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Etiology of recurrent abdominal pain in children

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Abstract
The commonest presentation is periumbilical pain associated with autonomic and functional symptoms and other painful conditions. Thus, on initial presentation RAP may mimic any acute abdominal disorder, and may prompt extensive evaluation and unnecessary invasive investigation. In their seminal study, Apley and Naish failed to identify an organic disease in 90% of children suffering from this problem but recent studies have found organic pathologies in a higher percentage of affected children.
Nevertheless, the majority of children with this condition still have no identifiable organic disorders. Numerous organic disorders lead to abdominal pain; in most, the pathophysiology is related to infection (e.g. urinary tract infection), inflammation (e.g. Crohn disease) or distension or obstruction of a hollow viscus (e.g. obstructive uropathy).

Keywords: Pain, Children, Disorder

1. Introduction
In 1909, a British paediatrician, G F Still wrote; "I know of no symptom which can be more obscure in its causation than colicky abdominal pain in childhood". Today, a century later, abdominal pain in children still remains a symptom which is often difficult to understand and managing it is a major challenge to paediatricians.
In some children, the episodes of abdominal pain may be severe enough to result in frequent visits to doctors, school absenteeism, poor concentration on studies, and inability to participate in sports and other extracurricular activities.
In 1958, J Apley, another British paediatrician, studied abdominal pain among children extensively. He named this symptom complex as "recurrent abdominal pain syndrome of childhood" and defined it as "at least three episodes of abdominal pain, severe enough to affect their activities over a period longer than three months". His findings formed the main guidelines for the paediatricians and researchers dealing with this problem. Often the term chronic is misused when referring to recurrent abdominal pain (RAP) since each episode of pain is distinct and separated by periods of well-being. According to previous epidemiological studies in the world RAP is the second common painful health problem in school-aged children, only second to headache.
In 1958, Apley and Naish reported a prevalence of 10.8% among British school children. Since then it has been studied all over the world, including Asian countries, and has been reported to occur in 8-12% of school aged children. 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).
Helicobacter pylori (H. pylori) infection is one of the commonest bacterial infections in the world, and it has been suggested as a possible cause for childhood RAP, but the link between H. pylori infection and RAP is still controversial. Some studies have identified H. pylori as a possible aetiological factor for RAP and suggest its eradication in the management while other studies contradict this finding.
Aetiology of RAP is complex in origin and does not lend itself to a single model of causation. The symptoms could not be explained by the traditional bio-medical model for aetiology which assumes that all conditions can be linearly reduced to a single aetiology. Therefore, a paradigm shift was clearly needed to explain abdominal pain in children with non-organic RAP when investigations such as haematology, biochemistry and endoscopy proved to be negative. The new "bio-psychosocial" model was introduced recently to look at this condition in an alternative way.
It proposes that RAP results from simultaneous interactions between biological, socio-cultural and psychological factors. Biological factors such as genetic make-up of a child interact with sociocultural factors and psychological factors, altering the physiology of the gastrointestinal tract and sensations giving rise to symptoms. Psychological and socio-cultural factors also alter the disease related behaviours such as health care consultation.
RAP is more common among children who have suffered stressful experiences and 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. The prevailing viewpoint is that the pathogenesis of the pain involves activation of brain gut axis resulting in gastrointestinal motility disturbances and visceral hypersensitivity.
Adult and paediatric patients with functional dyspepsia often have gastrointestinal motor and electrical abnormalities and delayed transit. Gastrointestinal myoelectrical and motility abnormalities are also reported in patients with irritable bowel syndrome. Very few studies have investigated the association between gastrointestinal motility disturbances and functional RAP. These studies have demonstrated altered fasting gastrointestinal motility patterns, abnormal electrical activity and impaired gastric accommodation. Without thorough knowledge on pathophysiology, childhood RAP is one of the most difficult conditions to manage.
Only basic urine, stool and blood investigations are recommended to exclude organic causes in the diagnostic workup. Extensive radiographic evaluation and invasive

investigations like endoscopy are rarely diagnostic or cost-effective.

The current recommendation in treating children with this condition includes support and empathy for the family, with reassurance that no serious disease is present. With this approach, approximately 30% to 40% of children have resolution of their pain46. However, the remainder continues to exhibit symptoms and go on to be adults with functional gastrointestinal disorders, anxiety, or other somatic disorders.

Pharmaceutical treatments are commonly used in an effort to manage symptoms despite the lack of data supporting their efficacy. This study has attempted to answer some of the questions related to epidemiology and pathophysiology of RAP in Indian children with emphasis on bio-psychosocial model of causation. This study was carried out in three phases.

2. Methods

In this school survey, four schools were randomly selected, one class each was chosen randomly from academic years 1 to 9. All students aged 5-15 years in the selected classes were included in the study. Written consent was obtained from parents or guardians. Pre-tested self-administered parental questionnaires were distributed to those who consented and were returned by post.

Reminders were sent twice to parents who failed to return the questionnaires. Information regarding demographic features, exposure to stressful life events, a history of RAP among first-degree relatives, associated symptoms and health care consultation was obtained. RAP was defined using Apley criteria.

3. Results and Discussion

Eight hundred and twenty five children were eligible for the study. Of them 810 (98.2%) parents consented to participate. After two reminders, a total of 734 (90.6%) questionnaires were returned. All of them were included in the analysis. [males 342 (46.6%), mean age of 10.5 years (SD 2.7years)]. Prevalence of recurrent abdominal pain Seventy seven (10.5%) children fulfilled the criteria for diagnosis of RAP.

The prevalence of RAP among Indian children and adolescents in our study was similar to those previously reported. In 1958, Apley and Naish reported a prevalence of 10.8% among British school children, with girls (12.3%) more commonly affected than boys (9.5%). More recent studies in Western countries and in Asia have reported similar prevalence; e.g. 11.8% in British children, 12% in Australian children, 11.5% among school children in Bangladesh and 10.2% in urban and rural school children in Malaysia (urban 8.2-9.6%, rural 12.4%).

Prevalence of RAP was highest in children between 10 and 11 years in our study which is in agreement with previous studies. During analysis, 657 children without recurrent abdominal pain were considered as controls. Clinical profile of the affected children Abdominal pain was defined as mild when the child was able to walk about and carry out regular activities during episodes of pain and as moderate when the child needed to sit down. Pain was classified as severe if the child had to lie down during pain episodes. If the child cried or screamed during pain episodes, it was considered very severe.

The majority of the affected children had mild to moderate abdominal pain (58.4%). In over half of the patients (58.4%) pain was felt in the periumbilical region, and similar results have been reported from other countries. The commonest symptoms associated with RAP that we found viz. headache (43%), anorexia (35%), lethargy (23%), joint pain (23%), nausea (22%) and vomiting (18%), were also similar to those reported in other studies. We found an independent association between RAP and the presence of abdominal pain among first degree relatives 55.8% vs. 44.2%, a finding that has been reported previously.

This may be due to genetic or environmental vulnerability, and further studies should be directed at identifying a definite genetic predisposition.

Table 1: Association between exposure to stressful life events and RAP

Stressful event	RAP *n* (%)	Controls *n* (%)
Change in school	15 (19.7%)**	54 (8.2%)
Frequent punishment in school	04 (5.2%)	15 (2.3%)
Change in class or a favourite teacher	07 (9.2%)	34 (5.2%)
Separation from best friend	09 (11.8%)	39 (5.9%)
Failure in an examination	03 (3.9%)	24 (3.7%)
Being bullied at school	12 (15.8%)***	32 (4.9%)
Change in address	16 (21.1%)**	60 (9.1%)
Severe illness in a close family member	19 (25.0%)***	66 (10.0%)
Death of a close family member	12 (17.1%)	87 (13.2%)
Loss of job by a parent	07 (9.2%)	34 (5.2%)
Mother starting work	05 (6.6%)	35 (5.3%)
Parent absent from home	05 (6.6%)	17 (2.6%)
Divorce or separation of parents	07 (9.2%)***	09 (1.4%)
Birth of a sibling	05 (6.6%)	22 (3.3%)
Frequent domestic fights	06 (7.9%)*	18 (2.7%)
Frequent punishment by the parents	07 (9.2%)*	22 (3.3%)
Hospitalisation of the child for other illness	07 (9.2%)	37 (3.3%)
Exposure to at least one stressful event	**22 (28.6%)****	**383 (58.3%)**

*$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$

In agreement with previous studies in Malaysia, the stressful life events independently associated with RAP were being bullied at school (p=0.02), severe illness in a close family member (p=0.028) and divorce or separation of parents (p=0.04)

Details regarding the child's academic performance were obtained from school records. The performance was categorised based on the performance in school end-of-term examinations during the year 2002. The top one third of the class (based on the ranking order of marks obtained) was considered as good, the middle one third as average and the bottom one third as poor. In contrast to the common belief that RAP is a disease of high achievers, this study failed to demonstrate significant associations between RAP and good academic performance (36.4% vs. 33.6% in controls) nor participation in sports or other extracurricular activities (28.6% vs. 24%). Similar results have been reported in previous studies.

In our study significantly higher numbers of children with RAP miss school compared to children without RAP (55.8% vs. 24.4%). Rasul and Khan found that children with RAP miss an average of 8 days per year because of abdominal pain.

Health care consultation in children with recurrent abdominal pain Fifty four (70.1%) children with RAP had consulted a doctor during the previous 12 months for the abdominal pain. Of them, only 5 (9%) had received in-patient care and the rest [49 (91%)] were managed as out-patients. The health care consultation in our children is higher than previously reported. Availability of free health services and easy access to health care, probably have contributed to the higher prevalence of health care consultation in our study. Health care consultation was significantly higher when the child with RAP was the eldest in family (p=0.04), a good academic achiever (p=0.02) and had pain associated with vomiting (p=0.007).

There was no significant association between the health care consultation and sex, younger age, pain severity, sleep interruption, family income, maternal employment, family size, school absenteeism, age of onset of RAP and frequency and duration of the pain episodes (p>0.05).

Many diseases can cause abdominal pain, but, in clinical practice, the majority of children and adolescents presenting with this symptom have no evidence of organic disease. To rule out underlying organic disorders, children with RAP do not require an exhaustive series of diagnostic investigations. Excessive testing may increase parental anxiety and put the child through unnecessary stress. A correct diagnosis can be suspected following a good history and physical examination.

Most researchers and clinicians suggest that investigation should be limited to a complete blood count, acute phase reactants, urine analysis and culture, and stool examination for parasitic infections. Further diagnostic testing should be based on clinical suspicion of a particular organic disorder.

To date the only community-based study to detect the aetiology of RAP was Apley's field survey which reported organic diseases in 10% of affected children. Investigations were limited during that period and recent advances in diagnostic facilities have probably contributed to the higher proportion of organic diseases seen in our patients with RAP.

Prevalence of organic diseases in our study was comparable to that reported by Dutta *et al*. (26%) in children with RAP attending a paediatric outpatient clinic in India and Alfven (25%) in abdominal pain clinic in Sweden. Some previous studies have reported higher percentage of organic diseases in children with RAP.

Inclusion of very young children may have accounted for the high percentage of organic diseases in these studies. Similar to our study,

Stordal *et al*. also reported constipation as a leading cause of RAP, while several Indian studies have recognized intestinal parasitic infections, including giardiasis, as the leading cause for RAP. Other diseases commonly recognized were urinary tract infection, Helicobacter pylori infection and lactose intolerance.

Table 2: Prevalence of abdominal pain related functional gastrointestinal diseases in children with RAP

FGD	Rome II criteria *n* (%)	Rome III criteria *n* (%)
Functional abdominal pain	13 (31%)	19 (45.2%)
Functional dyspepsia	9 (21.4%)	9 (21.4%)
Irritable bowel syndrome	9 (21.4%)	9 (21.4%)
Abdominal migraine	1 (2.4%)	1 (2.4%)
Aerophagia	1 (2.4%)	1 (2.4%)
FGD total	**33 (78.6%)**	**39 (92.9%)**
Non specific abdominal pain	**9 (21.4%)**	**3 (7.1%)**

4. Analysis

The concept of recognizing "red flags" that suggest organic disease has long been a tradition in management of childhood abdominal pain. Contrary to common beliefs and recommendations, the majority of pain characteristics and associated symptoms, including many alarm symptoms, were not commoner in patients with an organic aetiology compared to those with functional RAP. The symptom associated with organic aetiology in our study was presence of vomiting and nocturnal pain.

There has been no firm evidence to state that the nature of the abdominal pain or the presence of associated symptoms can discriminate between functional and organic disorders. In our study, a higher percentage of patients with functional RAP had a family history of RAP (42.9%) compared to those with organic RAP (23.2%), although the difference was not significant. We found no difference in health care consultation between organic (76.9%) and functional RAP (73.8%). Similar to the study done by Walker and Green, the present study found no difference in exposure to stressful life events in patients with organic and functional RAP (69.2% vs. 64.3%).

Table 3: Comparison of symptoms in patients with organic and functional RAP

	Organic RAP (*n*=13)	Functional RAP (*n*=42)
Severity		
Mild	2 (15.4%)	11 (26.2%)
Moderate	3 (23.0%)	8 (19.1%)
Severe	4 (30.8%)	14 (33.3%)
Very severe	4 (30.8%)	9 (21.4%)
Localization		
Periumbilical area	10 (76.9%)	28 (66.6%)
Epigastric area	2 (15.4%)	8 (19.1%)
Other	1 (7.7%)	4 (9.5%)
Undetermined	0	2 (4.8%)
Type of pain		
Burning	0	2 (4.8%)
Colicky/cramp like	7 (53.8%)	19 (45.2%)
Continuous	3 (23.0%)	15 (35.7%)
Undetermined	3 (23.0%)	6 (14.3%)
Associated symptoms†		
Headache	4 (30.8%)	19 (45.2%)
Anorexia	7 (53.8%)	10 (23.8%)
Lethargy	3 (23.0%)	10 (23.8%)
Weight loss	5 (38.5%)	10 (23.8%)
Dysuria	4 (30.8%)	6 (14.3%)
Joint pain	3 (23.0%)	7 (16.7%)
Nausea	4 (30.8%)	5 (11.9%)
Vomiting	5 (38.5%)*	3 (7.1%)
Diarrhoea	2 (15.4%)	1 (2.4%)
Nocturnal pain	4 (30.8%)**	3 (7.1%)

There have been only limited studies to detect the gastrointestinal motility abnormalities in children with RAP. Pineiro-Carrero *et al*. showed that the children with RAP had more migrating motor complexes compared to healthy children, but these were shorter in duration and showed impaired propagation down the intestine. These patients also had high-pressure duodenal contractions that were associated with abdominal pain.

Olafsdottir *et al*. showed an impairment in accommodation of the proximal stomach following a liquid meal in children with RAP compared to healthy children. This study failed to show a significant relationship between emptying of the distal stomach and RAP. We evaluated gastric myoelectrical activity, gastric emptying rate, antral motility and intestinal transit time in children with recurrent abdominal pain syndrome. Understanding the gastrointestinal motility abnormalities in such patients will widen the knowledge of the pathophysiology of the condition and potentially improve the management of the affected children.

5. Conclusions

In our study, the epidemiology of recurrent abdominal pain in India is similar to that of other countries, affecting nearly 10% of school children and adolescents. In agreement with previous studies the majority have mild to moderate central abdominal pain associated with other painful conditions like headache and limb pain, and autonomic symptoms such as lethargy, nausea and vomiting.

Recurrent abdominal pain has significant associations with exposure to recent stressful life events and a history of recurrent abdominal pain among first degree relatives. No associations were observed between this syndrome and socio-economic status or school performance. Approximately 70% of patients had consulted a doctor for their symptoms in contrast to previous studies in which the majority were non-consulters. We found organic pathology only in less than 25% of patients with RAP. Functional gastrointestinal diseases were present in over two third (75%).

The commonest functional gastrointestinal disorder observed in this study was functional abdominal pain, followed by irritable bowel syndrome and functional dyspepsia. 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. In agreement with previous studies, we did not find an association between Helicobacter pylori infection and RAP. For the first time, we have demonstrated, delayed gastric emptying, impaired antral motility and prolonged oro-caecal transit in patients with recurrent abdominal pain.

Our results indicate the importance of gastrointestinal motility disturbances in the pathogenesis of non-organic recurrent abdominal pain in children and adolescents. Cutaneous electrogastrography, gastric emptying ultrasound and lactulose breath hydrogen test are safe, noninvasive techniques, which are helpful in identifying altered gastrointestinal function in these children. Such information may be quite useful in understanding the pathophysiology of the condition and in directing an effective management plan. It remains to be established whether drugs that normalize the gastrointestinal motor activity result in improvement in symptoms. Future studies should be directed at establishing a possible therapeutic effect of prokinetic drugs in the management of this condition.

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