HHS Public Access

Author manuscript

Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2015 September 01.

Published in final edited form as:

Clin Gastroenterol Hepatol. 2014 September ; 12(9): 1468–1473. doi:10.1016/j.cgh.2014.01.031.

Subtypes of Irritable Bowel Syndrome in Children and Adolescents

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Abstract

Background & Aims—Pharmacologic treatments for IBS and medical management of symptoms are increasingly based on IBS subtype, so it is important to accurately differentiate patients. Few studies have classified subtypes of pediatric IBS, and conclusions have been challenged by methodologic limitations. We performed a prospective study to investigate the distribution of IBS subtypes among children and adolescents based on stool diary information, and compared subtypes according to demographic and pain characteristics.

Methods—We studied 129 subjects, 7–18 y old (mean 11.4 ± 2.8 y old, 60.5% female, 69.0% Caucasian) who met Pediatric Rome III IBS criteria and were part of larger studies of children with functional gastrointestinal disorders, recruited from primary and tertiary care centers. Children completed daily pain and stool diaries for 2 weeks. Participants were assigned IBS subtypes based on their reported stool information, per adult Rome III criteria. IBS subtypes were compared for demographic variables and pain characteristics.

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Disclosures: None.

Author contributions: Mariella M. Self, Ph.D. – Study design, data analysis and interpretation, drafting and revision of manuscript. This author approved the final version of this manuscript.
Danita I. Czyzewski, Ph.D. – Study design, interpretation of data, manuscript revisions. This author approved the final version of this manuscript.
Bruno P. Chumpitazi, M.D, M.P.H. – Study design, interpretation of data, manuscript revision. This author approved the final version of this manuscript.
Erica M. Weidler – Acquisition of data; administrative support, data analysis, manuscript revision. This author approved the final version of this manuscript.
Robert J. Shulman. M.D. – Obtaining funding, study design and supervision, interpretation of data, manuscript revision. This author approved the final version of this manuscript.

Results—IBS with constipation (IBC-C) was the most common subtype of the disorder (58.1% of subjects), whereas mixed IBS (IBS-M) was the least common (2.3% of subjects); 34.1% of subjects were unsubtyped (IBS-U) and 5.4% had IBS with diarrhea (IBS-D). The groups of different IBS subtypes did not differ significantly by sex, age, ethnicity, or pain characteristics.

Conclusions—In contrast to adults, IBS-C and IBS-U are the most common subtypes of IBS in children, whereas IBS-D and IBS-M are less common. Demographic and pain characteristics cannot distinguish subtypes.

Keywords

Irritable Bowel Syndrome; IBS Subtypes; Children; Pediatric Functional GI Disorders

Introduction

In the current absence of a reliable and valid biomarker for irritable bowel syndrome (IBS), diagnosis is made according to symptom based Rome III criteria.[1] Rome III criteria for adults use stool form to classify IBS patients into four subtypes: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed type (IBS-M), and unsubtyped (IBS-U). Medical management of symptoms and clinical trials evaluating pharmacological treatments for IBS are increasingly targeted to IBS subtype, underscoring the importance of reliably differentiating patients accordingly.[2-7]

In adults with IBS, the prevalence of subtypes varies by study, but in general subtype assignment by prospective diary data tends to yield a relatively even distribution among IBS-C, IBS-D, and IBS-U, with a smaller percentage of patients being classified as IBS-M.[8-13] Despite the importance of subtyping IBS from both a clinical and research perspective, few studies have described subtype classification in pediatric IBS, and only one small sample has been reported in a U.S. population.

Two pediatric school based Sri Lankan studies using self-report questionnaires describe an approximately equal distribution of IBS-C, IBS-D, and IBS-M, with a lower prevalence of IBS-U.[14-15] Results from these studies are limited by use of retrospective questionnaires, a method shown in adult and pediatric studies to be discordant with, and presumably less accurate than, prospective diaries of stool form.[8,10,13,16,17] While our collaborative work investigating the intestinal microbiomes of children with IBS did use assignment of IBS subtype via prospective diary data, the sample contained only 22 children.[18] Thus, we sought to investigate IBS subtype distribution in a significantly larger sample of children and adolescents based on prospective stool diary data and to compare subtype groups according to demographic and pain characteristics.

Methods

Recruitment & Data Collection

Participants were 129 patients, ages 7-18 years, with IBS as defined by Pediatric Rome III criteria who were part of larger studies of physiological and psychological characteristics of children with functional gastrointestinal (GI) disorders or who were part of dietary treatment

trials.[19] Only baseline data obtained prior to any interventions were used. Participants were recruited from primary (n = 52) and tertiary care (n = 77) clinics in a large academically-affiliated pediatric health care network. Potential participants had been identified through general pediatric and pediatric gastroenterology chart review with the ICD-9 codes 789.0 (abdominal pain) or 564.1 (irritable bowel syndrome). Parents of potential participants were contacted by mail and, if interested in participating, screened by phone for inclusion/exclusion criteria.

Children were excluded from participation if phone or chart review screening revealed organic GI illness (or it remained in the differential as a cause of the pain), a significant chronic health condition requiring daily medication or specialty follow-up care, decreased growth velocity, GI blood loss, unexplained fever, vomiting, chronic severe diarrhea, weight loss ≥5% of their body weight within a 3-month period, current use of anti-inflammatory medications, medications that would alter GI transit time, or previous use of GI medication that provided complete symptomatic relief. Additional exclusion criteria included lack of fluency in English (as the other studies required completion of psychological questionnaires only available in English) and learning or developmental challenges preventing diary completion. Participants who passed inclusion/exclusion criteria and qualified as IBS via mother-report on a phone screening based on Pediatric Rome III criteria[20] were considered eligible. The study was approved by the Baylor College of Medicine Institutional Review Board and parent consent and child assent were obtained.

Pain & Stool Diary

At a home visit parents and children were instructed on the completion of a daily pain and stool diary for two weeks. Parents were asked to remind children to complete the diaries daily but to allow children to independently rate abdominal pain and record stool occurrence and form without influencing their responses. Children rated abdominal pain for three intervals each day (morning, midday/afternoon, and evening/nighttime) using a 0-10 numerical scale anchored with the phrases “no pain at all” and “the worst pain you can imagine.”[21] Children also reported degree of activity interference due to pain using a 4-point scale, ranging from no interference to “could not participate because of pain.” Children recorded the time of each stool and rated its consistency using the Bristol Stool Form Scale (BSFS).[22]

Statistical Analysis

Statistics were performed using SPSS 20.0. Mean pain rating, maximum pain rating, and number of pain episodes (defined as pain rating ≥ 1) were calculated for each participant over the two weeks. An average interference rating for pain episodes was also calculated for each participant.

Participants were classified into IBS subtypes by applying Rome III criteria to their reported stool forms on diary. Specifically, the percent of stools reflecting constipation (i.e., rated as a 1 or 2 on the BSFS) or diarrhea (i.e., rated as a 6 or 7 on the BSFS) was calculated for each participant. Participants were classified into IBS subtypes as follows: IBS-C (hard stools ≥ 25% and loose stools < 25%), IBS-D (loose stools ≥ 25% and hard stools <25%), IBS-M

(hard stools and loose stools ≥ 25%), and IBS-U (hard stools and loose stools < 25%), as proposed by Longstreth.[1] Prevalence of each IBS subtype then was calculated.

Chi square tests were conducted to compare subtype groups according to sex and race/ethnicity. One-way ANOVAs were used to compare IBS subtypes on age, mean abdominal pain rating, maximum pain rating, number of pain episodes, and average pain interference. Data are shown as mean ± SD.

Results

Mean age of the participants was 11.4 ± 2.8 years (range 7-18) with 60.5% being female. Overall race/ethnicity distribution was: 69.0% Caucasian, 17.1% Black, 10.1% Hispanic, and 3.1% Asian, and 0.8% multi-racial. Regarding insurance status, 80.6% were covered by private insurance and 16.3% had Medicaid.

IBS Subtypes

The 129 children and adolescents were subtyped as follows: 75 (58.1%) IBS-C, 44 (34.1%) IBS-U, 7 (5.4%) IBS-D, and 3 (2.3%) IBS-M.

IBS Subtypes by Demographic Characteristics (Table 1)

Including all four IBS subtypes, distribution did not differ significantly by sex: χ^2 (3, *N*= 129) = 3.32; P=0.10. When omitting IBS-D and IBS-M subtypes due to low cell counts, distribution between IBS-C and IBS-U still did not differ significantly by sex: χ^2 (1, *N*= 119) = 2.15; P=0.14. IBS subtype distribution also did not differ significantly by age: $F(3,125) = 0.63$, P = 0.60, $\eta^2 = 0.01$. With respect to race/ethnicity, when including all IBS subtypes and omitting only the one participant with a multiracial designation, subtype distribution did not differ significantly by race/ethnicity: χ^2 (9, *N*= 128) = 9.85; P=0.36. Omitting IBS-D and IBS-M subtypes and both Asian and multiracial designations due to low cell counts, distribution between IBS-C and IBS-U still did not differ significantly by race/ethnicity: χ^2 (2, *N*= 114) = 1.42; P=0.49.

IBS Subtypes by Pain Characteristics (Table 2)

One-way ANOVAs reflected that subtype groups did not significantly differ according to mean abdominal pain rating, $F(3,125) = 2.27$, P = 0.08, maximum pain rating $F(3,125) = 1.08$, P = 0.36, number of pain episodes, $F(3,125) = 1.44$, P = 0.23, or interference due to pain, $F(3,125) = 0.86$, P = 0.47. All effect sizes were small (Table 2), but mean abdominal pain rating reflected the largest effect of the four.

Conclusions

To our knowledge, other than our previous microbiome research reporting pediatric IBS subtypes in a small sample[18], this is the first study to examine prevalence of IBS subtypes in a pediatric population in the United States using prospective diary data. In contrast to adult literature reporting similar prevalence among IBS-C, -D, and -U, over half of our participants were classified as IBS-C, approximately a third as IBS-U, and very few reported

stool patterns associated with IBS-D or IBS-M. In our view, these results emphasize the potentially different nature of childhood versus adult IBS.

Our results differ from findings of two pediatric questionnaire-based Sri Lankan studies, which reported a relatively equal distribution of IBS-C, IBS-D, and IBS-M and a lower prevalence of IBS-U.[14,15] The larger of the two studies based on the Pediatric Rome III diagnostic questionnaire reported IBS-C, IBS-D, and IBS-M having prevalences of 27-28% and IBS-U with 18%.[15] However, our previous work investigating intestinal microbiomes in 22 children yielded a very similar subtype distribution to the current results with a predominance of IBS-C (61.9%), approximately a third classified as IBS-U (33.3%), and very few subtyped as IBS-D (0.05%) or IBS-M (0%).[18]

Differences between our results and the two previous Sri Lankan pediatric studies likely are related, at least in part, to methodology. We used prospective stool and pain diaries whereas retrospective methods were used in the previous pediatric reports.[14,15] Data supporting the superiority of prospective diary data over retrospective self-report of bowel habits in IBS patients are increasingly robust, with prospective subtyping widely recommended in the existing literature and by the Rome III committee.[8,10,13,16] Adult data have demonstrated that subtyping distribution varies greatly by prospective versus retrospective symptom reporting, with poor agreement between subtype assigned by retrospective recall in contrast to prospective stool form diary.[8-10,13,16] Further, investigation of the accuracy of pain recall in children with chronic abdominal pain suggests that relatively few children accurately recall pain episodes even with a short recall interval, supporting reliance on diaries for research and meriting efforts to render their use feasible in clinical practice.[17] Another difference in methodology in the two previous Sri Lankan pediatric studies is that potential organic disorders were not considered.[14,15], whereas in our study children were excluded if organic GI illness remained in the differential following evaluation by their pediatrician or pediatric gastroenterologist. Finally, the lack of discrimination between health care consulters and non-consulters in the Sri Lankan studies, or the differing ethnic makeup of the populations may contribute to differences in findings.

The preponderance of IBS-C and relative infrequency of IBS-D in our sample suggest that children with IBS phenotypically differ from adults, as studies in adults tend to yield a relatively even distribution among IBS-C, IBS-D, and IBS-U and a smaller percentage of IBS-M. [8-13] Although it might be argued that the predominance of IBS-C in our study could be an artifact of incorporating children with functional constipation, children with constipation and pain who were treated and had resolution of their pain would have been disqualified from our study. Indeed, per medical record review, only a small percentage (10.8%) of children in our study had received a therapy for constipation prior to study onset (all subtyped IBS-C) and (by definition) without resolution of symptoms. However, given that the distinction between Rome III diagnosis of IBS-C and functional constipation has been challenged as artificial in adults[24], consideration of this as yet unexamined distinction in children is warranted as pediatric Rome criteria are refined.

We note that Rome III criteria do not account for stool frequency in IBS subtyping. Given subtype assignment is based solely on stool form and does not account for absence or

infrequency of stool, constipation may be underrepresented when assigning IBS subtype. In practicality this might result in a patient with infrequent stools subtyped as IBS-U when their stooling pattern might more accurately reflect IBS-C; or a patient classified as IBS-D might be more aptly considered IBS-M if days when they had no stool were considered. To explore this concept in the context of our IBS-U sample, we evaluated the number of days with no bowel movement for each IBS-U participant. Acknowledging that an every other day stooling pattern is considered in the normal range of stooling frequency, seven IBS-U participants had 7 or more days (≥50%) of the diary interval with no bowel movement. This suggests that if absence of stool were incorporated into the IBS subtyping criteria, some individuals otherwise subtyped as IBS-U might be reclassified as IBS-C. Classification of subtype based on percent of stool versus percent of days with a given stool form may also affect classification. Future revisions to the Rome III criteria may consider accounting for stool frequency as well as form in defining IBS subtypes.

We did not find that age, sex, or race/ethnicity were significantly different among the pediatric IBS subtypes (Table 1). However, examination of sex distribution suggests a possible trend toward a higher prevalence of IBS-C in girls compared with boys and a higher prevalence of IBS-D in boys versus girls. This is a cautious interpretation that warrants replication, but such findings would be consistent with most of the adult literature on sex differences in IBS[10,11,13,25-27], as well as the pediatric study by Rajindrajtih & Devanarayana, reporting females as more likely than males to be subtyped as IBS-C.[15]

In our study differences in pain characteristics (i.e., frequency, duration, location, pain interference in activities) according to subtype did not emerge. Rajindrajtih & Devanarayana's previous pediatric study also noted few differences in pain characteristics according to subtype, though self-report of severe pain occurred less commonly in those with IBS-D than the other three subtypes.[15] However, as previously mentioned, these results are limited by the retrospective questionnaire method, as children with functional gastrointestinal disorders generally exhibit poor recall for episodes of abdominal pain when compared with prospective pain diaries.[17] Relatively little adult research examining the relationship between pain characteristics and Rome III IBS subtype is available for comparison. Some adult data suggest that acute pain episodes and pain associated with individual bowel movements occur more with diarrhea than with hard stools.[10,28] In contrast, comparing IBS subtypes on mean abdominal pain ratings has suggested that adult IBS-C patients report more severe abdominal pain overall and more interference with activities than those with IBS-D[10], whereas other work has suggested greatest severity of discomfort/interference in the IBS-M subtype.[13]

Because no criteria have been specifically designed or tested in children to subtype IBS, our method relied on adult subtyping criteria. These criteria have long been in use and represent the basis for both clinical management and research design, including parameters set by the FDA. However, consideration of alternative pediatric criteria is warranted as the Rome IV criteria are developed. Given recent data on alterations of immune and gut barrier function in subgroups of pediatric and adult patients with IBS, alternative subgrouping may depend on laboratory versus the current clinically observable criteria.[29, 30]

Our study is limited in its short-term observation period, precluding knowledge of whether subtype distribution changes with time. Adult research has questioned the stability of IBS subtype classification.[8-10,12, 25-27, 31,32] Examining subtype stability in developing children presents an additional challenge but is an important area for future research. On the other hand, strengths of our study include the use of prospective diaries, the inclusion of primary and tertiary care patients, and evaluation by their physician to prevent inclusion of children with organic disease. Given the importance of identifying IBS subtypes for clinical care and research, our results warrant replication.

Acknowledgments

The authors would like to express appreciation to the pediatricians and pediatric gastroenterologists affiliated with Texas Children's Hospital who offered access to their patients for recruitment. The authors would also like to thank the research coordinators in the Center for Pediatric Abdominal Pain Research at Baylor College of Medicine for their assistance with study execution.

Financial support: This study was supported in part by R01 NR05337 and R01 NR013497 from the National Institutes of Health, the Daffy's Foundation, the USDA/ARS under Cooperative Agreement No. 6250-51000-043, and P30 DK56338 which funds the Texas Medical Center Digestive Disease Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This work is a publication of the USDA/ARS Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital. The contents do not necessarily reflect the views or policies of the USDA, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government. Funding was also provided by the NASPGHAN Foundation/Nestle Nutrition Young Investigator Development Award (BPC).

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Abbreviations

IBS	Irritable Bowel Syndrome
IBS-C	IBS with constipation
IBS-D	IBS with diarrhea
IBS-M	IBS mixed subtype
IBS-U	IBS unsubtyped

Table 1
Age, Sex, and Ethnicity Distribution among IBS Subtypes

	IBS-C (*n* = 75)	IBS-D (*n* = 7)	IBS-M (*n* = 3)	IBS-U (*n* = 44)
Age	11.3 ± 2.6*	11.9 ± 3.1	9.3 ± 2.0	11.5 ± 3.2
Sex				
Females (n = 78, 60.5%%)	51 (64.6%)	2 (2.6%)	1 (3.8%)	24 (30.4%)
Males (n = 51, 39.5%)	24 (47.1%)	5 (9.8%)	2 (3.9%)	20 (41.2%)
Race/Ethnicity (%)				
Caucasian (n = 89, 69.0%)	51 (57.3%)	4 (4.5%)	1 (1.1%)	33 (37.1%)
Black (n = 22, 17.1%)	14 (63.6%)	1 (4.5%)	2 (9.1%)	5 (22.7%)
Hispanic/Latino (n = 13, 10.1%)	6 (46.2%)	2 (15.4%)	0 (0%)	5 (38.5%)
Asian (n = 4, 3.1%)	3 (75.0%)	0 (0%)	0 (0%)	1 (25.0%)
Multi-racial (n = 1, 0.8%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)

*Mean ± SD

Table 2

Pain Ratings, Number of Episodes and Interference with Activities among IBS Subtypes

	IBS-C (*n* = 75)	IBS-D (*n* = 7)	IBS-M (*n* = 3)	IBS-U (*n* = 44)	η^2
Mean pain	1.2 ± 0.9*	2.1 ± 2.0	1.3 ± 0.7	1.1 ± 0.8	0.05
Maximum pain	6.2 ± 2.3	6.9 ± 3.1	7.0 ± 1.0	6.1 ± 2.3	0.03
Number of pain episodes	13.9 ± 9.5	21.3 ± 16.8	13.7 ± 5.0	13.2 ± 8.7	0.03
Mean interference rating due to pain#	0.7 ± 0.5	0.8 ± 0.7	0.8 ± 0.2	0.4 ± 0.5	0.02

Ps > .05

η^2 interpretation: .01 = small, .06 = medium, .14 = large.[23]

*Mean ± SD

#n = 126