

HEALTH-RELATED QUALITY OF LIFE IN CHILDHOOD INTERSTITIAL LUNG DISEASE PATIENTS

BY

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Abstract

Background: In uncommon diseases, the field of health-related quality of life (HR-QoL) has received little attention. Childhood interstitial lung diseases (chILD) are a diverse group of illnesses with a high rate of morbidity and mortality. These children's HR-QoL may be impacted by their reduced lung function, the effects of their nutrition, and the stressful nature of their medical regimens.

Aim of the work: to compare the HR-QoL in chILD to an aged-matched healthy population and to determine the parameters linked to a changed quality of life.

Patients and methods: This is a cross section controlled study conducted on 26 children aged from 2-16 years with chILD as well as 26 age and gender-matched healthy controls, they were selected by simple random method, during the period from October,2022 to June,2023. Clinical examination, imaging studies were done for the patients group to determine the severity grade of the disease. All participants were asked to complete the PedsQLTM 4.0 Generic Core Scale (0 to 100 points).

Results: The chILD group had significantly lower total mean score of PedsQL ($P=0.000$) in comparison to control group. The most significant predictors and influencing variables in the chILD group are prolonged oxygen therapy ($p=0.001$), radiological changes, higher Fan staging (Clinical severity score) ($P=0.041$), recurrent hospitalization ($p=0.021$), intensive care admission ($P=0.006$), Spo2 saturation and social class (0.040).

Conclusion: Since chILD is an incurable illness that progresses slowly and does not significantly improve lung function, we should concentrate more on possibly treatable factors affecting quality of life (QOL). Doing so could result in better care for individuals with chILD. Similar to how pulmonary function tests are evaluated, QOL assessment must be given proper weight when assessing chILD patients.

Key words: Health-Related Quality, Childhood, Interstitial Lung Disease Patients

Introduction

The term "chILD" refers to a broad category of respiratory conditions, the majority of which are chronic and affect lung function (Kurland et al., 2013). The presence of diffuse infiltrates on lung imaging and abnormal pulmonary function tests with indications of a restrictive ventilatory defect and/or poor gas exchange are characteristics of these disorders, which are linked to high morbidity and death (Abdelhady et al., 2021).

ChILD can have a range of clinical manifestations, including progressive, fibrotic, life-altering, and ultimately deadly conditions. In addition, failure to thrive, tiring during feeding, and weight loss are frequent symptoms in children (Bush et al., 2015). Patients with chILD and their parents face numerous obstacles as they might need many hospital stays, miss numerous days of school, have limited access to functional or recreational activities, and have their psychosocial development disturbed (Niemitz et al., 2018). Families could also feel uneasy about the prognosis and course of treatment (Lauby et al., 2019). So that, Children with chILD may have a

poorer HRQoL (health-related quality of life) than their counterparts without the condition. Moreover, Parents' HRQoL may also be impacted by the financial burden of the illness and its treatment (Kelada et al., 2021 & Cartland, 2013).

The Interstitial Lung Disease (ILD) specialists have made HRQOL a primary objective over the last ten years. Both ILD specialists and patients have expressed how critical it is to prioritise HRQOL as a primary area of focus in clinical practice and research investigations (Donohue et al., 2021, Cakici et al., 2020). There is currently a lot of interest in how interventions can effectively reduce the deterioration of HRQOL, even while a few medications are known to slow the progression of disease. However, there is a dearth of studies evaluating how chILD affects psychosocial status of children and their families (Aronson & Swigris, 2021). So this study aim was to compare the HR-QoL in chILD to an age and sex-matched healthy population and to identify the factors that were associated to an altered QoL.

patients and methods:

Ethical Considerations

1. The protocol was submitted for approval of the Ethics Committee of Ain Shams University, Faculty of Medicine (NO. FMASU M S 649/2022)

2. An Oral consent was taken from the patients' care givers before study enrollment.

3. The steps of the study, aims, potential benefits and hazards, were discussed with the patients and their care givers,

4. Confidentiality of all data was ensured and The patients had the right to withdraw from the study at any time without giving any reasons without penalties.

Inclusion Criteria:

The study included Children aged 2–18 years, who are diagnosed as chILD on the following aspects, if at least three of the following four criteria are present:

1. Respiratory symptoms (cough, rapid and/or difficult breathing, or exercise intolerance).

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This research has not received any funds regarding the study or publication.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/ or publication of this article.

Calculation of sample size: Using G Power program for sample size calculation, setting power at 80%, alpha error at 5% reviewing results from the previous study showed that health-related-QoL is significantly impaired in Interstitial lung disease in children (chILD) compared with a healthy population Lauby et al ,(2019) Assuming an effect size difference =0.8 between cases and controls regarding QoL score a sample size of at least 26 cases and 26 controls will be needed.

2. Respiratory signs (tachypnea, adventitious sounds, retractions, digital clubbing, failure to thrive, or respiratory failure).
3. Hypoxemia.
4. Diffuse abnormalities on a chest radiograph (CXR) or computed tomography (CT) scan.

Exclusion Criteria: Patients with other common causes of diffuse lung diseases (i.e. cystic fibrosis, primary ciliary dyskinesia, and congenital heart disease) were excluded. Also, child Patients who are in exacerbation are excluded temporarily till quiescence

Study procedure: all studied cases were subjected to the following :

Detailed history was taken from all enrolled participants and the missed the clinical data were retrieved from the medical files **with special emphasis on** personal information, living area, social class, frequency of pulmonary exacerbations/year, frequency of hospitalizations for the last year, drug history especially (steroids or immunosuppressive drugs), need for continuous oxygen treatment, pediatric Intensive care (PICU) admission, and family history of any lung disease.

Full Clinical examination was done also with special emphasis on clubbing, SPO₂, signs of respiratory distress (tachypnea, dyspnea on exertion or at rest, haemoptysis or persistent dry cough).

Fan Severity Score: Severity score was recorded for each subject on presentation as follows:

Grade 0: Asymptomatic

Grade 1: Symptomatic with normal oxygen saturation under all conditions, Grade 2: Symptomatic with normal resting room air saturation, but hypoxemia <90% with exercise or sleep,

Grade 3: Symptomatic with hypoxemia <90% at rest and Grade 4: Symptomatic with hypoxemia at rest and pulmonary hypertension.(Fan, 2004).

Pediatric Quality of Life Inventory™ (PedsQL™) 4.0 Generic Core Scale: We employed the PedsQL 4.0 Generic Core Scales, a validated generic paediatric quality of life questionnaire (PedsQL, Copyright 1998 JW Varni, PhD, all rights reserved). This non-specific disease questionnaire is made up of parent proxy reports for all age groups (1-12 months, 13-24

Study Design: our study was a case control study, conducted on 26 CHILD cases and 26 aged-and gender-matched healthy controls, they were selected by a simple random method. Study was conducted in the Ain Shams Pediatric hospital, Pulmonology and outpatient clinics between October, 2022 and June, 2023.

months, 2-4 years, 5-7 years, 8-12 years, 13-18 years) and child self-reports for children over the age of eighteen (8–12 years for children and 13–18 years for teenagers). The patients and parents were asked to consider the past month's condition) which are appropriate for assessing HRQoL in both healthy and chronically ill children, the response was given on a 5-point scale: 0 = never a problem; 1 = almost seldom a problem; 2 = occasionally a problem; 3 = frequently a problem; and 4 = almost always a problem. After that, each response was given a reverse score on a 0–100 scale (0 = 100; 1 = 75; 2 = 50; 3 = 25; 4 = 0). A total score was calculated, with a higher number denoting greater HR-QoL. The score ranged from 0 to 100. Several dimensions are reflected in the overall score: a psychosocial score (divided into emotional, social, and academic functioning scores) and a physical score (Varni, 1999).

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). **Independent-samples t-test** of significance was used when comparing between two means & **Mann Whitney U test:** for two-group comparisons in non-parametric data. **A one-way analysis of variance (ANOVA)** when comparing between more than two means & **Post Hoc test: Tukey's test** was used for multiple comparisons between different variables. The Comparison between groups with qualitative data was done by using **Chi-square test** and **Fisher's exact test** instead of Chi-square test only when the expected count in any cell less than 5

RESULTS:

All results will be demonstrated in the following tables and figures:

Table 1. Sociodemographic of all participants:

Personal Data	ChILD Group (n=26)	Control Group (n=26)	Test value	p-value
Sex				
Male	10 (38.5%)	17 (65.4%)	3.775	0.052
Female	16 (61.5%)	9 (34.6%)		
Age				
Median (IQR)	(5-13)10	7.5 (4-12)	0.712	0.403
Range	2-17	2-16		

There were no statistically significant differences between the chILD and control groups in age or sex but a slight female predominance observed in chILD Group. (table 1)

Table 2. Clinical data of all participants:

Personal Data	ChILD Group (n=26)	Control Group (n=26)	Test value	p-value
Age at Diagnosis (years)				
Median (IQR)	4 (2-8)			
Range	1-10			
Weight/ age centile				
Median (IQR)	25 (3 – 50)	62.5 (50 – 75)	-3.438	0.001
Range	3 – 90	25 – 90		
Height /age centile				
Median (IQR)	10 (3 – 25)	50 (25 – 50)	-3.722	0.000
Range	3 – 90	10 – 90		
Etiology of ILD				
Unknown	12 (46.2%)			
Genetic	3 (11.5%)			
Post viral	5 (19.2%)			
Immunological	4 (15.4%)			
Environmental	2 (7.7%)			
Resp. Dist. Grade				
Grade I	12 (46.2%)			
Grade II	13 (50.0%)			
Grade III	1 (3.8%)			
Spo2% During Rest				
Mean±SD	91.69±2.71	98.35±0.56	7.855	0.000
Range	87-97	97-99		
Spo2% During exercise				
Mean±SD	84.73±5.97	95.27±0.60	8.920	0.000
Range	75-92	94-97		
Cough				
No	2 (7.7%)			
Dry	8 (30.8%)			

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Wet	16 (61.5%)			
Clubbing				
No	16 (61.5%)			
Grade 1	7 (26.9%)			
Grade 2	1 (3.8%)			
Grade 3	2 (7.7%)			
Fan Staging (Clinical severity score)				
Grade 1	8 (30.8%)			
Grade 2	9 (34.6%)			
Grade 3	5 (19.2%)			
Grade 4	3 (11.5%)			
frequency of PICU admission in last year				
No Admission	18 (69.2%)			
1 time	8 (30.8%)			
frequency of ward Admission				
No admission	7 (26.9%)			
1 time	4 (15.4%)			
2 times	5 (19.2%)			
3 times	10 (38.5%)			
Radiological Changes				
Mild Changes	12 (46.2%)			
Moderate Changes	13 (50.0%)			
Severe Changes	1 (3.8%)			

The age of diagnosis, ranged from 1 to 10 years with a median of 4 years, chILD group showed poorer nutritional status presented in lower weight and height centiles in comparison to healthy controls, The chILD etiologies of the included patients were representative of the heterogeneity of chILD diagnoses, Regarding Fan staging that estimate clinical severity score of the chILD group, grade II was the most common, PICU admission once over the last year was experienced by 30.8% of the patients. Regarding radiology changes, 46.2% had mild changes within the lung parenchyma, 50% had moderate changes and only 3.8% had severe changes (Table 2).

Table 3. Comparison between ChILD group and control group according to QoL Scoring.

QoL Scoring	ChILD Group (n=26)	Control Group (n=26)	Test value	p- value
Physical scoring				
Mean±SD	46.94±12.68	70.77±8.06	7.254	0.000
Emotional scoring				
Mean±SD	56.73±12.57	76.73±7.34	7.008	0.000
Social functioning scoring				
Mean±SD	49.04±12.14	87.88±9.18	11.746	0.000
Cognitive scoring				
Mean±SD	49.73±12.67	81.46±7.28	9.364	0.000
Total Scoring% QoL				
Mean±SD	50.81±10.59	78.00±5.25	11.732	0.000

The PedsQL mean scores in chILD were significantly lower than those observed in a healthy population. (Table 3).

Table 4: Association between oxygen support and QoL scoring in ChILD Group

QoL Scoring	Need for oxygen support		Test value	p-value
	Yes	No		
Physical scoring				
Mean±SD	41.75±14.341	58.63±6.89	9.932	0.004
Emotional scoring				
Mean±SD	51.11±9.16	69.37±9.79	21.117	0.000
Social functiong scoring				
Mean±SD	43.33±12.37	61.87±8.43	14.756	0.001
Cognitive scoring				
Mean±SD	44.61±14.98	61.25±10.61	7.993	0.009
Total Scoring% QoL				
Mean±SD	46.05±8.78	61.50±4.93	21.409	0.000

Table 5: Association between Radiological Changes and QoL scoring in ChILD Group.

QoL Scoring	Radiological Changes			Test value	p-value
	Mild Changes	Moderate Changes	Severe Changes		
Physical scoring					
Mean±SD	55.87±9.80A	41.15±12.64B	15.00±0.00C	9.330	0.001
Emotional scoring					
Mean±SD	66.25±9.79A	49.62±7.48B	35.00±0.00C	14.748	0.000
Social functiong scoring					
Mean±SD	59.58±8.91A	39.62±11.63B	45.00±0.00B	11.541	0.000
Cognitive scoring					
Mean±SD	59.17±10.18A	41±15.64C	50.00±0.00B	5.808	0.009
Total Scoring% QoL					
Mean±SD	59.25±6.09A	43.92±8.08B	39.00±0.00B	15.552	0.000

There were significant associations between need for oxygen support, radiological changes and total QoL scoring and all domains of QoL, physical scoring, cognitive scoring, emotional scoring, social function scoring. (Table 4,5).

Figure (1): Correlations between HRQoL total score and frequency of PICU admissions in the last year.

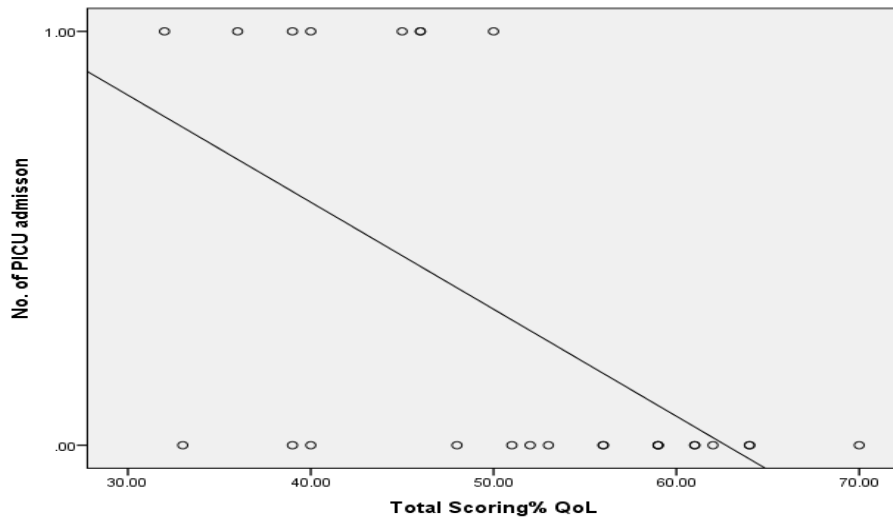


Figure (2): Correlations between HRQoL total score and grade of respiratory distress in the last year.

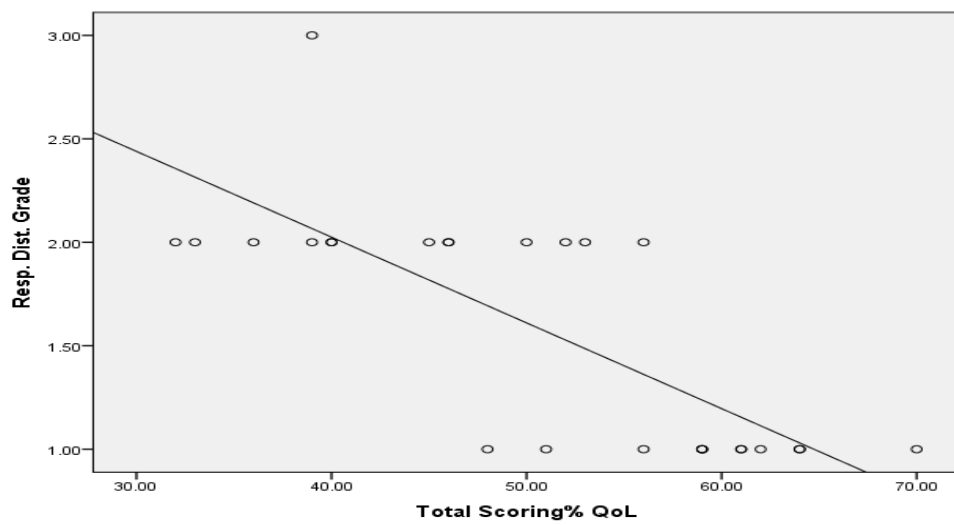


Table 6. Multiple linear regression analysis using total scoring of QoL as dependent variable in ChILD Group to identify the most predictor parameters.

Parameters	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	β	\pm SE	Beta		
(Constant)	281.245	153.601		1.808	0.076
Age" years"	1.015	4.555	0.013	0.223	0.824
Age/ w.t centile	-302.202	705.197	-0.030	-0.429	0.670
Age/ Ht. centile	-104.576	199.226	-0.085	-0.525	0.602
Age at Diagnosis (years)	-100.557	87.718	-0.089	-1.146	0.257
Fan Staging (Clinical severity score)	-84.319	27.592	0.158	2.167	0.041*
Resp. Dist. Grade	-19.072	62.618	0.313	2.452	0.022*
Clubbing	-0.547	0.185	-0.075	-1.213	0.246
Frequency of PICU admission	-1.578	0.557	-0.177	-2.917	0.006*
Spo2% During Rest	29.657	6.102	-0.073	-2.149	0.045*
Spo2% During exercise	2.532	0.541	-0.172	-2.832	0.006*
Social Class score	78.950	25.041	0.153	2.104	0.040*

β : Regression coefficient, SE: Standard error

Regarding the multiple linear regression analysis, Fan staging, respiratory distress grade, frequency of PICU admissions, Spo2 during rest and exercise and social class score were the most significant predictors and influencing variables in the ChILD group. (Table 6)

Discussion

HRQoL assessment is still not frequently utilised in rare diseases, despite its importance in all disorders. We attempted to evaluate HRQoL in children with chILD in an effort to identify the most significant determinants negatively affecting the HRQoL in these patients. Using the (PedsQL™) 4.0 Generic Core Scale, the main finding of this study is that 26 chILD patients had a significant impairment in HR-QoL.

According to *Ravens-Sieberer and Bullinger (1998)*, the HRQoL assessment is becoming a crucial tool for assessing children's mental and physical health, indicating its significance and wide range of applications in paediatric clinical practice. The HRQoL of children with asthma, recurrent respiratory tract infections, obesity, and cystic fibrosis has been the subject of numerous studies (*Williams et al., 2000 & Yackobovitch-Gavan et al., 2009, Jiang et al., 2013*). However, because chILD is an uncommon illness, little research has been done on this population particularly in the Middle East.

This study demonstrated that lower perceived QoL in patients with chILD.

Specifically, when compared to healthy children, this is in line with an earlier study by *Lauby et al., 2019* who evaluated QoL and parental adjustment in pediatric patients with chILD, in which parents reported significantly lower patient QoL than healthy standards in overall, psychological, and physical domains. The mean total score observed in chILD is significantly matching with scores reported in other chronic respiratory diseases, as documented by *Seid et al., (2010) and Thomas et al., (2006)* in diseases such as asthma and cystic fibrosis.

Physical activities like walking, running, bathing alone showed to be more affected in the chILD group who experienced easy fatigueability due decreased oxygen saturation with effort. Patients with chILD is associated with more frequent symptoms, e.g.: cough and dyspnea. Moreover, Children with uncontrolled ILD frequently experience increased anxiety about impending flare-ups.

Emotional well-being show also significant difference (P= 0.000) as negative emotional feelings like fear, stress, anxiety showed to be more experienced by the chILD

group. Patients with chILD experience panic attacks, and depression because to their social isolation and physical disability (*Nevel and Young, 2018*). Recent study by *Handler et al., (2019)* has found that symptom burden of cancer and of chronic lung disease are similar. Also, Cognitive abilities like mental abilities, ability to finish his/her school homeworks and regular school attendance significantly affected in chILD group which can be due to recurrent hospital admissions or long periods of keeping home due to oxygen support devices, These findings are similar to studies by *Seidl et al., (2022)*, *Lauby et al., (2019)*, and *Fuger et al., (2016)* that found overall QoL scores markedly low in chILD group compared to the control group.

Our study revealed that the physical domain was the most affected domain ($p < 0.001$) (Table 3), which agrees with *Farnik et al., (2010)* and *El-hosseiny et al., (2013)* that showed the physical domain was the most affected and revealed the negative effect of ILD symptoms on the QOL. On the other hand, studies done in more developed countries by *Niemitz et al., (2018)* and *Lauby et al., (2019)*, found that the emotional condition was the most affected domain. Our results regarding QOL may be attributed to the following as low-income cultures' poorer standards of life, laxer environmental regulations, dearth of adequate health care services beside ILD could all be contributing factors to our findings.

Our current findings show that numerous variables influence HRQOL. For example, we found that fan staging, radiological changes, frequency of hospital admission, frequency of PICU admission and basal oxygen saturation were key factors contributing to the HRQOL in children with chILD (Figure 1). *Lauby et al., (2019)*, also studied factors impairing HR-QoL in univariate and multivariable analysis, highlighting the impact of factors such as higher Fan scores, long-term oxygen therapy, nutritional support, and the number of oral medications on a lower total QoL score in children with ChILD.

Therefore, in order to restore normal daily activities and improve quality of life for children and their families, intensive efforts should be focused on achieving optimal ILD control and appropriate treatment for severe attacks.

Our study revealed that children with lower socioeconomic status (SES) had significantly lower total HRQoL scores compared to those with higher SES. This could be explained by the

assumption that parents from higher socioeconomic backgrounds typically had higher educational attainment, more knowledge about respiratory symptoms, and more fearful of the illness and its consequences, which caused them to overprotect their children.

In the chILD Group, an in-depth analysis of the association between radiological changes and Quality of Life (QoL) scoring revealed significant negative associations with physical scoring, emotional scoring, cognitive scoring, social functioning scoring, and total QoL scoring (Table 5). This aligns with *Wirnsberger et al., (1997)* who found that the radiographic stage was related to cognitive and emotional behavior, home management, and social interaction.

In addition, the need for oxygen support is negatively impacted all domains of QoL (Table 4). This finding is consistent with the results of *Bell et al., 2017* who also observed a significant negative correlation between HRQoL and the need for supplemental oxygen.

Assessments of quality of life are extremely useful in establishing clinical disease-management plans that offer ill children and their families' comprehensive treatment and education, Paediatricians can create focused support services for children and their families, like medical education about chILD and psychological counselling, by building on their knowledge of HRQOL (*Nevel and Young, 2018*).

Conclusion:

We concluded from our study the following:

- 1- significant poor scores were recorded in the chILD group in comparison to the control group.
- 2- Total (QoL) scoring in chILD group has been affected by factors as the clinical severity of the disease (Fan staging), respiratory distress grade, frequency of PICU and ward admissions, Spo2 during rest and exercise and social class score.
- 3- Children with ILD are frequently exposed to recurrent hospital admissions and recurrent oxygen support.

Recommendation:

Our study recommended that:

1. Efforts aimed at enhancing the overall quality of life in Egyptian children with chILD should extend beyond medical interventions.
2. Regular follow up sessions in the psychiatry clinic for better social rehabilitation.
3. Regular follow up in the nutrition clinic to provide regular balanced diet based on strict monitor to their growth parameters.
4. Working to develop educational curricula that suit their lifestyle and develop their cognitive skills.

Limitation:

We think that our research has significant implications for the chILD-affected children's quality of life. We do realise, though, that there are a number of limitations to our study as:

- 1- Small sample size due to difficulty of getting patients with ILD.

- 2- caregivers would have less influence on the children's HRQOL than the children themselves, so we did not objectively assess the mental and physical health of the carers
- 3- The HRQOL data from children treated in tertiary centre hospitals may not be indicative of the HRQOL of patients treated at various hospitals in various regions, which is another drawback of this study.

Even though our individuals might not be representative of all Egyptian children with chILD, our results do offer important insight into how chILD affects HRQOL, which is helpful for researchers and physicians.

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