

## Original Article



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

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### Conflict of Interest

The authors have no financial conflicts of interest.

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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

[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/m<sup>2</sup>) 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.

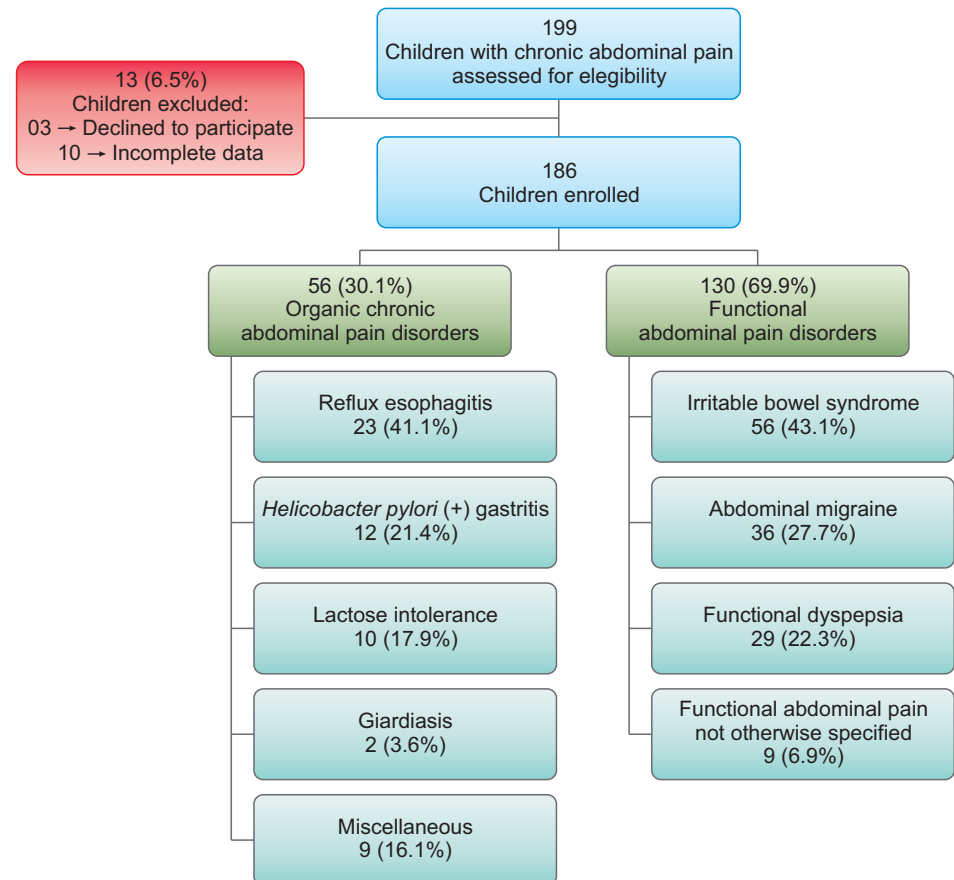
### Statistical analysis

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%).



**Fig. 1.** Flow diagram showing the Participant's identification, enrollment, and final diagnosis.

**Table 1.** Baseline characteristics of children with organic and functional abdominal pain

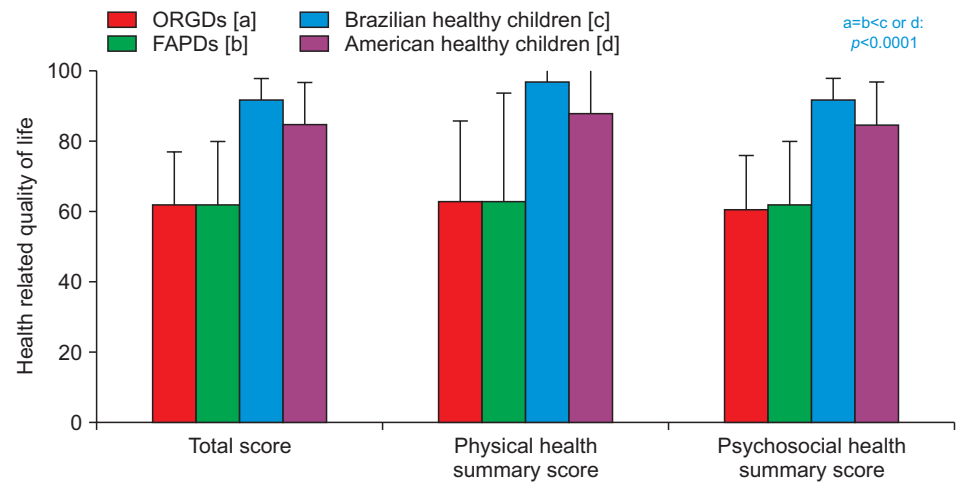
Variable	Organic (n=56)	Functional (n=130)	p-value
<b>Children characteristics</b>			
Age at the first visit, yr	10.2 (9.5–11.0)	9.7 (9.3–10.1)	NS
Duration of symptoms, mo	24.7 (17.6–31.9)	29.5 (24.9–34.0)	NS
Female sex	26 (46.4)	84 (64.6)	<0.02
First-born child	23 (41.1)	56 (43.1)	NS
Poor school performance	21 (37.5)	18 (13.8)	<0.0007
Bullying in school	19 (33.9)	22 (16.9)	<0.01
<b>Family characteristics</b>			
Mother's age, yr	37 (35–38)	36 (34–37)	NS
Father's age, yr	40 (38–42)	39 (37–40)	NS
Marital status (married)	33 (58.9)	90 (69.2)	NS
Couple's disagreement	11 (19.6)	45 (34.6)	<0.02
Mothers' schooling (12 years of education)	23 (41.1)	52 (40.0)	NS
Fathers' schooling (12 years of education)	19 (33.9)	63 (48.5)	NS
Crowding index (person/room)	0.8 (0.7–0.9)	0.8 (0.8–0.9)	NS
<b>Clinical features</b>			
<b>Pain characteristics</b>			
Frequency (weekly)	4.2 (3.0–5.0)	4.3 (3.0–5.0)	NS
Epigastric	38 (67.9)	32 (24.6)	<0.0001
Periumbilical	11 (19.6)	83 (63.8)	<0.0001
Retrosternal pain	16 (28)	2 (1.5)	<0.0001
Burning type	25 (44.6)	21 (16.2)	<0.0001
Colic	17 (30.4)	74 (56.9)	0.001
Vomiting	18 (32.1)	47 (36.2)	NS
Anorexia	21 (37.5)	37 (28.5)	NS
Visual analogue scale	7.4 (6.9–7.9)	6.9 (6.5–7.3)	NS
Facial affective scale	7.8 (7.4–8.3)	7.6 (7.2–7.9)	NS
<b>Nutritional status</b>			
Weight/age z score	0.7 (0.1–1.3)	0.5 (0.2–0.8)	NS
Height/age z score	0.02 (–0.2–0.3)	0.16 (–0.01–0.3)	NS
BMI/age z score	0.9 (0.5–1.3)	0.4 (0.1–0.6)	0.02
BMI (kg/m <sup>2</sup> )	20.1 (18.8–21.3)	18.0 (17.3–18.8)	0.005
Overweight and obesity	26 (46.4)	37 (28.5)	0.02

Values are presented as mean (95% confidence interval) or number (%).

BMI: body mass index, NS: not significant.

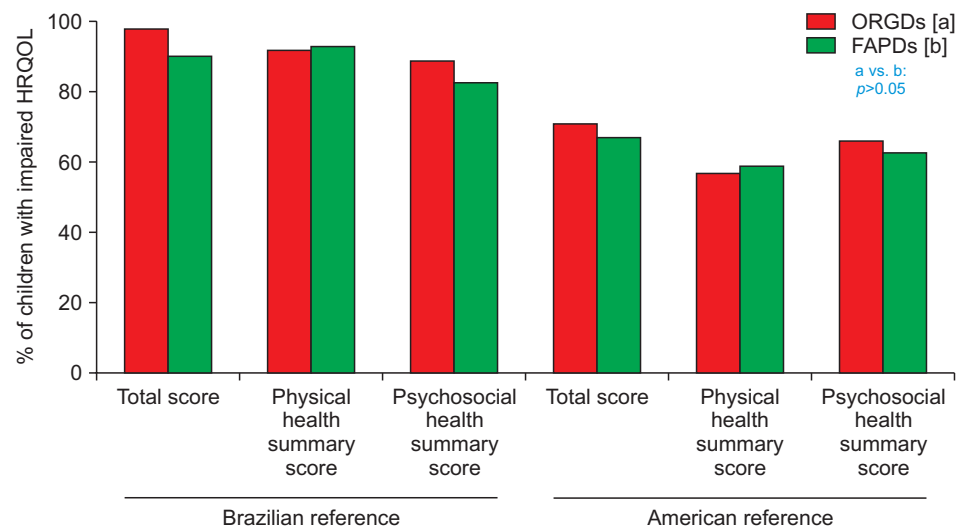
The baseline characteristics of the parents and children are presented in **Table 1**. Female sex (<0.02) and couple disagreement (<0.02) were higher in FAPDs than in ORGDs. In contrast, poor school performance ( $p<0.0007$ ) and bullying ( $p<0.01$ ) were more prevalent among ORGDs. Note that there 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.



**Fig. 2.** Comparison of the total scale score, physical health summary score, and psychosocial health summary score of PedsQL 4.0 generic cores scales parent proxy-report of children with chronic organic and functional abdominal pain with reference to healthy Brazilian and American children. FAPDs: functional abdominal pain disorders, ORGDs: organic abdominal pain disorders.

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.



**Fig. 3.** Percentage of children at risk for impaired HRQOL according to  $<1$  standard deviation of reference healthy Brazilian and American children. FAPDs: functional abdominal pain disorders, ORGDs: organic abdominal pain disorders, HRQOL: health-related quality of life.



## 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.

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