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## Research Submission

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# Abdominal Migraine: An Under-Diagnosed Cause of Recurrent Abdominal Pain in Children

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**Objective.**—Our objective was to demonstrate that, despite recognition by both the gastroenterology and headache communities, abdominal migraine (AM) is an under-diagnosed cause of chronic, recurrent, abdominal pain in childhood in the USA.

**Background.**—Chronic, recurrent abdominal pain occurs in 9-15% of all children and adolescents. After exclusion of anatomic, infectious, inflammatory, or other metabolic causes, “functional abdominal pain” is the most common diagnosis of chronic, idiopathic, abdominal pain in childhood. Functional abdominal pain is typically categorized into one, or a combination of, the following 4 groups: functional dyspepsia, irritable bowel syndrome, AM, or functional abdominal pain syndrome.

**International Classification of Headache Disorders—(ICHD-2)** defines AM as an idiopathic disorder characterized by attacks of midline, moderate to severe abdominal pain lasting 1-72 hours with vasomotor symptoms, nausea and vomiting, and included AM among the “periodic syndromes of childhood that are precursors for migraine.” Rome III Gastroenterology criteria (2006) separately established diagnostic criteria and confirmed AM as a well-defined cause of recurrent abdominal pain.

**Methods.**—Following institutional review board approval, a retrospective chart review was conducted on patients referred to an academic pediatric gastroenterology practice with the clinical complaint of recurrent abdominal pain. ICHD-2 criteria were applied to identify the subset of children fulfilling criteria for AM. Demographics, diagnostic evaluation, treatment regimen and outcomes were collected.

**Results.**—From an initial cohort of 600 children (ages 1-21 years; 59% females) with recurrent abdominal pain, 142 (24%) were excluded on the basis of their ultimate diagnosis. Of the 458 patients meeting inclusion criteria, 1824 total patient office visits were reviewed. Three hundred eighty-eight (84.6%) did not meet criteria for AM, 20 (4.4%) met ICHD-2 formal criteria for AM and another 50 (11%) had documentation lacking at least 1 criterion, but were otherwise consistent with AM (probable AM). During the observation period, no children seen in this gastroenterology practice had received a diagnosis of AM.

**Conclusion.**—Among children with chronic, idiopathic, recurrent abdominal pain, AM represents about 4-15%. Given the spectrum of treatment modalities now available for pediatric migraine, increased awareness of cardinal features of AM by pediatricians and pediatric gastroenterologists may result in improved diagnostic accuracy and early institution of both acute and preventative migraine-specific treatments.

**Key words:** abdominal migraine, pediatric, children

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Children with chronic recurrent abdominal pain have a high utilization of healthcare resources. As is observed with other chronic pain syndromes, recurrent abdominal pain leads to significant disability, including interference with family, school, and social activities. Accurate diagnosis as to the etiology of the

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*Conflict of Interest:* None

**Table 1.—International Classification of Headache Disorders 2004 Criteria<sup>4</sup>**


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Diagnostic criteria for abdominal migraine include the following:

- A. At least 5 attacks fulfilling criteria B-D.
  - B. Attacks of abdominal pain lasting 1-72 hours.
  - C. Abdominal pain has *all* of the following characteristics:
    1. Midline location, periumbilical or poorly localized.
    2. Dull or “just sore” quality.
    3. Moderate or severe intensity.
  - D. During abdominal pain, at least 2 of the following:
    1. Anorexia.
    2. Nausea.
    3. Vomiting.
    4. Pallor.
  - E. Not attributed to another disorder. History and physical examination do not show signs of gastrointestinal or renal disease or such disease has been ruled out by appropriate investigations.
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pain is integral to providing explanation and reassurance to the patient and family, as well as maximizing targeted therapeutic options.<sup>1</sup>

Chronic, recurrent abdominal pain occurs in 9-15% of all children and adolescents. The American Academy of Pediatrics Subcommittee on Chronic Abdominal Pain and North American Society of Pediatric Gastroenterology, Hepatology and Nutrition define “functional abdominal pain” as the most common cause of chronic, idiopathic abdominal pain in childhood, after exclusion of anatomic, infectious, inflammatory, or other metabolic causes, and categorize “functional abdominal pain” as 1, or a combination of, 4 clinical entities; functional dyspepsia, irritable bowel syndrome, *abdominal migraine (AM)*, and/or functional abdominal pain syndrome.<sup>1</sup>

First described nearly a century ago, AM occurs in 1% to 4% of children and has received considerable attention as one of many potential etiologies of recurrent abdominal pain in children.<sup>2,3</sup> In 2004, the International Headache Society (ICHD-2) included AM among its “periodic syndrome of childhood that are precursors for migraine” (Table 1).<sup>4,5</sup> In 2006, Rome III Gastroenterology established separate, but similar, criteria for AM, confirming AM as a well-defined cause of recurrent abdominal pain (Table 2).<sup>6</sup>

International Classification of Headache Disorders—2nd Version defined AM as an idio-

pathic disorder characterized by attacks of midline, moderate to severe abdominal pain lasting 1-72 hours with vasomotor symptoms, nausea, and vomiting. A key feature of AM is the complete resolution of symptoms between attacks. The pain is of moderate to severe intensity. In 2001, Dignan et al introduced a comprehensive guideline which included valuable exclusionary criteria for patients with the following features: mild symptoms not interfering with daily activities, burning pain, non-midline abdominal pain, symptoms consistent with food allergy or other gastrointestinal disease, attacks less than 1 hours, or persistence of symptoms between attacks.<sup>7</sup>

Abdominal migraine is more common in those with a family history of migraine headaches and emerges between the ages of 3 and 10 years.<sup>8</sup> While AMs rarely persist into adulthood, evidence suggests an evolution of AM into migraine headaches, ergo a “precursor for migraine.”<sup>7</sup> In a 10-year prospective study of nearly 150 children referred for recurrent abdominal pain, Bentley et al identified 70 children whose symptoms were consistent with AM.<sup>9</sup> An equal number of males and females were affected by this condition, and 90% had a positive family history of migraines in a first-degree relative. Consistent with other reports, diagnosis was made between the ages of 6 and 10 years.<sup>8-10</sup>

**Table 2.—Rome III Functional Gastrointestinal Disorders 2006 Criteria<sup>6</sup>**


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Diagnostic criteria for abdominal migraine include all of the following, with 2 or more episodes in the preceding 12 months:

- A. Paroxysmal episode of intense, acute periumbilical pain that lasts 1 hours or more.
  - B. Intervening periods of usual health lasting weeks to months.
  - C. The pain interferes with normal activities.
  - D. The pain is associated with 2 or more of the following:
    - a. Anorexia.
    - b. Nausea.
    - c. Vomiting.
    - d. Headache.
    - e. Photophobia.
    - f. Pallor.
  - E. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process.
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One of the curious issues regarding the entity of AM is the apparent *trans*-Atlantic dissociation. The overwhelming body of literature pertaining to AM arises from Europe, primarily Scotland, with very little coming from US centers. Is the diagnosis made more commonly in Europe and uncommonly in the USA? Is there inadequate awareness among US clinicians about AM? Russell et al proposed that the limited recognition of AM among clinicians can be explained, in part, by referral patterns and biases. Children with recurrent abdominal pain are typically referred to gastroenterologists, where organic causes are explored and migraine is rarely considered.<sup>11</sup> Do gastroenterology services in the USA consider AM among the potential causes of unexplained abdominal pain? We hypothesize that despite the recognition of AM by the gastroenterology and headache communities, AM is likely being under-diagnosed in the USA.

The purpose of this study was to assess the population of children within a single academic pediatric gastroenterology clinic who present with “recurrent abdominal pain” to ascertain whether there is an unrecognized subset of patients who fulfill the diagnostic criteria for AM.

## METHODS

Study population included subjects 1-21 years of age, males and females, who have been evaluated in the Pediatric Gastroenterology Clinic at the Children’s Hospital of The King’s Daughters. The subject population was identified by International Classification of Diseases—Ninth Revision (ICD-9) code for “recurrent abdominal pain” among gastroenterology clinic patients from 1/1/2006 to 12/31/2007 and their medical records were reviewed. Those patients who were found to have an etiology for their recurrent abdominal pain were excluded as, by definition, AM cannot be attributed to another disorder. These diagnoses included: eosinophilic esophagitis, ulcerative colitis, Crohns disease, celiac disease, irritable bowel syndrome, or food allergies; renal disease; autism spectrum disorder; pre-existing neurologic disorder; metabolic disease; hydrocephalus and/or ventricular shunt.

*Idiopathic* recurrent abdominal pain was isolated for evaluation by the criteria listed above, eliminating

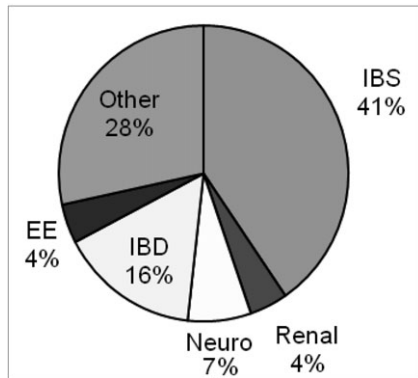
patients with additional diagnoses that may explain the etiology of the abdominal pain. For each subject meeting inclusion criteria, information regarding demographics, medical and family history to specifically include history of migraine, as well as previous gastroenterology work-up and attempted therapies were recorded. Details describing the nature of abdominal pain episodes were transferred to a data collection sheet, and subsequent database managed by the principle investigator. Based on ICHD-2 criteria AM, characteristics of abdominal pain episodes included frequency, duration, location, quality, intensity, and associated symptoms were recorded.

Data were analyzed using SPSS version 16.0 for Windows. Descriptive statistics were determined for the patient population that met the criteria for AM. Odds ratio was determined for family history and medical history between individuals with recurrent abdominal pain that did or did not meet the criteria for AM. Chi-square analysis was completed to determine any differences between the 2 groups, those that meet or do not meet the criteria for AM, such as demographic information, medical history, and family history.

## RESULTS

The search for gastroenterology clinic patients by ICD-9 code revealed 2443 children evaluated at least once from 1/1/2006 to 12/31/2007 with the diagnosis of recurrent abdominal pain on 1 or more visits. From this patient list, 600 charts were randomly selected and evaluated, with all visits included as data, regardless of time period, such that the complete work-up and pattern of disease was recorded for each included patient.

From an initial cohort of 600 children (ages 1-21 years; 59% females) with recurrent abdominal pain, 142 (23.5%) were excluded on the basis of their ultimate diagnosis in accordance with ICHD-2 AM criteria (Table 1). Reasons for exclusion included irritable bowel syndrome (41%), renal disease (4%), pre-existing neurologic disorder (7%), inflammatory bowel disease (16%), eosinophilic esophagitis (4%), and “other” (28%) which included food allergies, celiac disease, cystic fibrosis, autism spectrum disorder, and anatomic abnormalities (Fig. 1).

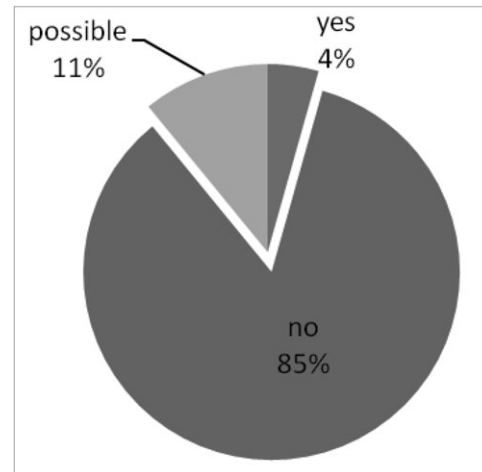


**Fig 1.—Reasons for exclusion.** EE = eosinophilic esophagitis; IBD = inflammatory bowel disease; IBS = irritable bowel syndrome.

Of 458 patients meeting inclusion criteria, a total of 1824 total patient visits were reviewed. Three hundred eighty-eight (84.6%) children did not meet criteria for AM, 20 (4.4%) met formal ICHD-2 criteria for AM (age 5-17 years, mean 11 years) and another 50 (11%) had documentation lacking at least 1 criterion, but were otherwise consistent with AM (“probable AM”; age 4-18 years, mean 12 years; Fig. 2). Data on race revealed 36% Caucasian, 14% African American, 5% other, 1% Asian, 0.5% Hispanic, and were unavailable for 43% of included patients. There was no significant difference ( $P > .05$ ) in race or gender among those who met criteria for AM.

Of the included 458 patients, 75% had a family history of recurrent abdominal pain and 46% had a family history of migraine. Among the 20 patients who met formal criteria for AM, 62.5% had a family history of migraine. Personal history of migraine was noted in 15% of all included patients but found in 38% of children meeting formal AM criteria, indicating that it is 4 times more likely for a patient with recurrent abdominal pain to have AM if they also have migraine headache ( $P < .024$ , 95% CI 1.56-11.92). Other clinical features reported more frequently among suspected AM patients included nausea ( $P < .001$ ), vomiting ( $P < .038$ ), and anorexia ( $P < .001$ ).

Patients meeting AM criteria were also significantly more likely to have had an esophagogastroduodenoscopy as part of their diagnostic evaluation ( $P .008$ ), confirming that no other organic etiology was involved. Among the 4-15% of patients



**Fig 2.—Suspected abdominal migraine.**

with suspected AM based on ICHD-2 criteria, 63% reported abdominal pain as periumbilical, 11% midline, 5% poorly localized, and 21% “other” which included diffuse abdominal pain and cases in which no location was noted in the documentation.

During the assessment period January 2006 through December 2007, no children received a diagnosis of AM in the Pediatric Gastroenterology Clinic.

## DISCUSSION

Until recently developed diagnostic criteria were published, the existence of AM was controversial, and therefore prevalence data were rare. The majority of data originated in Europe, with 1 UK study demonstrating that the prevalence of AM was 2.4%.<sup>8</sup> In a study using diagnostic criteria similar to ICHD-2, Abu-Arafeh and Russell reported the prevalence of AM was 4.1% in 2165 children aged 5-15 years.<sup>12</sup> Comparable to those results, our data from a US academic gastroenterology practice determined the prevalence of AM to be 4% among children 1-21 years with recurrent abdominal pain. An additional 11% of patients were deemed as “probable” AM based on having met diagnostic criteria except for 1 criterion for which documentation was lacking.

The major limitations of this study are inherent to retrospective designs, with only the recorded data being available for review. Frequently, not every

portion of the ICHD-2 diagnostic criteria was addressed. For example, the severity, duration, or location of abdominal was not noted on a particular visit. Oftentimes, not all of the target associated symptoms were commented upon, and therefore it is not possible to know if they did not occur, they were not discussed, or they were discussed and not recorded. In addition, each chart was reviewed as a whole, with characteristics of abdominal pain recorded from each visit. Occasionally, the description of abdominal pain and associated symptoms varied significantly visit to visit. At times this was attributed to disease evolution, or treatment. The accuracy of the report by the patient also must be questioned, as it is often difficult for children to qualify many of these characteristics or to quantify the duration of symptoms.

A paucity of literature exists regarding the treatment and management of AM. However, anecdotal evidence demonstrates that many of the strategies used in the treatment of migraine headaches may also be efficacious in the management of AMs. This experience is supported by evidence that children with AM have similar demographic and social characteristics to those of children with migraine, as well as similar patterns of trigger and relieving factors, and associated symptoms during attacks.<sup>13</sup>

Russell et al reported success with a series of measures that include reassurance that there is no serious abdominal pathology. Also recommended is avoidance of triggers that are thought to instigate migraine headaches such as chocolate, caffeine and amines, as well as alterations in sleep patterns and skipping meals. A “few-foods diet” is employed by restricting the diet and gradually reintroducing foods in an attempt to identify specific foods that may be affecting the individual patient.<sup>11</sup>

Little evidence exists regarding the use of drugs to manage AM. For acute treatment of attacks, there is no data regarding ibuprofen or acetaminophen, the 2 agents for which controlled data exist for migraine without aura in young children. There are likewise not data regarding the use of triptans for AM. Preventive medications that have demonstrated efficacy in clinical trials include pizotifen, propranolol, and cyproheptadine for prevention of recurrent attacks.<sup>14</sup> One double-blind placebo-controlled trial demonstrated

pizotifen syrup was superior to placebo in the prophylaxis of AM.<sup>15</sup>

Improved recognition and diagnosis of AM as a relatively frequent cause of recurrent abdominal pain in children would facilitate further investigation into the nature and underlying mechanisms of AM, as well as studies to define effective treatment options. Future directions call for prospective, controlled trials of migraine-specific therapies, the acute and prophylactic treatment of AM in children with AM.

## CONCLUSIONS

According to the American Academy of Pediatrics and North American Society of Pediatric Gastroenterology, Hepatology and Nutrition, “long-lasting, constant or intermittent abdominal pain in childhood remains one of ambiguity and concern for most pediatric healthcare professionals.”<sup>1</sup> The differential diagnosis is broad and requires a systematic approach to exclude anatomic, metabolic, infectious, and inflammatory causes. Ultimately, functional abdominal pain will be the most common diagnosis and this condition is composed of 4 entities; functional dyspepsia, irritable bowel syndrome, functional abdominal pain syndrome, and/or AM.

Abdominal migraine represents 4-15% of pediatric gastroenterology patients followed for idiopathic recurrent abdominal pain. Despite recognition by the gastroenterology and headache communities with reliable diagnostic criteria (ICHD-2 and Rome III 2006), AM is under-diagnosed in the USA, and represents an example of diagnostic substitution. Given the spectrum of treatment modalities now available for pediatric migraine, increased awareness of cardinal features of AM by pediatricians and pediatric gastroenterologists may result in improved diagnostic accuracy and early institution of both acute and preventative migraine-specific treatments.

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