



Factors influencing the quality of life in children after biliary atresia treatment

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Background: Despite surgical treatment, children with biliary atresia (BA) may face many problems which seriously affect their quality of life. However, there is a paucity of studies in China examining the quality of life of these children after BA treatment. This study investigated the current status of the quality of life of children after BA treatment and analyzed the influencing factors so as to provide a scientific basis for the development of targeted interventional measures.

Methods: From May 1 to May 31, 2021, the STAR questionnaire method was used to conduct cross-sectional surveys in children following BA surgery in the West China Hospital of Sichuan University, China. The basic information questionnaire was used to investigate the general characteristics of the children. The children were also given quality of life questionnaires during follow-up sessions after surgical treatment for BA. In addition, a 12-point health survey was used to assess the physical and mental health of the children's caregivers. Age- and gender-matched healthy children were recruited as controls. Correlation analysis and multiple linear regression equations were established to explore the influencing factors of the quality of life of children after surgery for BA.

Results: After surgery, children with BA experienced significantly lower physical health, emotional function, social function, cognitive function, and quality of life compared to healthy children ($P < 0.050$). Co-existing diseases had a statistically significant impact on the quality of life of children with BA ($b = -12.566$; $t = -2.343$; $P = 0.021$), and the caregiver's understanding level of liver transplantation also had a statistically significant impact on the quality of life of these children ($b = 6.481$; $t = 2.376$; $P = 0.021$).

Conclusions: The quality of life of children after BA surgery was significantly lower than that of age-matched healthy children. Co-existing diseases and the caregiver's understanding level of liver transplantation were the main factors affecting the quality of life of these children.

Keywords: Biliary atresia (BA); children's quality of life questionnaire; 12-item health survey; quality of life; influencing factors

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Introduction

Biliary atresia (BA) is a serious congenital hepatobiliary disease characterized by dysfunction and occlusion of the intrahepatic and extrahepatic bile ducts and liver fibrosis, the pathogenesis is still unclear, and the current main point of view is that it is related to viral infection in the embryonic or perinatal period. The incidence of BA ranges from 1 in 5,000 to 1 in 12,000 (1), with a higher incidence in Japan and China compared to that in Europe and America. Without treatment, the average survival period is less than 1 year and approximately 75% of children will require liver transplantation for long-term survival (2). At present, the main form of treatment for children with BA is the Kasai operation. Advances in this technique and improved public cognition of the condition have seen the 2-year autologous liver survival rate approach 60% (3). However, children with BA can still face many serious complications after surgery, including postoperative cholangitis, portal hypertension, variceal bleeding, biochemical abnormalities, hepatic osteodystrophy, growth problems, and problems associated with long-term use of high-dose hormones. All this can lead to a significant decline in the quality of life and serious financial burden. However, the few studies reporting the quality of life of BA children after surgery remain controversial. Some studies have reported that about 50% of children experienced a low quality of life after BA (4), especially in the 5–12 year age group (5). On the contrary, other reports have suggested that children with BA experience the same quality of life as healthy children in adulthood (6–8). This current study investigated the current quality of life of children after BA treatment and analyzed the influencing factors. We present the following article in accordance with the SURGE reporting checklist (available at <https://dx.doi.org/10.21037/tp-21-391>).

Methods

Participants

Children with BA who were diagnosed and underwent surgery in the West China Hospital of Sichuan University from May 1 to May 31, 2021, were recruited for this study. Age- and gender-matched healthy children were enrolled as the control group. The STAR questionnaire method was used to survey the children during follow-up consultations. Children were included in the study if they met the following inclusion criteria: (I) a confirmed BA diagnosis and all operations were completed in the West China Hospital

of Sichuan University; (II) the quality of life questionnaire was administered 3 months or more after the completion of the surgery; (III) the questionnaire was completed with no conflicting content; and (IV) the caregiver spent ≥ 4 hours/day caring for the child in the past month and voluntarily participates in this investigation. The following exclusion criteria were applied: (I) children presenting with co-existing diseases that seriously affect the quality of life, such as esophageal atresia, chromosomal abnormalities, cyanotic heart disease, and other organ dysfunctions; and (II) the caregiver cannot correctly understand and complete the questionnaire due to cultural, medical, or other reasons.

Research tools

Questionnaire for the basic characteristics of the child

This form was designed in-house and includes the following basic information: the child's age, gender, place of residence, number of siblings, family plans to have another child, the child's feeding routine, co-existing diseases, method of surgery, and the child's age at the time of surgery.

Questions related to the child's family include the following: the marital status of the child's family, the type of family where the child lives, the main daily caregiver of the child, the education status of the main caregiver, the caregiver's understanding level of BA and liver transplantation, the monthly family income, the payment method for medical expenses, and the average monthly costs associated with the child post-surgery.

Questions related to post-surgical status include the following: duration of oral antibiotic administration post-surgery, regular follow-up visits to the hospital, presence or absence of cholangitis, when cholangitis occurs and whether it is complicated with other systemic infections, and the work conditions and emotional well-being of the caregivers post-surgery.

Chinese Mandarin version of the Pediatric Quality of Life Inventory [TM] (PedsQL[TM]) 4.0 (9)

The Pediatric Quality of Life Inventory scale was released in 2011 and is divided into a standard version and a short-term version. For children over 5 years old, there is a self-filled version and a parent-filled version. This study used the standard version and the parent-filled version to investigate the quality of life of children up to 18 years old. There are four dimensions to this questionnaire: physical health, emotional function, social function, and cognitive function. The latter three dimensions collectively reflect

the psychological and social well-being of the children. The number of items and behavior descriptions in each dimension differ slightly for different age groups. Each item is a survey of the frequency of an event in the most recent month. There are 5 possible answers ranging from 0 to 4, with 0 representing never, 1 representing almost never, 2 representing sometimes, 3 representing often, and 4 representing almost always. These scores are then converted to 100 points, 75 points, 50 points, 25 points, and 0 points, respectively. The total score for each dimension is the sum of the scores of the answered items divided by the full marks of these items. The scores of each dimension range from 0 to 100. The higher the score, the better the quality of life. The use of the PedsQL[™] scale has been authorized by Professor JW Varni and the translated Chinese version has been verified by the issuing agency.

The 12-item short form health survey (SF-12)

The 12-item short form health survey (SF-12) (10,11) is an abbreviated form of the 36-item health survey with the advantages of being concise, easy-to-understand, and quick to fill in. SF-12 has been widely used in different countries and regions to assess health-related quality of life. The SF-12 scale has 12 items and 8 dimensions for assessing health-related quality of life, including physical functioning (PF), role-physical (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Among them, PF, RP, BP and GH are included in the physical component summary (PCS), while VT, SF, RE, and MH are included in the mental component summary (MCS). The higher the score, the better the health-related quality of life.

Research methods

This study adopted a cross-sectional survey method and the STAR questionnaire method was used. Surveys were carried out in the follow-up group of BA children in West China Hospital of Sichuan University. The basic information questionnaire was used to collate the general data of the children, the PedsQL[™] was used to assess the quality of life of children after BA, and the SF-12 scale was used to evaluate the physical and mental health of the caregivers of the children. Information regarding the purpose, meaning, medical ethics, confidentiality, and voluntary nature of the questionnaire, as well as the filling requirements and precautions were provided to the participants prior to completion of the survey. After the questionnaire was

completed, it was verified by 3 investigators, and a pre-survey was conducted among the family members of the children, and the questionnaire was released after confirmation. There were 6 investigators in the follow-up group, including 1 associate professor, 2 attending physicians, 1 pharmacist, 1 nurse-in-charge, and 1 nurse. All investigators have been uniformly trained. Data export, sorting, and analysis was verified by two independent researchers.

Sample size

According to the rough estimation method of sample content proposed by Kendall, the sample size is generally determined as 10–20 times the survey index (12). In this study, the PedsQL[™] scale has 4 dimension items, and SF-12 has 8 dimension items, that is, 80 examples around the sample.

Statistical analysis

The SPSS 26.0 software was used for data processing and statistical analysis. Normally distributed measurement data is represented by mean \pm standard deviation ($\bar{x}\pm s$), non-normally distributed measurement data is represented by median (interquartile range) [M (IQR)], and count data is represented by frequency and composition ratio. The bivariate rank correlation analysis method was used for single-factor correlation analysis, and the variables with statistical differences in the single-factor correlation analysis were included as independent variables to construct a multi-factor linear regression equation. A two-sided test was used, and the test level was set to $\alpha=0.05$.

Ethical principles

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study has been reviewed and approved by the Biomedical Ethics Committee of the West China Hospital, Sichuan University, China (approval number: #20191082) and informed consent was taken from parents of all the patients.

Results

Inclusion of research subjects

Between May 1 to May 31, 2021, 79 questionnaires were

Table 1 Comparison of quality of life scores between children with biliary atresia and age-matched healthy children (points)

Projects	Physical health summary	Emotional function	Social function	Cognitive function	Total
BA	47.31±20.12	42.98±21.04	54.41±20.53	50.97±21.99	46.84±18.11
Health	76.21±19.41	70.56±22.40	79.03±20.20	73.09±22.15	74.00±18.25
t	7.822	6.852	6.480	5.385	8.026
Point probability	<0.001	<0.001	<0.001	<0.001	<0.001
Mean difference (95% CI)	28.89 (21.58 to 36.21)	27.58 (19.61 to 35.55)	24.62 (17.10 to 32.14)	22.12 (13.98 to 30.25)	27.1 (20.46 to 33.86)

BA, biliary atresia; CI, confidence interval.

received. A total of 10 questionnaires were excluded, including 4 repeated questionnaires, 2 questionnaires with incorrect information, and 4 mismatches in filling in the 3 scales. A total of 70 valid questionnaires (88.61%) from 70 children were enrolled, including 31 males and 39 females, with an average age of 11 months (IQR, 34.5 months). A total of 49 questionnaires were collected from age- and gender-matched children. The average age of children in the normal group was 11 months (IQR, 32.9 months), with 22 males and 27 females. The negative emotions of the caregivers were mainly manifested as fatigue (61.4%) and depression (44.3%), while 11.4% felt unbalanced, 20.0% felt lonely, and 27.1% felt that they were easy to anger. Unfortunately, only 27.1% of caregivers did not report any particular feelings.

A comparison of the quality of life scores between BA children and age-matched healthy children

Following surgery, children with BA had significantly lower scores for physical health, emotional function, social function, cognitive function, and quality of life compared to age-matched healthy children ($P < 0.050$; *Table 1*).

Univariate analysis of the factors affecting the quality of life in BA children after treatment

The quality of life of BA children post-surgery was significantly correlated with co-existing diseases ($r = -0.277$; $P = 0.020$), understanding level of liver transplantation ($r = 0.254$; $P = 0.034$), the payment method of medical expenses ($r = -0.275$; $P = 0.021$), the average monthly medical expenses post-surgery ($r = -0.301$; $P = 0.011$), and the duration of oral antibiotics administration ($r = 0.358$; $P = 0.002$). See *Table 2* for details.

Multiple linear regression analysis of the quality of life of children after BA treatment

Taking the total score of the physical health of the children after BA as the dependent variable, and statistically significant variables in single-factor correlation analysis were included as independent variables to construct a multivariate linear regression equation. The results showed that co-existing diseases had a statistically significant impact on the quality of life of children with BA ($b = -12.566$; $t = -2.343$; $P = 0.021$). Furthermore, the caregiver's understanding level of liver transplantation also exerted a significant impact on the quality of life of BA children after surgery ($b = 6.481$; $t = 2.376$; $P = 0.021$). The model fit (adjusted R^2 value) was 0.208. The hypothesis test result of the regression model showed $F = 4.630$ and $P = 0.001$ (*Table 3*).

Discussion

Health-related quality of life (HRQoL) is an important reference index for providing long-term comprehensive care for children with chronic diseases, and can enable medical workers to better understand the health status of such children (13,14). Problems related to the quality of life have gradually become the "hidden pathology" of chronic diseases such as BA, but there are few studies on the quality of life of children with BA, especially in China. Consistent with the findings of Sundaram *et al.* (5), this study confirmed that the scores of all dimensions of quality of life were significantly lower in BA children post-surgery compared to those of healthy children. Furthermore, when children with BA have co-existing diseases, their quality of life will further decline, and thus developing management and support strategies for these patients is crucial.

Kasai portojejunostomy is currently the preferred treatment for BA (15) to relieve cholestasis and inflammation

Table 2 The univariate correlation analyses of the factors affecting the quality of life of children with biliary atresia

Variables	N (%) / ($\bar{x}\pm s$) / M (IQR)	r	Point probability
Gender		0.014	0.912
Male	31 (44.3)		
Female	39 (55.7)		
Current age (m)	11 (34.5)	0.119	0.327
Place of residence		0.058	0.635
City	44 (62.9)		
Rural	26 (37.1)		
Only child		-0.098	0.421
Yes	29 (41.4)		
No	41 (58.6)		
Plans to have another child		0.090	0.460
Yes	18 (25.7)		
No	52 (74.3)		
Feeding method		-0.150	0.215
Breastfeeding	16 (22.9)		
Mixed feeding	25 (35.7)		
Artificial feeding	29 (41.4)		
Co-existing diseases		-0.277	0.020
No	58 (82.9)		
Yes	12 (17.1)		
Surgical approach		0.162	0.180
Kasai operation	58 (82.9)		
Others	12 (17.1)		
Children's age at the time of surgery (m)	2 (1.25)	-0.046	0.708
Marital status of the family		-0.227	0.059
Married	68 (97.1)		
Divorced	2 (2.9)		
Family types		0.052	0.668
Nuclear family (a family of three or living with parents and siblings)	38 (54.3)		
Single parent (divorced or widowed)	1 (1.4)		
Extended family (living with grandparents)	31 (44.3)		
Primary caregiver		0.092	0.450
Parents	56 (80.0)		
Grandparents	9 (12.9)		
Others ^a	5 (7.1)		

Table 2 (continued)

Table 2 (continued)

Variables	N (%) / ($\bar{x}\pm s$)/M (IQR)	r	Point probability
Education status of primary caregiver		0.051	0.675
Elementary school or below	9 (12.9)		
Junior high school	14 (20.0)		
Senior school or technical secondary school	19 (27.1)		
University or above	28 (40.0)		
Understanding level of biliary atresia		0.203	0.092
Never heard of it, don't know at all	2 (2.9)		
Heard of it, but don't know much	5 (7.1)		
Have consulted the information and know part of it	34 (48.6)		
Well-known	29 (41.4)		
Understanding level of liver transplantation		0.254	0.034
Never heard of it, don't know at all	2 (2.9)		
Heard of it, but don't know much	11 (15.7)		
Have consulted the information and know part of it	39 (55.7)		
Well-known	18 (25.7)		
Family monthly income		0.539	0.075
Below 775 USD	29 (41.4)		
775–1,549 USD	22 (31.4)		
1,549–3,098 USD	12 (17.1)		
Above 3,098 USD	7 (10.0)		
Method of payment for medical expenses		–0.275	0.021
All at your own expense	13 (18.6)		
Social security	54 (77.1)		
Other methods ^b	3 (4.3)		
Average monthly post-operative medical costs (USD)	310 (310)	–0.301	0.011
Duration of oral antibiotics administration after surgery (m)	5 (3.25)	0.358	0.002
Do the children go to hospital regularly for follow-up?		0.012	0.920
No	3 (4.3)		
Yes	67 (95.7)		
Has the child experienced cholangitis post-operatively?		–0.107	0.379
No	36 (51.4)		
Yes	34 (48.6)		
Did cholangitis occur with other systemic infections?		–0.228	0.058
No	58 (82.9)		
Yes	12 (17.1)		

Table 2 (continued)

Table 2 (continued)

Variables	N (%) / ($\bar{x}\pm s$)/M (IQR)	r	Point probability
Work status of the main caregiver after the child's operation		-0.177	0.142
Full time job	13 (18.6)		
Half-work and half-rest	13 (18.6)		
No job	44 (62.9)		
Physical health of caregiver after the child's surgery (PCS)	44.60±5.53	0.158	0.191
Psychological health of caregiver after the child's surgery (MCS)	44.81±7.81	0.223	0.064

^a, other options for the main caregiver of the child's daily life refer to the combination of parents and (grand) parents or the combination of nanny and other people; ^b, other methods of payment of medical expenses refer to hospitals or poverty subsidies and a combination of methods including own expense. IQR, interquartile range; m, months; USD, United States Dollar; PCS, physical component summary; MCS, mental component summary.

Table 3 Multiple linear regression analysis of the quality of life of children after biliary atresia

Variables	b	Std. Error	Sig.	P	95% CI for b
Co-existing diseases ^a	-12.566	5.317	-2.343	0.021	-23.189 to -1.943
Understanding level of liver transplants	6.481	2.728	2.376	0.021	1.031 to 11.930
Method of payment for medical expenses	-3.668	2.237	-1.640	0.106	-8.136 to 0.800
Average monthly post-operative medical costs	-0.001	0.000	-1.799	0.077	-0.001 to 0.000
Duration of oral antibiotics administration after surgery (m)	0.543	0.298	1.835	0.073	-0.051 to 1.138

^a, no other diseases are used as a reference. *, P values indicate that the independent variable has a statistical significance on the dependent variable in the regression equation.

in the portal area (16). However, liver fibrosis may progress even after surgery (17), especially with recurring cholangitis which causes continuous damage to the liver (18). Studies have shown that about 60% of children still require liver transplantation before the age of 20 (19-21), and some studies have also shown that patients undergoing liver transplantation have a higher long-term survival rate than those undergoing Kasai surgery (22). Increasingly, families of children with BA have realized that eventually liver transplantation may be required and has high expectations for liver transplantation. Unfortunately, at present, there is a lack of readily available information regarding pediatric liver transplantation. This lack of knowledge can cause anxiety in caregivers, which indirectly translates to a decline in the children's quality of life. This study confirmed that the caregiver's knowledge of liver transplantation affects the quality of life of the child. Therefore, medical staff should take the initiative to provide relevant knowledge about liver transplantation and answer the questions of caregivers of

children with BA. At the same time, the writing of popular science books on pediatric liver transplantation and the popularization of pediatric liver transplantation scientific knowledge should be strengthened.

Studies have found that the method of payment of medical expenses is related to the social living standard and quality of life of children after liver transplantation, and children with medical insurance have a higher quality of life than children without medical insurance (23,24). However, no similar reports have been found in children with BA. As BA is also a disease that exerts a huge financial burden on families, the method of payment of medical expenses may be related to the quality of life of these children. Unexpectedly, multiple linear regression analysis revealed that the payment method of medical expenses and the monthly medical costs incurred did not affect the quality of life of children with BA. It is possible that with improvements in China's social security system, the vast majority of rural and urban residents can access a basic social medical insurance or

other subsidies. In this survey, the hospitalization expenses were fully self-funded in only 18.57% of children, with the remainder of children being funded by medical insurance or other subsidies. Therefore, families with reasonable medical insurance will experience less financial burden, which translates to improved quality of life for the sick child.

Cholangitis is the most common complication following Kasai surgery, with a reported incidence of 30–60%, and it also affects a considerable number of adult patients (7,25,26). Patients with more frequent and severe the postoperative cholangitis will experience poorer bile drainage, more obvious itching and nutritional deficiencies, and rapidly deteriorating liver fibrosis (27–29). Moreover, studies have shown that there is a correlation between the quality of life of children undergoing liver transplantation and the occurrence of postoperative complications (30). Therefore, one might speculate, that recurrent cholangitis may have a significant impact on the quality of life in children, there is a lack of literature to support this. The current study examined the incidence of cholangitis in children with BA, however, there was no correlation between the incidence of cholangitis and the quality of life of these children. This may be related to the establishment of a comprehensive follow-up system after BA surgery in the hospital, including an online booking system for postoperative follow-up appointments. Furthermore, postoperative management is conducted by a multi-disciplinary team which includes surgeons, clinical pharmacists, and nursing experts. All this facilitates the early detection and treatment of cholangitis in these children, thereby relieving caregiver stress and improving the quality of life of the children.

This study also investigated the emotional feelings of caregivers of BA children and found that only 27.1% had no particular emotional feelings. Nearly half of the caregivers felt tired and depressed. As the emotional response of caregivers can be transmitted to children through long-term daily contact, medical staff should pay attention to the mental well-being of caregivers and provide psychological counseling and support if required, so as to avoid negatively impacting the physical and mental health of the children.

This study had certain limitations. The cross-sectional survey design could not provide sufficient information on changes in the quality of life. Future studies should lengthen the follow-up period to investigate the changes in the quality of life of the same population over 1, 2, 3, and 5 years. Furthermore, the impact of liver transplantation on the quality of life of children with BA should be assessed.

Conclusions

This study demonstrated that the quality of life of BA children after surgery is significantly lower than that of age-matched healthy children. The main influencing factors on the quality of life are co-existing diseases, the caregiver's understanding level of liver transplantation, and the caregiver's emotional coping ability. Thus, there should be a particular focus on BA children with co-existing diseases by providing accessible treatment and nursing care. It is also vitally important to provide knowledge and emotional support to caregivers so as to prevent their stress exerting a negative impact on the quality of life of BA children after surgery.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Biomedical Ethics Committee of the West China Hospital, Sichuan University, China (#20191082) and informed consent was taken from parents of all the patients.

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