Abdominal Pain and Health Related Quality of Life in Pediatric Inflammatory Bowel Disease

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Objective To summarize rates of abdominal pain in pediatric inflammatory bowel disease, and to examine associations of abdominal pain, disease activity, and health-related quality of life (HRQoL). Methods 44 youths aged 11–18 years completed ratings of abdominal pain, whereas youths and mothers provided ratings of HRQoL at Time 1 (T1) and Time 2 (T2; 6 months later). Disease activity was rated by physicians at T1. Results At T1, 55% of participants reported pain in the past week, with most in clinical remission. Approximately one-third reported abdominal pain at neither (absent), either (transient), or both (chronic) T1 and T2, respectively. T1 abdominal pain did not contribute significant variance to T1 HRQoL beyond disease activity. However, pain group uniquely predicted T2 HRQoL, with chronic abdominal pain associated with lower HRQoL. Conclusions Abdominal pain is prevalent in pediatric inflammatory bowel disease, even during clinical remission. Interventions to address abdominal pain also may enhance HRQoL.

Key words inflammatory bowel disease; pain; quality of life.

Inflammatory bowel disease (IBD) is a chronic relapsing condition of the gastrointestinal (GI) tract comprising Crohn’s disease, ulcerative colitis, and indeterminate colitis. Frequently diagnosed before age 18, IBD affects approximately 71 in 100,000 youths (Kapplman et al., 2007). IBD is characterized by chronic inflammation of the GI tract caused by an abnormal immune system response. IBD treatment focuses primarily on immunosuppression to reduce inflammation and induce remission, with additional adjunctive treatment as needed to address associated symptoms. IBD is unpredictable both across and within individuals. Some experience frequent relapses, others prolonged periods of remission, and some only sporadic relapses (Markowitz, 2008). Common symptoms of IBD include persistent diarrhea, fever, and rectal bleeding, along with loss of appetite, weight loss, and growth delay. Abdominal pain may occur as an associated symptom of inflammation in the GI tract in IBD, short-term sequelae of IBD-related procedures, and/or a side effect of treatment (Banez & Cunningham, 2003). Moreover, abdominal pain may occur in the absence of disease activity from the sensitization of sensory pathways during inflammation that leads to enduring changes in afferent neurons and central nervous system pain processing (Bielefeldt, Davis, & Binion, 2009).

Despite the multiple possible causes of abdominal pain in pediatric IBD, surprisingly little is known about the prevalence and frequency of persistent abdominal pain in this group. Crandall, Halterman, and Mackner (2007) examined abdominal pain duration among a group of 20 youths with IBD presenting for a first-time colonoscopy, all of whom endorsed pain. They found an
average abdominal pain duration leading up to diagnosis of 11.8 weeks (SD = 14.24 weeks, range = 0–52 weeks). Data obtained via medical chart review from adults with IBD suggests that 50–70% experience abdominal pain at the time of diagnosis or during disease flares, whereas 20% experience abdominal pain even in the context of disease remission (Biefeleldt, et al., 2009). The pattern of persistent abdominal pain during disease remission appears similar in pediatrics. In a cross-sectional study of 301 youths aged 9–17 years with Crohn’s disease, 46% reported abdominal pain (Srinath et al., 2010). Of those with abdominal pain, the majority was in remission; further, 23% met criteria for functional abdominal pain, indicating pain duration of at least eight weeks (Zimmerman et al., 2010).

Although the few studies cited earlier suggest that abdominal pain may be a common problem in IBD populations, our understanding of which subgroups of youths may be at particular risk for experiencing abdominal pain is limited. For example, youths with disease activity would presumably be at a greater risk of experiencing abdominal pain than those in clinical remission, as abdominal pain often is associated with disease flares. Similarly, girls may be more at risk for pain than boys, based on the pattern found in other pediatric conditions (Perquin et al., 2000), but this has not yet been established in IBD. Further, the extent to which youths experience intermittent versus chronic pain in the context of IBD and the implications of persistent pain for health-related quality of life (HRQoL) has not yet been examined in this group. A more complete understanding of the prevalence, frequency, and severity of abdominal pain in the context of pediatric IBD is important, given that ongoing pain has been associated with significant disability and impaired HRQoL among other pediatric chronic illnesses groups (Kashikar-Zuck, Goldschneider, Powers, Vaught, & Hershey, 2001; Palermo, Harrison, & Koh, 2006; Panepinto, O’Mahar, Debaun, Loberiza, & Scott, 2005; Sawyer et al., 2004). Furthermore, attention to abdominal pain among adolescent patients may be of particular value, given the potential for disease symptoms to interfere with achievement of key developmental milestones related to social functioning and autonomy development in this group (Williams, Holmbeck, & Greenley, 2002).

Broadly, HRQoL of youths with IBD is generally poorer than that of healthy youths, although comparable with youths with other chronic conditions (Greenley et al., 2010) Youths with IBD may be at particular risk for HRQoL deficits in the school functioning domain (Kunz, Hommel, & Greenley, 2010). Among youths with IBD, there is evidence to suggest that disease factors (e.g., greater disease activity) may contribute to poorer HRQoL (Hommel, Densone, & Baldassano, 2011; Perrin et al., 2008). However, no research has explicitly examined cross-sectional or longitudinal associations between abdominal pain and HRQoL in pediatric IBD. This seems an important omission, given that abdominal pain has been associated with impaired HRQoL in other pediatric chronic conditions (Palermo, et al., 2006; Panepinto, et al., 2005; Sawyer et al., 2004), and insight into such relationships in pediatric IBD may help to inform efforts to enhance HRQoL in this at-risk group. Among adults with IBD, data support links between pain and psychosocial functioning deficits (Palm, Berndt, Moum, & Gran, 2005; Schirbel et al., 2010), but the focus of this research has been broad and not limited to abdominal pain.

Thus, although the existing literature is informative in several respects, it remains limited. It is important that we understand the prevalence and sequelae of abdominal pain in pediatric IBD for several reasons. Understanding whether demographic factors (e.g., gender, age) are related to abdominal pain may help to identify at-risk subgroups. Moreover, knowledge about abdominal pain that exists in the presence or absence of disease activity has value in determining at what point(s) in the disease process one should focus pain assessment and intervention efforts. Finally, to the extent that abdominal pain is related to HRQoL, effective pain management may have broad implications for promoting healthy physical and psychosocial functioning over the lifespan (Kashikar-Zuck, et al., 2001). Thus, the aims of the current study are to: (1) summarize rates of abdominal pain at two separate intervals (i.e., baseline and 6-month follow-up); (2) determine whether abdominal pain rates vary based on gender or age; (3) examine the unique contribution of transient and more chronic abdominal pain to youth HRQoL after accounting for the impact of disease activity; and (4) determine whether the proportion of youths with clinically significant impairments in HRQoL differs depending on whether abdominal pain is absent, transient, or chronic. It was hypothesized that: (1) abdominal pain would be prevalent cross-sectionally, affecting approximately 50% of youths at each time point, and would occur with equal frequency among those with and without disease activity (Srinath et al., 2010); (2) abdominal pain would occur more frequently among girls than boys; (3) abdominal pain would be uniquely associated with poorer HRQoL both cross-sectionally and longitudinally; and (4) youths with any abdominal pain during the study period would be overrepresented among those with clinically significant impairments in HRQoL, with the greatest impairment among those with chronic pain, followed by the transient pain group.
Method
Procedure
Participants were recruited in Gastroenterology Clinics of two Midwestern Tertiary Care Children’s Hospitals. After providing informed consent or assent, families completed a set of baseline questionnaires (Time 1; T1) assessing HRQoL and abdominal pain. Questionnaires were completed again via mail at approximately 6 months post recruitment (Time 2; T2). Data for the current manuscript were drawn from a larger longitudinal study that aimed to examine predictors of oral medication adherence in youths with IBD. Youths were eligible for participation if they were (1) 11–18 years old; (2) English speaking; (3) able to read and understand study questionnaires; (4) accompanied by an English-speaking parent or guardian who was willing to participate; (5) diagnosed with IBD based on medical record confirmation; (6) prescribed an oral thiopurine for IBD treatment for a period of at least three months immediately preceding recruitment; and (7) willing to use a Medication Events Monitoring System (MEMS) cap electronic monitor for their thiopurine medication. Inclusion criteria 1, 6, and 7 related to the broader aim of the study, namely, examining oral medication adherence among adolescents, a group known to be at high risk for nonadherence (Rapoff, 2010; Williams et al., 2002). These criteria also served to exclude youths who had just begun treatment and could not yet be expected to have achieved disease remission.

Participants
Fifty-two of 59 families (86%) consented to participate. Seven declined participation (citing being too busy or a desire to continue to use a weekly pill box for medication rather than switch to the MEMS cap). Of the 52 who consented, 44 completed study procedures (85%); four withdrew from the study citing they were “too busy” to complete study tasks, and four became ineligible when they were discontinued from their oral IBD maintenance medication by their physician. Study completers (n = 44) were demographically similar to noncompleters (n = 15) in patient age [t(57) = −0.323, p = .748] and sex (Φ = 0.087, p = .503). Participants ranged in age from 11 to 18 years (M = 14.84, SD = 2.17). Slightly more males (n = 25; 57%) than females participated. Youths were primarily Caucasian (n = 41; 93%), with fewer youths of African American (n = 1; 2%), Asian (n = 1; 2%) or biracial (n = 1; 2%) ethnicities. Median annual family income fell in the $100,000–$119,999 category. All participating caregivers were biological mothers. See Table 1 for additional descriptive information about the sample.

Measures
Demographics
Mothers provided demographic information for the patient, including age, sex, and ethnicity, as well as information about household income, using a questionnaire developed for the study.

Disease Information
Disease information was abstracted from the patient’s medical record, including diagnosis, date of diagnosis, and a physician rating of clinical disease activity at T1 using the Physician Global Assessment (PGA) scale (Hanauer et al., 1993). PGA ratings were unavailable at T2 because T2 data collection did not coincide with clinic visits during which physicians could perform an examination and provide PGA ratings. The PGA is a global assessment of patient disease activity, in which patients are assigned a rating of no disease activity/clinical remission, mild disease activity, moderate disease activity, or severe disease activity. It correlates highly with more complex measures of disease status, including the Pediatric Crohn’s Disease Activity Index (Hyams et al., 1991). In the current study, disease activity was categorized as “no active disease” or “active disease” (a rating of mild, moderate, or severe) for regression analyses, given the significant skew of the distribution.

Abdominal Pain
Youths provided ratings of abdominal pain in the past 1 week at T1 and T2 using a 4-point Likert scale (i.e., none, mild, moderate, or severe) developed for this study. In cross-sectional analyses, participant’s T1 pain ratings were dichotomized into “no pain” (a rating of none) or “pain” (a rating of mild, moderate, or severe) groups, given the significant skew of the distribution. In longitudinal analyses, participants’ pain ratings across T1 and T2 were categorized as absent (no pain at either time point), transient pain (pain reported at 1 time point), or chronic pain (pain reported at both T1 and T2).

Health-Related Quality of Life
Youths completed age-appropriate versions the PedsQL 4.0 Generic Core Scales (Varni, Seid, & Kurtin, 2001), a 23-item measure of youth HRQoL at T1 and T2. Mothers completed a parallel parent-proxy report. Respondents rate on a 5-point scale, the extent to which each issue has been a problem for the youths during the past 1 month. Raw scores are reverse coded and linearly transformed to a 0–100 scale with higher scores reflecting better HRQoL. The Total Score, which consists of the average of all 23 items, was used in the present study. Internal consistency reliabilities for the current study were 0.87 and
0.92 for child and maternal-proxy report of the Total Scores, respectively.

**Data Analytic Plan**

The prevalence and severity of T1 abdominal pain, the proportion of participants reporting pain with and without active disease, and the extent to which abdominal pain persisted over time were evaluated with descriptive statistics. Independent samples \( t \)-tests or \( \chi^2 \) analyses examined links between demographics and T1 abdominal pain.

Hierarchical multiple regressions were used to examine differences in Total HRQoL as a function of disease activity and abdominal pain. Cross-sectional analyses were conducted as follows: T1 disease activity (coded dichotomously as present or absent) was entered in the first block, and T1 abdominal pain (coded dichotomously as present or absent) was entered in the second block. The dependent variable was T1 Total HRQoL. For longitudinal analyses, a similar strategy was used, with T2 Total HRQoL as the dependent variable in hierarchical multiple regressions. T1 disease activity (coded dichotomously) was entered in the first block, whereas two dummy variables were included in block two to represent the three pain group categories: (1) absent, (2) transient, and (3) chronic. Dummy variables were coded such that the reference group was the chronic pain group.

For cross-sectional and longitudinal analyses, the squared semi partial correlation was the effect size index for individual variables, whereas Multiple \( R^2 \) was the effect size index for the full model. For longitudinal models, the \( \Delta R^2 \) of step 2 represented the unique contribution of pain on the given dependent variable. All effect sizes were interpreted as follows: 0.01 = small effect, 0.09 = medium effect, 0.25 = large effect (Cohen, 1988). Effect size estimates were emphasized over results of statistical significance tests, given that the study had >80% power to detect a medium effect with a sample size of 44. An \( n = 76 \) is required to ensure 80% power with \( \alpha = 0.05 \) and three independent variables in the regression model. Of note, this study was adequately powered to detect a large effect (i.e., required \( n = 34 \) with \( \alpha = 0.05 \) and three independent variables). For all analyses, regressions were conducted separately for child report (CR) and maternal-proxy report (MR) Total HRQoL.

Analysis of the presence of clinically significant impairments in MR T2 Total HRQoL was conducted using the cutoff scores established by Huang et al. (2009). The focus was limited to MR Total HRQoL because published cutoffs exist only for this version of the scale. The percentage of youths with (Total HRQoL score \( \leq 78 \)) or without (Total HRQoL score \( >78 \)) clinically significant impairment for each of the pain conditions (i.e., absent, transient, chronic) was calculated, and we examined whether the frequency of clinical impairments in HRQoL differed by pain group with \( \chi^2 \) analysis, using Cramer’s V as a measure of effect size.

**Results**

**Prevalence and Severity of Abdominal Pain at T1**

At T1, 55% of youths (\( n = 24 \)) reported some abdominal pain in the past week. Of those with abdominal pain, 92% (\( n = 22 \)) had mild pain, and 8% (\( n = 2 \)) had moderate pain. Of the 24 participants with abdominal pain at T1, 13 had no disease activity, eight had mild, and three had moderate
disease activity. Thus, over half (54%) of those with T1 abdominal pain were in clinical remission. Additionally, all participants with disease activity at T1 reported the presence of T1 abdominal pain. Of the 11 participants with T1 disease activity, 10 reported mild pain and one reported moderate pain. Of the 13 participants in clinical remission, 12 had mild pain and one reported moderate pain, a pain intensity distribution comparable with those with active disease.

**Differences in Abdominal Pain at T1 as a Function of Demographic Factors**

Consistent with prediction, a greater proportion of females experienced T1 abdominal pain (74%; n = 14/19) than males (40%; n = 10/25; Φ = 0.34, p = .026). Age was not significantly associated with T1 abdominal pain (r = .12, p = .423).

**Stability of Abdominal Pain From T1 to T2**

At T2, 39% of youths (n = 17) reported abdominal pain in the past week. Seventy-one percent (n = 12) of those with abdominal pain reported mild pain, 24% (n = 4) reported moderate pain, and 6% (n = 1) reported severe pain. Thirty percent (n = 13) reported chronic abdominal pain (i.e., pain at both T1 and T2), 34% reported transient abdominal pain (n = 15; n_{T1} = 11, n_{T2} = 4), and 36% (n = 16) endorsed no abdominal pain at either T1 or T2.

**Abdominal Pain and HRQoL at T1**

In cross-sectional analyses, T1 disease activity accounted for 19% of the variance in the T1 CR Total HRQoL, a statistically significant amount and the equivalent of a medium effect size (see Table II). Similarly, T1 disease activity accounted for 43% of the variance in T1 MR Total HRQoL, a statistically significant amount and a large effect size (see Table III). T1 abdominal pain failed to predict significant variance beyond that accounted for by T1 disease activity, with small effect sizes ranging from 0.03 to 0.05 (see Table III).

**Abdominal Pain and HRQoL at T2**

T1 disease activity failed to consistently account for significant variance at step 1 in the prediction of T2 CR or MR Total HRQoL outcomes. Effect sizes were 0.001 and 0.08 for MR and CR, respectively, neither of which exceeded a small effect size (see Table IV). In contrast, pain group classification (chronic, transient, or absent pain) contributed a significant proportion of variance to T2 HRQoL in both CR and MR analyses, with effect sizes of medium magnitude in both cases [CR Total HRQoL: ΔR² = 0.23; ΔF(2, 40) = 6.77, p = .003; MR Total T2 HRQoL: ΔR² = 0.15; ΔF(2, 37) = 3.33, p = .047; See Table IV].

Differences between the chronic, transient, and absent pain groups were further examined via analysis of the dummy-coded pain variable beta weights and associated t statistics (see Table III). Specifically, because the first dummy-coded variable (i.e., Dummy Pain 1) compares the transient pain group with the chronic pain group (see Data Analytic Plan section for details about the dummy coding system), a positive beta value for this variable reflects higher HRQoL for the transient pain group compared with the chronic pain group. Similarly, because the second dummy-coded variable (i.e., Dummy Pain 2) compares the absent pain group with the chronic pain group, a positive beta value for this variable reflects higher HRQoL for the absent pain group compared with the chronic pain group. Thus, examination of beta weights (see Table IV) showed that T2 CR Total HRQoL was significantly higher for the transient group compared with the chronic pain group. In addition, T2 Total HRQoL was significantly higher for the absent pain group compared with the chronic pain group for both child and maternal reports (see Table IV).
Clinical Significance of HRQoL Findings

Using the Huang criteria (Huang et al., 2009), we categorized youths in each of the three pain groups into a clinical impairment group (score of ≤ 78) or a no impairment group (score > 78) based on their MR T2 Total HRQoL scores. Results suggested a medium effect size Cramér’s $V (1) = 0.31$ (Cohen, 1988) that failed to reach statistical significance, given the small $n$ ($\chi^2(2) = 4.09$, $p = .130$). Overall, 21% had clinically significant impairments in MR T2 Total HRQoL scores. Of those with clinically significant impairments, 55% had chronic pain, 22% had transient pain, and 22% had absent pain, suggesting that the chronic pain group was overrepresented among those with clinically significant impairments in T2 HRQoL.

Discussion

The current findings suggest that abdominal pain is prevalent in pediatric IBD. Consistent with our hypotheses, a prevalence of approximately 50% was found for abdominal pain at a single point in time (T1). Although this might be expected for those with active disease, this held true even among those with clinical remission of symptoms, with youths reporting current abdominal pain split evenly between those with active disease and those deemed to be in clinical remission. As expected, girls were more likely to report abdominal pain than boys, whereas no differences in abdominal pain prevalence were documented as a function of age. This information has potential utility in defining the scope of the issue, as well as in identifying specific at-risk subgroups.

Beyond the issue of prevalence, results of the present investigation suggest that abdominal pain does in fact have a significant negative impact on HRQoL. Further, the relationship between abdominal pain and HRQoL differs depending on whether that pain is transient or chronic. Although the presence or absence of abdominal pain at an isolated time point (T1) failed to explain variance in HRQoL after accounting for the impact of concurrent...
disease activity, pain group classification contributed significant variance to later (T2) HRQoL. In general, youths with pain at both T1 and T2 had lower HRQoL than those with pain at neither T1 nor T2, and lower CR HRQoL than those with pain at only one time point. Moreover, youths with chronic pain were overrepresented in the clinically impaired HRQoL groups compared with youths absent of pain or youths with transient pain. However, data on disease activity at T2 were not available. Controlling for T2 disease activity may have lead to a reduced impact of pain group on T2 HRQoL, given cross-sectional findings, which show strong concurrent relationships between disease activity and HRQoL at T1.

Thus, not only is abdominal pain associated with poorer HRQoL but also in a subset of youths who experience chronic pain; their HRQoL is impaired to a clinically significant degree. These findings, indicating a meaningful relationship between chronic pain and diminished HRQoL, are consistent with research in other pediatric populations, such as youths with cystic fibrosis, juvenile idiopathic arthritis, and sickle cell disease (Palermo et al., 2006; Panepinto et al., 2005; Sawyer et al., 2004). Taken together, findings suggest that abdominal pain is an important issue in terms of clinical patient management for youths with IBD. These findings are particularly important in light of our focus on youths aged 11–18 years. For youths with chronic illnesses such as IBD, key developmental tasks of adolescence include developing a greater sense of autonomy from parents and learning key self-management skills to facilitate successful transition to adulthood (Williams et al., 2002). The presence of abdominal pain has the potential to disrupt such developmental processes and as such, may pose unique risks for this age-group.

Although these findings contribute to our understanding of the prevalence of abdominal pain among youths with IBD and the impact of such pain on HRQoL, the study is not without limitations. The current sample was underpowered, necessitating a relatively greater focus on effect size analyses rather than traditional statistical significance tests. Moreover, although representative of the clinic demographics of the recruitment sites, the sample was limited in ethnic and socioeconomic diversity. Additionally, data for this manuscript were drawn from a larger study that focused on adolescents and required youths to have been on an oral maintenance medication for at least three months. Thus, youths on other forms of treatment and those who had just begun treatment were excluded, limiting the generalizability of our findings to these groups. Overall, these limitations argue for replication with other samples to ensure that findings are not idiosyncratic to this sample. However, the fact that current findings are in line with the limited previous data from IBD populations (Srinath et al., 2010), as well as from other pediatric chronic conditions (Kashikar-Zuck et al., 2001; Palermo et al., 2006; Panepinto et al., 2005; Sawyer et al., 2004), provides some interim support for the validity of current findings. Furthermore, our method of abdominal pain assessment was broad and did not allow for application of the Rome III criteria for diagnosis of functional abdominal pain (Rasquin et al., 2006) to categorize the subgroup of youths with chronic pain identified in this study. This would be particularly relevant for youths deemed to be in clinical remission, as abdominal pain existing outside of disease activity may be functional in nature and may require a different type of treatment. With new awareness that abdominal pain is common during clinical remission, future work should endeavor to better define the specific location, frequency, duration, and chronicity of this pain, with an eye toward intervention efforts to minimize chronic abdominal pain across the disease process and enhance HRQoL in youths with IBD.

Beyond addressing the limitations of the current study, it may be of value for future research to examine additional predictors of pain among youths with IBD beyond the demographic factors evaluated in this study. Among other pediatric pain populations, parental modeling, solicitousness, and reinforcement of pain behaviors have been associated with increased pain, as has family dysfunction (Palermo & Chambers, 2005). Additionally, youth-perceived stress and internalizing symptoms also predict higher levels of pain in other pediatric populations (Stanford, Chambers, Biesanz, & Chen, 2008; Varni et al. 1996). Future examination of the extent to which these variables influence the experience of pain in youths with IBD may be of value in further defining at-risk subgroups and in identifying associated treatment targets. Moreover, building on the current results, future research that examines interactions between (rather than main effects of) pain and other known correlates of youth HRQoL would be of value. For example, drawing from Wallander & Varni’s (1992) risk and resilience model, relevant domains for future study may include assessment of interactions between pain and intrapersonal factors (e.g., self-efficacy), socio-ecological factors (e.g., family environment), and stress-processing skills (e.g., coping strategies) in predicting HRQoL. Finally, examining how the presence of abdominal pain may disrupt attainment of key developmental milestones and self-management skills in this group may also be of value.

In sum, the current findings have several implications for clinical practice. The combined prevalence and impact...
of abdominal pain in pediatric IBD suggest that routine screening for abdominal pain is warranted, even for youths in clinical remission. Youths with enduring abdominal pain, even mild, may benefit from interventions to help reduce pain and/or more directly enhance their HRQoL. Adequate identification and management of abdominal pain in those youths with and without active disease has the potential to enhance their HRQoL.

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