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Health Related Quality of Life in Patients with Biliary Atresia Surviving with their Native Liver

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Abstract

Objectives—To quantify health related quality of life (HRQOL) of patients with biliary atresia with their native livers and compare them with healthy children and patients with biliary atresia post-liver transplant (LT) and to examine the relationship between HRQOL and medical variables.

Study design—A cross-sectional HRQOL study of patients with biliary atresia with their native livers (ages 2–25 years) was conducted and compared with healthy and post-LT biliary atresia samples using PedsQL™ 4.0 child self and parent proxy reports, a validated measure of physical/psychosocial functioning.

Results—221 patients with biliary atresia with native livers (54% female, 67% white) were studied. patient self and parent proxy reports showed significantly poorer HRQOL than healthy children across all domains ($p < 0.001$), particularly in emotional and psychosocial functioning. Child self and parent proxy HRQOL scores from patients with biliary atresia with their native livers and post-LT biliary atresia were similar across all domains ($p = \text{NS}$). Child self and parent proxy reports showed moderate agreement across all scales, except social functioning (poor to fair agreement). On multivariate regression analysis, black race and elevated total bilirubin were associated with lower Total and Psychosocial HRQOL summary scores.

Conclusions—HRQOL in patients with biliary atresia with their native livers is significantly poorer than healthy and similar to post-LT biliary atresia children. These findings identify significant opportunities to optimize the overall health of patients with biliary atresia.

Keywords

Biliary Atresia; Quality of Life; Health Related Quality of Life; Liver Transplant; PedsQL

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*A list of members of the Childhood Liver Disease Research and Education Network is available at www.jpeds.com (Appendix).

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Biliary atresia is a progressive obliterative cholangiopathy that presents in infancy with jaundice due to biliary obstruction (1). Despite the use of surgical hepatic portoenterostomy (HPE) to reestablish bile flow, biliary atresia progresses to end-stage liver disease in 80% of patients over a variable length of time. Approximately one-half of affected infants will require liver transplantation in the first two years of life due to complications of cirrhosis and cholestasis, including severe malnutrition, ascites, portal hypertension and coagulopathy (2). The remainder of children with biliary atresia may live many years with their native livers, despite the chronic, progressive cirrhosis that develops. The impact on quality of life (QOL) for these relatively healthy children with biliary atresia surviving without liver transplantation has not been well established.

An assessment of health-related QOL (HRQOL), a multidimensional construct that assesses physical, psychological (including emotional and cognitive), and social health dimensions, is an important determinant in providing comprehensive long-term care to children with chronic disease (3). The inclusion of such measures allows providers to understand the global impact of changes in health status from the perspective of the patient, which may otherwise be overlooked (4, 5).

The primary focus of HRQOL studies in pediatric liver disease to date has been the post-liver transplant period (4, 5). Pediatric liver transplant recipients demonstrate lower HRQOL than healthy children, with the greatest differences observed in school functioning, although it is not clear how functioning was affected by pre-transplant versus post-transplant morbidities (4, 5). HRQOL in patients with biliary atresia surviving with their native livers has not, however, been systematically evaluated using a well-validated instrument. A study of Japanese and British adolescents with biliary atresia surviving with their native livers suggested that general, physical, social and emotional health were all impaired compared with healthy children (6). This study was limited, however, by its small size, inability to assess children younger than 14 years of age, as well as exclusion of parental perceptions of HRQOL (6). A systematic study of HRQOL in biliary atresia may help to clarify additional determinants of severity of their chronic disease. The potential impact of this valuable information may promote refinements in personalized health care, advocating for early educational interventions, support in social integration and perhaps even as an indication for liver transplant.

Therefore, the objectives of this study were to address this knowledge gap in the literature by quantifying HRQOL in a cross section of patients with well-characterized biliary atresia with their native livers and comparing it with healthy children and to patients with biliary atresia who have undergone liver transplant and examining the relationship between HRQOL and medical variables.

Methods

The biliary atresia Research Consortium (biliary atresiaRC) was formed in 2002 as an NIDDK/NIH supported cooperative network of 10 pediatric clinical centers and a data coordinating center. biliary atresiaRC was subsequently expanded and renamed the Childhood Liver Disease Research and Education Network (ChiLDREN). These 10 clinical

centers enrolled children with a confirmed diagnosis of biliary atresia with their native liver, between the ages of 6 months and 25 years into the prospective biliary atresia Study of Infants and Children (biliary atresiaSIC). At entry, demographic, clinical and laboratory data were collected and physical examinations performed. In addition, past medical histories were obtained by chart review at individual centers. Medical events in the previous 12 months, obtained by a combination of recall and chart review, were recorded. Laboratory tests obtained as part of routine management were also recorded. In patients with biliary atresia surviving with their native liver, optimal health was defined as no cholangitis or gastrointestinal (GI) bleeding in the previous 12 months, platelet count $80 \times 10^3/\text{mm}^3$, albumin 3 g/dL and total bilirubin 2 mg/dL . The final study cohort was limited to subjects who completed the Pediatric Quality of Life Inventory™ (PedsQL™) 4.0 Generic Core Scales, administered to children ages 8 and older and to the parents of children 2 years to 18 years of age.

A cohort of healthy children was derived from the previously conducted PedsQL™ 4.0 Generic Core Scales initial field test (7) and a statewide State Children's Health Insurance Program (SCHIP) evaluation (8). This healthy population was matched by age group (ages 2-4, 5-7, 8-12, 13 -18 and 18-25 years), sex, and race/ethnicity to patients with biliary atresia surviving with their native livers. In addition, PedsQL™ 4.0 Generic Core Scales data were obtained from patients with biliary atresia post-liver transplant in an ancillary study of Studies of Pediatric Liver Transplantation (SPLIT), and included a cross-section of pediatric liver transplant recipients, ages 2 and 18 years, who had survived liver transplant (LT) by at least 12 months, collected from 22 participating North American centers between July 2005 and August 2010 (4). Demographic and medical variables for this post-transplant biliary atresia cohort were obtained from data collected by SPLIT at the time of survey administration. Optimal health in this post-transplant population was defined as having no allograft rejection, biliary or vascular complications in the previous 12 months, albumin 3 g/dL , and a total bilirubin 2 mg/dL .

Measurement of HRQOL

The 23-item PedsQL™ 4.0 Generic Core Scale encompasses physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items). These scales produce a Total, Psychosocial and Physical Summary Score (7). The PedsQL™ Generic Core Scales is composed of parallel child self-report and parent proxy-report versions. Items are reverse scored and linearly transformed to a scale of 0-100, with higher scores indicating better HRQOL. HRQOL scores were examined by age group (ages 2-4, 5-7, 8-12, 13 -18 and 18-25 years) and in aggregate for both child self-report and parent proxy-report.

This study was approved by Institutional Review Boards at each participating center and informed consent was obtained from parents/guardians or subjects 18 years or older.

Statistical Analyses

Mean PedsQL™ Scale and Summary scores were calculated for the biliary atresia sample surviving with their native liver, the post-transplant biliary atresia sample, and the matched

healthy control population. A healthy population was randomly matched to patients with biliary atresia surviving with their native livers by age group, sex, and race/ethnicity, utilizing an SPSS statistical software random sample case selection command. This command allows the percentage of children in the healthy sample to be matched to the biliary atresia native liver sample on the targeted demographic characteristic (e.g., age, sex, race/ethnicity). Independent samples *t*-tests were utilized to compare PedsQL™ 4.0 Generic Core Scale Scores between patients with biliary atresia surviving with their native livers and the healthy sample. Mean PedsQL™ scores were also compared between patients with biliary atresia surviving with their native livers and the biliary atresia post-transplant sample utilizing independent samples *t*-tests. In order to determine the magnitude of differences, effect sizes were calculated by subtracting the biliary atresia native liver sample and healthy sample means and dividing by the pooled standard deviation. This same approach was used to compute the effect sizes between the biliary atresia native liver and biliary atresia post-LT samples (9). Effect sizes are designated as small (0.20), medium (0.50) and large (0.80) in magnitude (9). In addition, in order to identify the poorest performing segment, the cohort of patients with biliary atresia with their native livers were dichotomized based on PedsQL™ Total Scale scores, with an “at risk” cut off score set at 1 SD below the population mean (8).

Agreement between child self-report and parent proxy-report was determined through Intra-class Correlation Coefficients (ICCs) (10). ICCs are designated as poor to fair agreement (< 0.40), moderate agreement (0.41-0.60), good agreement (0.61-0.80), and excellent agreement (0.81-1.00) (11).

Univariate regression analysis was conducted to identify demographic and health status variables that were associated with impairments in Total, Physical and Psychosocial summary HRQOL scores. Factors identified on univariate analysis as potential predictors of HRQOL, at the $p < 0.1$ level, entered a multivariate model. Separate analyses were conducted for the child self-report and parent proxy report, given the possibility that different predictors could emerge.

All statistical analyses were conducted using SAS v9.2 or SPSS.

Results

Two hundred and ninety-eight patients with biliary atresia with their native livers were enrolled into the BASIC study, 221 of whom completed HRQOL assessments (at a mean age 9.75 ± 5.25 years) and were included in the final study cohort. These subjects were 54% were female and 67% white, with a mean age of 2.75 ± 9.14 months at the time of HPE, similar to the 77 patients who did not complete HRQOL assessments (Table I). Subjects who completed HRQOL assessments had good overall nutritional status, with rare episodes of cholangitis and GI bleeding in the 12 months prior to study. In addition, laboratory studies at the time of HRQOL evaluation (Table I), indicated optimal health in 62% of patients surviving with their native livers (no cholangitis or GI bleeding in the previous 12 months, platelet count $80 \times 10^3/\text{mm}^3$, albumin 3 g/dL, and total bilirubin 2 mg/dL). Patients with optimal health reported higher Physical Health scores compared with those without optimal health (85.5 ± 13.2 vs. 80.1 ± 17.1 , $p=0.03$), but similar Psychosocial and

Total Summary Scores. Patients with biliary atresia who did not complete HRQOL assessments, however, had evidence of more advanced liver disease, with lower triceps skin fold z scores, and higher total bilirubin, ALT and INR levels (Table I).

There were 954 healthy children in the matched sample used as a comparison for patients with biliary atresia with their native livers. They were 54.5% female and 70.3% white, with a mean age of 9.51 ± 3.57 years.

The post-transplant biliary atresia group included 151 children that were used as a comparison for patients with biliary atresia with their native livers. They were 64.2% female and 57.8% white, with a mean age at survey of 7.2 ± 3.8 years, demographically similar to patients with biliary atresia with their native livers ($p=NS$). Optimal health in patients with biliary atresia after liver transplant (no rejection, biliary or vascular complications in the previous 12 months, albumin ≥ 3 g/dL, and total bilirubin ≤ 2 mg/dL) was present in 78% of subjects.

Comparison of patients with biliary atresia with their native livers and Healthy Sample

The mean and standard deviations of the PedsQL 4.0™ Generic Core Scale Scores for patients with biliary atresia surviving with their native livers and the healthy comparison population are presented in Table II (available at www.jpeds.com). Among patients with biliary atresia surviving with their native livers, 29.5% of self-reported PedsQL™ Total Scale scores were at least 1 SD below the population mean of 76.96, indicating significantly impaired overall HRQOL. Self-reported comparisons of Physical Health, Psychosocial Health and Total Summary HRQOL scores (Figure) demonstrate significantly poorer HRQOL in patients with biliary atresia than healthy children across all measured domains ($p < 0.001$), with the majority of effect sizes in the moderate range. The greatest differences occurred in school functioning, with moderate to large effect sizes. Child self-reports of social functioning were lower in school age children (mean of 74.05 ± 18.02 in 5-7 year olds and 78.33 ± 17.48 in 8-12 year olds) as compared with older adolescents (mean of 84.55 ± 14.60 in 13-18 year olds) and young adults (mean of 87.92 ± 11.77 in > 18 years), $p=0.02$. No differences among age groups were noted across other HRQOL domains.

Using parent proxy-reports, 20.3% of reported PedsQL™ Total Scale scores were at least 1 SD below the population mean of 77.69, indicating significantly impaired overall HRQOL. Parent proxy-report comparisons of Total, Psychosocial and Physical Health Summary HRQOL scores in patients with biliary atresia with their native livers (Figure) were also significantly lower than the healthy children across all measured domains (<0.001), with medium effect sizes. In addition, parent proxy reports demonstrated the greatest differences in school functioning ($p < 0.001$), with medium to large effect sizes.

Parent proxy scores of school functioning were significantly lower in school age children and adolescents (mean of 69.76 ± 16.60 in 5-7 year olds, 68.25 ± 18.62 in 8-12 year olds, and 70.16 ± 21.23 in 13-18 years) than younger children (mean of 84.31 ± 21.83 in 2-4 year olds), $p=0.01$. Parent proxy-report scores of psychosocial functioning were also lower in older age groups (mean of 74.40 ± 12.66 in 5-7 year olds, 74.00 ± 14.60 in 8-12 year olds, and 74.69 ± 16.69 in 13-18 years), as compared with younger children (mean of $86.27 \pm$

14.19 in 2-4 year olds), $p=0.007$. No differences among age groups were noted across other HRQOL domains.

Comparison of patients with biliary atresia with their native livers and patients with biliary atresia after liver transplant

The mean and standard deviations of the PedsQL 4.0™ Generic Core Scale scores for child self-reports and parent proxy-reports of patients with biliary atresia with their native livers compared with patients with biliary atresia after liver transplant are presented in Table II. Physical Health, Psychosocial Health and Total Summary HRQOL scores (Figure) by child self-report and parent proxy-report HRQOL in patients with biliary atresia with their native livers and those post-LT were similar across all measured domains, $p=NS$.

Comparison of Child Self-report and Parent Proxy-report for patients with biliary atresia with their native liver

There were 159 child self and parent proxy-report pairs available in patients with biliary atresia surviving with their native livers. Intra-class correlation coefficients (ICCs) were determined on this subset to assess agreement in HRQOL perceptions by child self-report and parent proxy-report. Assessed in aggregate, ICCs showed moderate agreement across all scales, with the notable exception of social functioning, which demonstrated only poor to fair agreement between child and parent (Table III). Differences in perceptions of HRQOL between parent and child were also assessed by age group (Table III). Among 5-7 year olds, there was poor to fair agreement between child and parent across all assessed scales. Among 8-12 year olds, there was moderate agreement in social and physical functioning, with good agreement in other domains. Among 13-18 year olds, social, emotional and school function showed moderate agreement, with all other scales showing good agreement.

Demographic and Medical Predictors of HRQOL

Univariate linear regression analysis was performed in patients with biliary atresia surviving with their native livers to understand the association between child self-reports of Total, Physical and Psychosocial Health Summary scores of HRQOL and demographic and medical factors. Risk factors found to be significant at the $p < 0.1$ level on univariate analyses were entered into a multivariate logistic regression model, and included sex, ethnicity, race, ascites, hepatopulmonary syndrome, total bilirubin and hemoglobin. In addition, because of its potential clinical importance, age at HPE was placed in the multivariate model. Non-significant factors on univariate analysis included height and weight z scores, cholangitis, GI bleeding, sepsis or peritonitis in the previous 12 months, ALT, albumin, GGTP, white blood cell and platelet count. On multivariate regression analysis, there were no identified factors significantly associated with lower Total, Physical or Psychosocial summary scores of HRQOL by child self report. The absence of hepatopulmonary syndrome and higher hemoglobin, however, were associated with higher Total and Physical summary scores of HRQOL by child self report.

Univariate linear regression analysis was also performed to understand the relationship between parent proxy reports of Total, Physical and Psychosocial Health Summary scores of HRQOL and demographic and medical factors among patients with biliary atresia surviving

with their native livers. Risk factors found to be significant at the $p < 0.1$ levels on univariate analysis were entered into a multivariate logistic regression model, and included race, age at survey, ascites, hepatopulmonary syndrome, total bilirubin and platelet count. In addition, sex and age at HPE were placed in the multivariate model because of their potential clinical importance. Non-significant factors on univariate analysis included height z scores, triceps z scores, cholangitis, GI bleeding, sepsis or peritonitis in the previous 12 months, ALT, albumin, GGTP, white blood cell and platelet count. On multivariate regression analysis, black race was associated with lower Total and Psychosocial summary scores of HRQOL by parent proxy report. Additionally, an elevated total bilirubin was associated with lower Total, Physical and Psychosocial summary scores of HRQOL by parent proxy report.

DISCUSSION

This multicenter study evaluates HRQOL in a large cohort of children affected by biliary atresia surviving with their native livers, and compares them across a spectrum of health, from children who are healthy to those with biliary atresia who have undergone liver transplant, in order to understand the complete impact of this chronic disease. This study captures children with biliary atresia across a broad range of ages and simultaneously reports both the perspective of the child and parent, providing the most comprehensive assessment of HRQOL in biliary atresia to date. This cohort of patients with biliary atresia was generally healthy, with 62% having a state of health considered by the research team to be optimal for a child with this diagnosis. Their HRQOL, however, was significantly poorer than healthy children. In addition, contrary to our expectations, their HRQOL was surprisingly similar to that of patients with biliary atresia who had previously undergone liver transplant and therefore experienced very different medical problems related to the post-transplant state.

Psychosocial functioning in children with biliary atresia surviving with their native livers was significantly impaired compared with a matched healthy population. Psychosocial problems are increasingly identified as “hidden morbidities” across an array of pediatric conditions, now including biliary atresia (12-14). As such, these findings support the need for psychological counseling and the development of peer support groups for children with biliary atresia.

The most significant differences between patients with biliary atresia surviving with their native livers and healthy children occurred in school functioning, a construct that measures missed days of school (which was not assessed in this study) and school-related cognitive functioning (4, 18, 19). Infants and toddlers with biliary atresia are known to have subtle delays in gross motor and language development (20, 21). Cognitive and learning disabilities in older children living with biliary atresia, however, have yet to be quantified. Neurodevelopmental testing that is ongoing in patients with biliary atresia participating in the ChILdREN study may provide further insights into this area in the future.

Self reports of social functioning were poorer among young children (ages 5-12 years) than older adolescents and young adults. This finding may imply a “response shift”, whereby over time children accommodate their perceptions of the negative impacts of biliary atresia

on their lives (17, 23, 24). Furthermore, modeling that included markers of disease severity did not identify a survivor bias in this study, despite the cross sectional nature of the study. Future longitudinal analyses of HRQOL in patients with biliary atresia with their native livers may provide additional insight into this finding.

Unexpectedly, patients with biliary atresia with their native livers were noted to have nearly identical impairments in HRQOL as patients with biliary atresia who had undergone liver transplant. Seventy seven biliary atresia subjects with evidence of more advanced liver disease did not, however, complete HRQOL assessments, which may have skewed these results towards better HRQOL. In addition, although the degree of portal hypertension in patients with biliary atresia with their native livers was difficult to quantify based on recorded physical findings, it is expected that many had a degree of portal hypertension, which might contribute to subclinical or minimal hepatic encephalopathy. In cirrhotic adults with evidence of minimal hepatic encephalopathy on neurocognitive testing, abnormalities improve, but are not completely reversed after liver transplantation (26, 27). Therefore, this may suggest that cognitive deficits associated with portal hypertension in the pre-transplant period in patients with biliary atresia may still contribute to HRQOL in post-transplant follow-up. Longitudinal assessment of neurocognitive deficits and school performance in children with biliary atresia before and after LT will be necessary to fully understand this evolution in pediatric patients.

Self reports by patients with biliary atresia living with their native livers had only moderate agreement with parental HRQOL reports, consistent with previous literature in other chronic diseases (4, 28, 29). The weakest correlation was noted in social functioning, which occurs primarily outside the home in children of school age and beyond and may not be directly observed behavior. This reiterates that simultaneous evaluation of child and parent perceptions of HRQOL should remain the standard practice, providing complimentary but unique perspectives.

In this study, black race in patients with biliary atresia was independently associated with poorer HRQOL. This study did not collect data on socioeconomic status, marital status or education, and therefore, the potential impact of such confounders cannot be assessed. Higher total bilirubin was also associated with poorer HRQOL in patients with biliary atresia. One might speculate that the addition of the biliary atresia children who did not undergo HRQOL testing and who demonstrated significant cholestasis (Table I), could make this association even more robust. Children with more pronounced cholestasis may have more visible signs of disease, including pruritus, nutritional deficiencies, poorer growth, and more frequent medical visits, all of which may contribute to poor HRQOL.

A limitation of this study is that 77 biliary atresia subjects and their families chose not to complete the HRQOL assessment. These subjects had evidence of more advanced liver disease. We speculate that those subjects would have had poor overall HRQOL based on the relationship we found between total serum bilirubin and parent proxy reports of HRQOL. Therefore, our findings in patients with biliary atresia with native livers should be viewed as representing a better outcome than is most likely present in all biliary atresia subjects with their native liver.

In conclusion, despite generally good medical health, patients with biliary atresia with their native livers have significantly impaired HRQOL, similar to that in patients with biliary atresia post-LT. Recognition of this allows for the initiation of a dialogue between the care provider, patient and family, designed to promote individualized long term care to children pre-LT. These findings identify significant deficits in the functioning of patients with biliary atresia that should form the basis for development of comprehensive care plans, with the goal to achieve optimal health.

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Appendix

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Figure.

Mean physical, psychosocial and total summary scores by child self report and parent proxy report were significantly lower (*p: <0.001) than the healthy comparison population, as well as the biliary atresia population post-liver transplant.

Child self-report and parent proxy reports of PedsQL™ 4.0 Physical, Psychosocial and Total Summary Scores

Mean physical, psychosocial and total summary scores by child self report and parent proxy report were significantly lower (*p: <0.001) than the healthy comparison population, as well as the BA population post-liver transplant.

Table 1

Demographic and Medical Characteristics of Biliary Atresia patients surviving with their native livers.

Variable	BA With QoL assessment (n=221)	BA Without QoL Assessment (n=77)	P value
Female (%)	54	62	0.20
White (%)	67	62	0.81
Mean Age at HPE (months)	2.75 ± 9.14	2.72 ± 4.15	0.86
Mean Weight z score	0.37 ± 1.18	-0.33 ± 5.59	0.30
Mean TSF z score	0.16 ± 0.97	-1.02 ± 1.17	0.0008
Mean MAC z score	0.07 ± 1.49	-1.80 ± 2.12	0.0007
Cholangitis (%) *	13.4	22.1	0.07
GI Bleeding (%) *	4.9	10.4	0.09
Total Bilirubin (mg/dL)	1.54 ± 2.36	5.32 ± 8.69	0.007
ALT (mg/dL)	86 ± 108	110 ± 70	0.02
Albumin (g/dL)	4.10 ± 0.54	3.53 ± 0.74	0.09
GGTP (U/L)	139 ± 182	221 ± 238	0.08
INR	1.10 ± 0.15	1.22 ± 0.32	0.02
Hemoglobin (g/dL)	13.4 ± 8.9	11.5 ± 1.7	0.004
WBC (10 ³ /mm ³)	5.9 ± 4.0	11.1 ± 24.4	0.18
Platelet (10 ³ /mm ³)	159 ± 95	172 ± 112	0.46

QoL: Quality of Life; HPE: Hepatopertoenterosotomy; TSF: Triceps Skin Fold; MAC: Mid Arm Circumference; GI: Gastrointestinal;

* Cholangitis or GI bleeding in previous 12 months.

Table 2

A comparison of child self and parent proxy reports of PedsQL™ 4.0 Generic Core Scale Scores in biliary atresia patients with their native livers versus healthy children and biliary atresia after liver transplant.

Scale	Biliary Atresia Native Liver		Healthy Sample		Differences	Effect Size	Biliary Atresia Post-LT		Differences	Effect Size
	Mean	SD	Mean	SD			Mean	SD		
Child Self Report	(n=173)		(n=954)				(n=151)			
Total Score	76.96	13.70	84.70	12.16	7.74*	0.62	75.22	14.56	1.74	0.12
Physical Score	83.41	14.99	88.86	12.31	5.45*	0.43	81.15	16.38	2.26	0.14
Psychosocial Score	73.51	15.53	82.49	14.03	8.98*	0.63	71.95	15.97	1.56	0.10
Emotional Functioning	70.92	20.96	80.56	18.08	9.64*	0.52	71.28	19.07	0.36	0.02
Social Functioning	80.49	16.59	85.51	16.82	5.02*	0.30	78.96	20.92	1.53	0.08
School Functioning	69.13	20.26	81.25	16.49	12.12*	0.71	65.77	17.47	3.36	0.18
Parent Proxy Report	(n=197)		(n=1266)				(n=437)			
Total Score	77.69	16.40	84.58	13.30	6.89*	0.50	78.05	16.83	0.36	0.02
Physical Score	82.04	21.50	87.28	16.35	5.24*	0.31	82.22	16.92	0.18	0.01
Psychosocial Score	75.28	15.91	83.10	13.78	7.82*	0.56	75.66	17.25	0.38	0.02
Emotional Functioning	73.74	17.08	81.86	16.01	8.12*	0.50	73.70	19.42	0.04	0.00
Social Functioning	80.94	18.37	86.49	16.75	5.55*	0.33	80.97	20.19	0.03	0.00
School Functioning	68.35	20.39	80.64	17.69	12.29*	0.68	69.73	21.51	1.38	0.07

Note:

* p < 0.001 based on independent samples t-tests. Effect sizes are designated as small (0.20), medium (0.50) and large (0.80). SD=standard deviation; post-LT=post-liver transplant.

Table 3

Age based Intra-class Correlations (ICC) between Child Self and Parent Proxy-Reports Of the PedsQL™ 4.0 Generic Core Scales for Biliary Atresia Patients surviving with their native livers.

PedsQL™ Scale	Parent-Child Agreement ICC All Ages (n=157)	Parent-Child Agreement ICC 5-7 years (n=54)	Parent-Child Agreement ICC 8-12 years (n=54)	Parent-Child Agreement ICC 13-18 years (n=49)
Total Score	0.49**	0.07	0.66**	0.71**
Physical Health	0.42**	0.12	0.54**	0.71**
Psychosocial Health	0.46**	0.08	0.68**	0.62**
Emotional Functioning	0.39**	0.18	0.65**	0.51**
Social Functioning	0.27**	0.05	0.42*	0.57**
School Functioning	0.48**	0.22	0.65**	0.57**

ICC: Intra-class Correlation. Statistically significant correlations (* $p < .01$, ** $p < .001$) between child self and parent proxy reports of the PedsQL™ 4.0 Generic Core Scales by individual ages groups are indicated in this table.