Childhood Irritable Bowel Syndrome Characteristics Are Related to Both Sex and Pubertal Development

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Objective To determine the relationship of both pubertal development and sex to childhood irritable bowel syndrome (IBS) clinical characteristics including gastrointestinal symptoms (eg, abdominal pain) and psychological factors.

Study design Cross-sectional study with children ages 7-17 years (n = 143) with a pediatric Rome III IBS diagnosis recruited from both primary and tertiary clinics between January 2009 and January 2014. Subjects completed 14-day prospective pain and stool diaries, as well as validated questionnaires assessing several psychological factors (somatization, depression, anxiety) and Tanner stage. Stool form ratings were completed using the Bristol Stool Form Scale.

Results Girls with higher Tanner scores (more mature pubertal development) had both decreased pain severity and pain interference; in contrast, boys with higher Tanner scores had both increasing pain severity ($\beta = 0.40$, $P = .02$) and pain interference ($\beta = 0.16$, $P = .02$). Girls (vs boys), irrespective of pubertal status, had both increased somatic complaints ($P = .005$) and a higher percentage ($P = .01$) of hard (Bristol Stool Form Scale type 1 or 2) stools. Pubertal status and sex did not significantly relate to IBS subtype, pain frequency, stooling frequency, anxiety, or depression.

Conclusions In children with IBS, both pubertal development and/or sex are associated with abdominal pain severity, stool form, and somatization. These differences provide insight into the role of pubertal maturation during the transition from childhood to adult IBS. *(J Pediatr 2017;180:141-7).*

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Irritable bowel syndrome (IBS) is highly prevalent in both children and adults throughout the world. Large school and community-based studies identify IBS-type symptoms in 8%-25% of children and up to 20% of adults.[1-5] Up to 66% of children with IBS will transition to have adult IBS.[6-10]

Despite both its worldwide prevalence and impact, the differences in childhood IBS phenotype at various pubertal developmental stages is poorly characterized. Both IBS gastrointestinal symptoms and psychological characteristics have been evaluated in children of various ages using school- and/or community-based questionnaires without attention to developmental pubertal stage.[1-3] These data may be unreliable as questionnaire-based recall differ significantly vs prospective diaries.[11,12] The lack of knowledge as to whether pubertal development affects IBS clinical presentation represents a barrier to efforts aimed at halting the transition from childhood to adult IBS.

Sex may also play a role in the transition from childhood IBS to adult IBS. Children with IBS have different sex-specific physiological responses.[13] Though at times conflicting, several studies have identified several sex-based differences in adult IBS gastrointestinal symptoms and psychological factors.[14] Therefore, elucidating the relationship of both pubertal stage and sex in childhood IBS may provide insight into the common progression of pediatric to adult IBS.[15] Given this, the objective of our study was to determine the relationship of both pubertal development and sex to childhood IBS clinical characteristics including gastrointestinal symptoms (eg, abdominal pain) and psychological factors (eg, depression).

Methods

Children ages 7-17 years included in this study were part of larger, prospective studies in children with functional gastrointestinal disorders. Only data prior to any intervention were used. The data were captured between January 2009 and January 2014. All recruitment and study procedures were reviewed and

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approved by the Baylor College of Medicine Institutional Review Board. Informed consent was obtained from the parent and assent from the child.

Participants were identified by medical chart review based on the *International Classification of Diseases, Ninth Revision* codes of 789.0 (abdominal pain) or 564.1 (irritable bowel syndrome) from a large academic pediatric gastroenterology practice and general pediatrician offices within the same affiliated hospital system.

Children were excluded if chart review or phone screening identified: an organic gastrointestinal illness; a co-occurring significant chronic health condition; vomiting ≥2 times a month for the preceding 3 months; unexplained weight loss; blood in stool; current use of any medication that completely alleviated the pain; lack of fluency in English (as some of the questionnaires are only available in English); and significant developmental delay (preventing questionnaire or diary completion). Participants were included in the study if they qualified as having IBS using Pediatric Rome III criteria by phone screening using a modification of the Pediatric Rome III questionnaire.[16] The modification asked about presence or absence of symptoms rather than the percentage of time the symptom occurred.

Pain and Stool Diaries

Children completed 14-day pain and stool diaries as we have described previously.[17] Parents were instructed only to remind children to complete the diaries, and children were instructed to record the data without parental influence. Children rated their pain 3 times a day using a 0-10 scale anchored with the phrases "no pain at all" and "the worst pain you can imagine." Mean pain severity was defined as each child's average pain severity for intervals when pain was present over the course of 2 weeks. Pain frequency was defined as the number of pain episodes a child reported over the 2-week period. With each rating, degree of interference with activities because of pain was rated on a 4-point scale (0 = no interference; 1 = a little interference; 2 = a lot of interference; 3 = could not participate because of pain), and the mean of the interference ratings during pain episodes was calculated.[17] Children were instructed to call in their responses to a dedicated phone line linked to a computerized database at the end of each day. Research coordinators contacted the family for any missing entries.

Stool frequency and stool form were recorded using the Bristol Stool Form Scale; constipated stools were classified as stool form types 1 or 2 and diarrheal stools were classified as types 6 or 7.[18] Mean stool frequency per day and stool form percentages for constipation and diarrhea over the 14 days were calculated for each participant. IBS subtypes were determined based on stool form as per Rome III criteria.[19]

Children were shown sex appropriate Tanner staging drawings and asked to choose the representation that best matched their own bodies.[20] The self-report staging drawings consist of 2 pictures: for girls, 1 picture depicting breast development and 1 depicting pubic hair growth; for boys, 1 picture depicting genital size and 1 depicting pubic hair growth.[20] The 2 ratings were averaged for each participant.[20] Tanner self-assessment ratings of pubertal status have been shown to correlate well with physical examination by physicians.[21-24] In addition self-assessment ratings of pubertal status have been reported to correlate with hormonal markers of pubertal development.[20]

The Children's Somatization Inventory was used to assess somatic symptoms in children.[25] The child rates the degree to which each of 35 symptoms bothered him/her in the past 2 weeks on a 5-point scale ("not at all" to "a whole lot"). Total scores are calculated by summing the values for each item.

The Behavior Assessment System for Children-Second Edition is a psychometrically robust instrument used to measure a range of behavioral and emotional problems in children.[26] This study used T scores on the anxiety and depression scales from the child self-report forms.

Data Analyses

IBM SPSS Statistics v 23, 2015 (IBM Corporation, Armonk, New York) was used for statistical analysis. Generalized linear models were used to evaluate the degree to which both Tanner stage and sex predicted pain, stooling, somatization, and psychological factors. Tanner stage and sex main effects were included in the same step along with the interaction of the 2 variables. With each regression analysis, potential interactions between independent variables were evaluated. If a statistically significant ($P < .05$) interaction effect was not identified, the interaction evaluation was removed from the model, and the main effects of each independent variable were assessed. A χ^2 analysis was performed to evaluate the relationship between sex and IBS bowel pattern subtype. A Kruskal-Wallis test was used to assess the relationship between IBS subtypes and Tanner stage. Data are presented as mean ± SD.

Results

A total of 143 participants were included in the study; the mean age was 12.9 ± 2.8 (SD) years. Demographic and pubertal stage classification breakdown is listed in the **Table** (available at www.jpeds.com). No statistically significant demographic differences were found between boys and girls. As expected, pubertal stage and age were highly but not completely correlated ($r = 0.77$, $P < .001$).

Prediction of Abdominal Pain Characteristics by Sex and Pubertal Status

There was no difference within the studied population with respect to the sex distribution across Tanner stages (t [1,141] = −1.646, $P = .15$). When evaluating pain severity, a significant interaction between pubertal stage and sex emerged ($\beta = 0.40$, CI 95% 0.07-0.72, $P = .02$; **Figure 1**). Girls with higher Tanner scores (more pubertal development) had lower pain severity, and boys with higher Tanner scores had increased pain severity. There was no interaction or identified independent relationship between pain frequency and either pubertal stage or sex.

When evaluating the degree of interference with activities because of pain, there was also a similar significant interaction between pubertal stage and sex ($\beta = 0.16$, CI 95%