Impaired Health-Related Quality of Life in Brazilian Children with Chronic Abdominal Pain: A Cross-Sectional Study

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ABSTRACT

Purpose: We compared the health-related quality of life (HRQOL) of children and adolescents with functional abdominal pain disorders (FAPDs) and organic abdominal pain disorders (ORGDs).

Methods: This was a single-center, cross-sectional, observational study. The PedsQL 4.0 generic cores scales parent proxy-report was administered to parents/caregivers of 130 and 56 pediatric patients with FAPDs and ORGDs respectively on their first visit. The self-reported pain intensity in the patients was assessed using a visual analog scale (VAS) and facial affective scale (FAS).

Results: Irritable bowel syndrome was the most prevalent FAPDs, and the most prevalent ORGDs were reflux esophagitis (41.1%) and gastritis associated with Helicobacter pylori (21.4%). There was no difference in HRQOL among patients diagnosed with ORGDs and FAPDs (p>0.05). Patients with ORGDs and FAPDs had lower HRQOL Scale scores than healthy Brazilian and American children’s references, with a high proportion of children at risk for impaired HRQOL (p<0.0001). There was no difference in the VAS and the FAS scores between the ORGDs and the FAPDs. FAPDs had a higher prevalence of girls’ and couples’ disagreement (p<0.02), although poor school performance (p<0.0007) and bullying (p<0.01) were higher in patients with ORGD.

Conclusion: This study revealed that there was a difference in impaired HRQOL between patients with ORGDs and FAPDs. Thus, considering the high prevalence of chronic abdominal pain in children, a well-founded treatment plan is necessary for a multidisciplinary cognitive-behavioral Pain management program.

Keywords: Abdominal pain; Functional gastrointestinal disorders; Quality of life; Helicobacter pylori; Pain measurement; Reflux esophagitis

INTRODUCTION

Chronic abdominal pain (CAP) is defined according to the American Academy of Pediatrics as long-lasting intermittent or constant abdominal pain that is functional or organic
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[1] and is a common clinical condition in children and adolescents. A meta-analysis of epidemiological studies on abdominal pain from 1957 to 2014 reported a global pooled prevalence of 13.5% [2]. Most children and adolescents (almost 90%) who seek healthcare advice for CAP suffer from functional abdominal pain disorders (FAPDs) [3]. The diagnostic criteria for these disorders comprise four conditions: irritable bowel syndrome, abdominal migraine, functional dyspepsia, and functional abdominal pain-not otherwise specified [4]. On the other hand, reflux esophagitis and non-ulcer dyspepsia caused by *Helicobacter pylori* are common causes of organic chronic abdominal pain (ORGDs) as well as in our pediatric gastroenterology outpatient clinic [5,6].

CAP is a serious problem for children and their families. In daily clinical practice, children with chronic pain experience increased psychological distress and reduced health-related quality of life (HRQOL) [7,8]. CAP is intensely impaired, places a heavy psychosocial burden on children, and is commonly associated with parental stress [9-11]. Furthermore, it is associated with high economic costs owing to increased healthcare utilization [12,13].

Calvano and Warschburger [14] reported that parents’ perception of pain influences healthcare-seeking and the number of medical visits for childhood CAP. Consequently, a study comparing the HRQOL between FAPDs and ORGDs using parent reports would be valuable in assessing children with CAP. To date, three studies have compared the HRQOL of children with FAPDs and ORGDs [11,15,16].

This study aimed to evaluate HRQOL in children and adolescents with CAP using the PedsQL 4.0 generic cores scales parent proxy-report, comparing FAPDs and ORGDs HRQOL scores to healthy children, FAPDs and ORGDs HRQOL scores with one another, and to analyze the association of HRQOL with demographics, anthropometric, and clinical variables.

**MATERIALS AND METHODS**

**Study design, setting and selection of participants**

This single-center, observational, cross-sectional study included a convenience sample of consecutive children/adolescents referred from July 2018 to December 2019 for initial evaluation of CAP at the outpatient pediatric gastroenterology clinic of Botucatu Medical School, Botucatu, São Paulo, Brazil. All children and adolescents were in the same geographic area and had good education, food, and general health conditions. The inclusion criteria were defined as CAP according to Apley and Naish [17] and Di Lorenzo et al. [18], age between 5-18 years; and living with the parent or caregiver. The exclusion criteria were underlying chronic disorders (genetic, metabolic, immune, cardiac, hepatic, or renal diseases), neurodevelopmental delay, previous surgery, and inability to self-report pain. This study was approved by the medical and Institutional Review Board (CAAE 05721218.3.0000.5411). Written parental informed consent and child assent (when age was appropriate) were obtained during the first visit.

**Data collection**

Questionnaires were administered to pediatric patients and their parents in a private room at the clinic before their medical evaluation. Data collection was based on a standardized form developed according to the Rome IV diagnostic questionnaire for pediatric functional gastrointestinal disorders and included demographics, gastrointestinal symptoms,
gastrointestinal symptoms, and alarm symptoms and signs. Anthropometric measurements
of body weight (kg) and height (cm) were obtained at the initial visit according to the World
Health Organization guidelines by experienced pediatric nurses [19]. The body mass index
(BMI, kg/m²) and z-scores were evaluated [20].

**Pain intensity**

The patients' self-reported pain intensity was assessed using the visual analog scale (VAS)
[21] and Facial Affective Scale (FAS) [22], each on one side of a sheet. Children were inquired
to mark the “Pain over the past month” [23] that appears similar when they have pain. The
numerical values for faces vary from 0.4 to 9.7. The pain intensity was adjusted in the FAS and
VAS on a 0–10 numeric scale [24].

**Diagnosis of chronic abdominal pain**

Complete blood cell count, C-reactive protein level, urinalysis, stool for ova and parasites,
and *H. pylori* serology were performed for all patients. The diagnosis of CAP of organic origin
was based on diagnostic testing performed at the gastroenterology team’s discretion. The
routine diagnosis of esophagitis and *H. pylori* gastritis has been described elsewhere [6].

Briefly, all children and adolescents with chronic dyspeptic syndrome underwent
esophagogastroduodenoscopy. Non-ulcer dyspepsia associated with *H. pylori* was diagnosed
if both a positive rapid urease test and the presence of the bacterium on histological
examination were present. Dyspepsia associated with chronic esophagitis was based on
clinical symptoms/signs, endoscopy [25], and histologic evaluation [26]. Diagnosis of lactose
intolerance was based on hydrogen breath tests, and diagnosis of FAPDs was based on the
Rome IV criteria [4]. The final diagnosis was determined after three months of follow-up by
two experienced pediatric gastroenterologists (MAC and NCM).

**HRQOL evaluation: PedsQL 4.0 generic cores scales parent proxy-report**

PedsQL 4.0 generic cores scales parent proxy-report [27] age-appropriate (5–7 years, 8–12
years, and 13–18 years) was applied to assess parents’ perceptions of their child’s HRQOL. The
questions assessed how many problems each item experienced during the previous month.
This instrument was adapted cross-culturally and validated in a Brazilian Portuguese version
[28] and comprises four domains: physical functioning (8 items), emotional functioning
(5 items), social functioning (5 items), and school functioning (5 items). The total scale
score (23 items) was computed as the sum divided by the number of items answered on the
physical, emotional, social, and school functioning scales. Higher scores indicated better
HRQOL. The physical health summary score was the same as that of the physical functioning
scale. The Psychosocial Health Summary Score (15 items) was computed as the sum divided
by the number of items answered on the emotional, social, and school functioning scales.

Analysis of children's at-risk status for impaired HRQOL was established using the
percentage of children with <1 standard deviation below the media of reference healthy
Brazilian [28] and American children [8]. After the questionnaire ended, the researcher
checked and the respondent was requested to complete the questionnaire if there was an
omitted answer.

**Statistical analysis**

The analysis was performed using GraphPad Prism version 8.4.0 for Windows (GraphPad
Software, San Diego, CA, USA, www.graphpad.com). The normality of data distribution was
tested using the Shapiro-Wilk test. Categorical data were reported as counts and percentages and analyzed using Fisher's exact test. Continuous variables are expressed as means, standard deviations, and 95% confidence intervals of the mean. Independent t-tests and one-way ANOVA followed by Tukey's multiple comparisons test were used to compare the total scale score, physical health summary score, psychosocial health summary score, emotional functioning, social functioning, and school functioning with reference means and standard deviation of Brazilian [24] and American children [6]. Spearman's rank correlation was used to calculate associations between the total scale score of the PedsQL 4.0 generic cores scales parent proxy-report with demographic, anthropometric, and clinical variables. The correlation coefficients were designated as small (0.10–0.29), medium (0.30–0.49), and large (>0.50). The internal consistency reliability scale was determined by calculating the Cronbach's alpha coefficient [23]. All statistical tests were performed at a significance level of p<0.05.

RESULTS

Fig. 1 displays a flow diagram of children/adolescents with CAP assessed for eligibility, exclusion, and enrolment over 18 months. IBS was the most prevalent FAPDs (43.1%), and the most prevalent ORGDs were reflux esophagitis (41.1%) and gastritis associated with *H. pylori* (21.4%).

![Flow diagram](https://doi.org/10.5223/pghn.2022.25.6.500)
The baseline characteristics of the parents and children are presented in Table 1. Female sex (<0.02) and couple disagreement (<0.02) were higher in FAPDs than in ORGDs. In contrast, poor school performance (p < 0.0007) and bullying (p < 0.01) were more prevalent among ORGDs. Note that there was a long duration of symptoms before the first visit: organic (24.7 months) and functional (29.5 months), with no statistical difference. There was no difference in pain intensity between ORGDs and FAPDs for both the VAS and FAS scales. Children with ORGDs had higher BMI z-scores than those with FAPDs. The proportion of items with floor effects is low. However, the ceiling effect was high for the ORGDs and FAPDs groups. The Cronbach’s alpha coefficients showed excellent scale scores consistency, with values between 0.82 and 0.89 for Total Scale Score and all 23 Items of PedsQL 4.0 domains. There was no redundancy between the items as the values were less than 0.90.

Fig. 2 compares the total scale score, physical health summary score, and psychosocial health summary score of children with ORGDs and FAPDs with Brazilian and American healthy children’s references. In ORGDs and FAPDs, the scores were lower than those in healthy controls (p<0.0001). Conversely, there was no significant difference between children with ORGDs and FAPDs in the total scale, physical health summary, psychosocial health summary, emotional functioning, social functioning, and school functioning scores.
The percentage of children at risk of impaired HRQOL is shown in Fig. 3. Data were evaluated for the total scale, physical health summary, and psychosocial health summary scores. A high proportion of children were at risk for impaired HRQOL using the reference of healthy Brazilian children (−83–98%) and an intermediary proportion utilizing the healthy American reference (57–71%). In the ORGDs group, the correlation of the total scale score was negatively related to VAS ($p<0.01; r=-0.33$) and FAS ($p<0.04; r=-0.27$) with r-value medium and small, respectively. The correlations of the total scale score with the age of the children, duration of symptoms, and BMI z-score were not statistically significant for ORGDs and FAPDs.
DISCUSSION

This study evaluated the HRQOL of children and adolescents with ORGDs and FAPDs. The questionnaire was easily administered and was highly acceptable. According to the methodology of this study, there were no open items. The high values of Cronbach's alpha coefficient determine greater congruence and homogeneity in measuring HRQOL in children with ORGDs and FAPDs.

There were no differences in pain intensity, total scale score, physical health summary score, or psychosocial health summary score. Nevertheless, the scores were lower than those of the healthy Brazilian and American references. Consequently, the PedsQL 4.0 generic cores scales parent proxy-report is recommended for evaluating and comparing patients with organic and functional CAP.

The mother answered the PedsQL 4.0 generic cores scales parent proxy-report questionnaire in 88% of the cases. Since parents of children with CAP have higher anxiety, depression, or somatization than healthy controls [29,30], individually focused care planning must be offered for the dyad child-mother. The two groups demonstrated similarities in age at first visit, duration of symptoms, and housing and family characteristics. However, the pain characteristics were different, with no difference in pain intensity between the groups.

The first research question analysis suggested that ORGDs and FAPDs significantly affect HRQOL scores. There was a significant difference between children with CAP (ORGDs and FAPDs) and healthy Brazilian and American children. However, there was no difference in the proportion of children with ORGDs and FAPDs at risk for impaired HRQOL. Varni et al. [8] determined the cut-off points for the total score that defined the risk of compromising HRQOL. The Brazilian cutoff points were slightly larger. Thus, the proportion of children who did not reach this average was higher in the Brazilian than in the American reference.

In 2006, two studies assessed HRQOL using the Rome II criteria for CAP functional diagnosis. Youssef et al. [15], evaluated children with functional abdominal pain and organic gastrointestinal diseases (Inflammatory Bowel Disease or Gastroesophageal reflux disease) and reported identical scores for both groups but lower HRQOL compared with healthy children. Additionally, parents' perceptions were lower than their children's scores. Varni et al. [16], in three outpatient pediatric gastroenterology clinics, investigated HRQOL using the PedsQL 4.0 Generic Core Scales and demonstrated that children with irritable bowel syndrome manifest significantly impaired HRQOL compared to healthy children and is comparable to patients with functional abdominal pain and organic diagnoses (including Inflammatory Bowel Disease and Gastroesophageal reflux disease). In 2013, Warschburger et al. [11] also evaluated children with functional and organic gastrointestinal disorders and reported significantly lower HRQOL scores than reference values from normative data of a generic QOL questionnaire. HRQOL was not significantly associated with age, sex, or pain duration. In conclusion, the emotional burden associated with organic and functional CAP is enormous.

The findings of the current study with CAP based on the Rome IV criteria agree with those of previous studies using the Rome II [15,16] and Rome III criteria [11]. Therefore, CAP, whether organic or functional, impacts HRQOL in the same way in different scenarios and different Rome criteria. The authors suggested that it may provide insight into the
disease’s biopsychosocial etiology and that these findings need targeted interventions to impair HRQOL. Integrative approaches increase the acceptability of behavioral health recommendations by placing all treatment components (biological, psychological, and social) into a single comprehensive framework [31].

Accordingly, this study supports the notion that pain is not only a signal following anatomic or biochemical pathology. Chronic pain is a complex, multidimensional phenomenon that results from the dynamic integration of biological, psychological, and sociocultural contexts. Consequently, HRQOL assessment of pain disorders could include the child’s prior pain experience, behavioral and emotional factors, and the caregiver’s response and attitudes [32,33]. The association of the HRQOL total scale score with the pain intensity scales shows that the evaluation of pain intensity could be appropriate during visits [16,34]. Accordingly, by the age of five, most children can verbally express pain and indicate its severity [32]. Indeed, pain intensity is probably the most natural dimension to assess, and pain rating scales have a central place in clinical practice. Emphasizing that pain intensity did not differ between organic and functional groups through evaluation using the two scales.

This study had several strengths. First, to our knowledge, no study has evaluated HRQOL in children with FAPDs using the Rome IV criteria. Second, the study included children with dyspepsia associated with H. pylori gastritis. However, this study has some limitations. First, we used a cross-sectional design; therefore, the outcomes were not evaluated. Second, this was a tertiary center study and the generalizability of these results is not recommended.

In conclusion, the results of this study validated the anterior conclusion regarding HRQOL in children with CAP, both organic and functional. However, there are different scenarios and diverse organic etiologies. Overall, the data emphasize that CAP increases psychosocial stress in children. Thus, considering the high prevalence of children with CAP, the risk of bullying in school, particularly for parental protective behaviors, such as excusing the child from school [30,35], well-founded treatment for children and adolescents should be necessary with a multidisciplinary team. Therefore, studies in children with CAP analyzing pain intensity and HRQOL as outcome measures could be valuable for therapeutic programs.

ACKNOWLEDGEMENTS

The authors would like to thank all the parents and children's participants in the study.

REFERENCES

1. American Academy of Pediatrics Subcommittee on Chronic Abdominal Pain. Chronic abdominal pain in children. Pediatrics 2005;115:812-5.
   PUBMED | CROSSREF
2. Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. PLoS One 2015;10:e0126082.
   PUBMED | CROSSREF
3. Spee LA, Lisman-Van Leeuwen Y, Benninga MA, Bierma-Zeinstra SM, Berger MY. Prevalence, characteristics, and management of childhood functional abdominal pain in general practice. Scand J Prim Health Care 2013;31:197-202.
   PUBMED | CROSSREF
4. Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, van Tilburg M. Functional disorders: children and adolescents. Gastroenterology 2016;150:1456-68.e2.
PUBMED | CROSSREF

5. Correa Silva RG, Machado NC, Carvalho MA, Rodrigues MA. Helicobacter pylori infection is high in paediatric nonulcer dyspepsia but not associated with specific gastrointestinal symptoms. Acta Paediatr 2016;105:e228-31.
PUBMED | CROSSREF

6. Carvalho MA, Machado NC, Ortolan EV, Rodrigues MA. Upper gastrointestinal histopathological findings in children and adolescents with nonulcer dyspepsia with Helicobacter pylori infection. J Pediatr Gastroenterol Nutr 2012;55:523-9.
PUBMED | CROSSREF

7. Gulewitsch MD, Enck P, Schwille-Kiunte J, Weimer K, Schlarb AA. Rome III criteria in parents’ hands: pain-related functional gastrointestinal disorders in community children and associations with somatic complaints and mental health. Eur J Gastroenterol Hepatol 2013;25:1223-9.
PUBMED | CROSSREF

8. Varni JW, Bendo CB, Nurko S, Shulman RJ, Self MM, Franciosi JP, et al.; Pediatric Quality of Life Inventory (PedsQL) Gastrointestinal Symptoms Module Testing Study Consortium. Health-related quality of life in pediatric patients with functional and organic gastrointestinal diseases. J Pediatr 2015;166:85-90.
PUBMED | CROSSREF

9. Lisman-van Leeuwen Y, Spec LA, Benninga MA, Biemser-Zeinstra SM, Berger MY. Prognosis of abdominal pain in children in primary care--a prospective cohort study. Ann Fam Med 2013;11:238-44.
PUBMED | CROSSREF

10. Assa A, Ish-Tov A, Rinawi F, Shamir R. School attendance in children with functional abdominal pain and inflammatory bowel diseases. J Pediatr Gastroenterol Nutr 2015;61:553-7.
PUBMED | CROSSREF

11. Warschburger P, Häning J, Friedt M, Posovszky C, Schier M, Calvano C. Health-related quality of life in children with abdominal pain due to functional or organic gastrointestinal disorders. J Pediatr Psychol 2014;39:45-54.
PUBMED | CROSSREF

12. Groenewald CB, Wright DR, Palermo TM. Health care expenditures associated with pediatric pain-related conditions in the United States. Pain 2015;156:951-7.
PUBMED | CROSSREF

13. Dhroove G, Chogle A, Saps M. A million-dollar work-up for abdominal pain: is it worth it? J Pediatr Gastroenterol Nutr 2010;51:579-83.
PUBMED | CROSSREF

14. Calvano C, Warschburger P. Chronic abdominal pain in children and adolescents: parental threat perception plays a major role in seeking medical consultations. Pain Res Manag 2016;2016:3183562.
PUBMED | CROSSREF

15. Youssef NN, Murphy TG, Langseder AL, Rosh JR. Quality of life for children with functional abdominal pain: a comparison study of patients’ and parents’ perceptions. Pediatrics 2006;117:54-9.
PUBMED | CROSSREF

16. Varni JW, Lane MM, Burwinkle TM, Fontaine EN, Youssef NN, Schwimmer JB, et al. Health-related quality of life in pediatric patients with irritable bowel syndrome: a comparative analysis. J Dev Behav Pediatr 2006;27:451-8.
PUBMED | CROSSREF

17. Apley J, Naish N. Recurrent abdominal pains: a field survey of 1,000 school children. Arch Dis Child 1958;33:165-70.
PUBMED | CROSSREF

18. Di Lorenzo C, Colletti RB, Lehmann HP, Boyle JT, Gerson WT, Hyams JS, et al. Chronic abdominal pain in children: a clinical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 2005;40:245-8.
PUBMED | CROSSREF

19. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995;854:1-452.
PUBMED | CROSSREF

20. WHO. WHO AnthroPlus for personal computers manual: software for assessing growth of the world’s children and adolescents [Internet]. Geneva: WHO; 2009 [cited 2022 Jan 10]. Available from: https://cdn.who.int/media/docs/default-source/child-growth/growth-reference-5-19-years/who-anthroplus-manual.pdf?sfvrsn=dd24b2_1

https://doi.org/10.5223/pghn.2022.25.6.500
21. Gragg RA, Rapoff MA, Danovsky MB, Lindsley CB, Varni JW, Waldron SA, et al. Assessing chronic musculoskeletal pain associated with rheumatic disease: further validation of the pediatric pain questionnaire. J Pediatr Psychol 1996;21:237-50.

22. McGrath PA. Pain in children: nature, assessment, and treatment. New York: Guilford Press, 1989.

23. Gold II, Mahrer NE, Yee J, Palermo TM. Pain, fatigue, and health-related quality of life in children and adolescents with chronic pain. Clin J Pain 2009;25:407-12.

24. Hirschfeld G, Zernikow B. Variability of “optimal” cut points for mild, moderate, and severe pain: neglected problems when comparing groups. Pain 2013;154:154-9.

25. Lundell LR, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut 1999;45:172-80.

26. Knuff TE, Benjamin SB, Worsham GF, Hancock JE, Castell DO. Histologic evaluation of chronic gastroesophageal reflux. An evaluation of biopsy methods and diagnostic criteria. Dig Dis Sci 1984;29:194-201.

27. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr 2003;3:329-41.

28. Klatchoian DA, Len CA, Terreri MT, Silva M, Itamoto C, Ciconelli RM, et al. Quality of life of children and adolescents from São Paulo: reliability and validity of the Brazilian version of the Pediatric Quality of Life Inventory version 4.0 Generic Core Scales. J Pediatr (Rio J) 2008;84:308-15.

29. Campo JV, Bridge J, Lucas A, Savorelli S, Walker L, Di Lorenzo C, et al. Physical and emotional health of mothers of youth with functional abdominal pain. Arch Pediatr Adolesc Med 2007;161:131-7.

30. van der Veek SM, Derkx HH, de Haan E, Benninga MA, Boer F. Abdominal pain in Dutch schoolchildren: relations with physical and psychological comorbid complaints in children and their parents. J Pediatr Gastroenterol Nutr 2010;51:481-7.

31. Palermo TM, Long AC, Lewandowski AS, Drotar D, Quittner AL, Walker LS. Evidence-based assessment of health-related quality of life and functional impairment in pediatric psychology. J Pediatr Psychol 2008;33:983-96; discussion 997-8.

32. von Baeyer CL. Children's self-report of pain intensity: what we know, where we are headed. Pain Res Manag 2009;14:39-45.

33. McGrath PJ, Walco GA, Turk DC, Dworkin RH, Brown MT, Davidson K, et al. Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. J Pain 2008;9:771-83.

34. Greenley RN, Kunz JH, Schurman JV, Swanson E. Abdominal pain and health related quality of life in pediatric inflammatory bowel disease. J Pediatr Psychol 2013;38:63-71.

35. Walker LS, Claar RL, Garber J. Social consequences of children's pain: when do they encourage symptom maintenance? J Pediatr Psychol 2002;27:689-98.