

According to a clinical trial performed, famotidine (an H₂-receptor antagonist) is effective in children with RAP who have predominantly dyspeptic symptoms. Pizotifen, a serotonin antagonist, has been found to be effective when used prophylactically in children with abdominal migraine(47). Their effects on the majority of RAP patients with typical periumbilical pain are still not clear.

Local remedies

Many local remedies are used to alleviate symptoms in children with RAP, but to date there are very few treatment trials to assess their effect on the affected children. One study evaluated the therapeutic value of peppermint oil in the treatment of irritable bowel syndrome in children. Improvement in symptoms was reported in 71% of the peppermint oil group versus 43% in the placebo group(48).

Dietary modifications

There is a lack of high quality evidence on the effectiveness of dietary interventions on childhood RAP. According to the systematic reviews available, the treatment trials of fibre supplements and lactose restricting diets are inconclusive(49). Feldman, *et al.*(50) and Christiansen(51) studied the effect of dietary fibre on the symptoms of RAP. Feldman, *et al.*(50) reported a significant benefit for the children in the fibre group. The percentage of those with the fibre intervention having at least a 50% decrease of pain episodes was 50% compared with only 27% in the placebo group ($P < 0.05$). Less severe pain was also noted in the fiber group(50). Although not mentioned in the original study, it was recently reported that the P value was calculated from a 1-sided statistic. Reanalysis of the same data found no difference between the 2 treatment groups(49). Christiansen(51) also failed to find a difference in the number of pain episodes reported by parents following fibre supplementation versus placebo. Liebman(15) studied lactose malabsorption in children with RAP and reported significant or total pain relief following a lactose elimination diet for 4 week. In contrast to this, Wald, *et al.*(16) and Boey(17) did not find significant improvement of symptoms in RAP children following periods of lactose free diet.

Box: Guidelines for Management of Recurrent Abdominal Pain

1. *Explain and reassure.* Carefully explain to the family and the child the concepts and reasoning behind all investigations. Ask the parents about any particular concerns or diseases they believe to be the culprit of the child's pain. Once organic cause has been systematically ruled out, reassure the patient and family that no major illness is present.
2. *Identify red flags.* Make sure that the parents fully understand objective changes and provide guidelines for what to do if they occur.
3. *Avoid psychological "labelling".* Unless evidence supports the contrary, do not suggest that the child's pain is psychological or that the child may be malingering.
4. *Allow normal activity.* Encourage normal activity between times of pain.
5. *Watch out for withdrawal.* If the child begins to withdraw from normal activity, psychological referral should be considered over escalating pain management.
6. *Establish regular follow-up.* Establish a system of regular return visits to monitor the symptoms.
7. *Be available.* Assure parents that you are available to see the child if changes occur or the parents become anxious. Allow appropriate time, in an unrushed environment, for them to be seen.
8. *Beware the placebo response.* Avoid making an immediate diagnosis based on a therapeutic response. Placebo effects, particularly involving the gastrointestinal tract, can be misleading.
9. *Make judicious use of "second opinions".* Be open to requests for second opinions, particularly for anxious patients and families. Assure the parents that you will continue to help manage their child's problem even after a second opinion is obtained.

Low fat diet is suggested as a possible treatment option in FGID, including functional dyspepsia and irritable bowel syndrome(52), but to date no studies have evaluated the value of this in children with RAP.

Cognitive behavior therapy

Cognitive behavior therapies have been tried in patients with RAP, and some have demonstrated significant effects. They have been used with the idea that pain behaviors produce secondary gain (special attention, school avoidance, etc.) that in future reinforces the pain behaviors. Robins, *et al.*(54) has reported significant improvement of symptoms and fewer school absences in children with RAP following a short period of cognitive-behavioral family treatment. In agreement with this, a study by Youssef, *et al.*(54) also demonstrated significant improvement in symptoms in children with chronic abdominal pain following two cognitive behavior techniques; guided imagery and progressive relaxation.

Combined treatment options

Humphreys and Gevirtz have analyzed the effect of four treatment protocols: (i) fiber only, (ii) fiber and biofeedback, (iii) fiber, biofeedback and cognitive behavior therapy, (iv) fibre, biofeedback, cognitive behavior therapy and parental support, on outcome of RAP(55). In this study, all groups showed improvement in self-reported pain. However, the active treatment groups showed significantly more improvement than the fiber-only group. In contrast to Robins, *et al.*(53) and Youssef, *et al.*(54), who showed significant effect of cognitive behavior therapy in management of RAP, in the study done by Humphreys and Gevirtz(55), the cognitive and parental support components did not seem to independently increase treatment effectiveness.

HEALTH CARE UTILIZATION OF CHILDREN WITH RAP

There have been relatively few studies on health care utilization among children with RAP. In 2000,

Huang, *et al.*(2) showed a health care consultation rate of 34.0% among Australian children. Two studies done in Malaysia have shown health care consultation rates of 45.5% among urban and 48.4%, among rural school children(56,57). Recent study has reported health care consultation of 70% in Sri Lankan school children(6). It was significantly associated with age of the affected child, age at onset of symptoms, severity, frequency and duration of pain, school absenteeism, interruption of sleep and presence of vomiting(6,56,57).

RAP AND EDUCATION

Although RAP does occur in preschool children, it is rare in children below 5 years and above 15 years(1). It is most frequently encountered in school aged children; this might be a result of psychological difficulties these children experience during school. Irish pediatrician O'Donnell observed that RAP almost never occurs during summer holidays and many children got symptoms on return to school after vacation(58). This was compatible with a study done by William, *et al.*(59), which showed that the admission of children to British hospitals with non-specific abdominal pain was significantly higher during the school term compared with school holidays.

Very few studies have been done so far to detect the impact of RAP on education and schooling of affected children. Some studies have shown that the majority of children with RAP do not attend schools regularly, and school absenteeism is significantly higher among these children(5,6). Even though, general consensus regarding RAP is that it is most common among the high academic achievers; research data available up to date failed to show any association between RAP and school academic performance(1,6,58) or the child's participation in sports(6).

PROGNOSIS

Two long-term studies done by Apley and Hale(44) and Christensen and Mortensen(45) reported that nearly half of the children with functional RAP experience pain as adults. According to Christensen and Mortensen, offspring do not have a significant risk of RAP. Other studies have reported

development of irritable bowel syndrome in 25-29% of them in later life(8,60).

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