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Health-related quality of life (HRQOL) in children and adolescents with congenital heart disease: a cross-sectional survey from South India

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ABSTRACT

Objective There are limited data on health-related quality of life (HRQOL) for children and adolescents with uncorrected congenital heart disease (CHD) from low-income and middle-income countries where late presentation is common. We sought to compare HRQOL of children and adolescents with uncorrected CHD to that of controls using the Pediatric Quality of Life Inventory (PedsQL 4.0).

Methods The study design is a cross-sectional analytical survey. The study setting was (1) Hospital-based survey of patients with CHD and their parents. (2) Community survey of controls and their parents. Subjects included (1) Children/adolescents with CHD between the ages of 2 years and 18 years and their parents enrolled in a previous study (n=308). (2) Unmatched community controls (719 children/adolescents, aged 2–18 years) and their parents. Participants were given PedsQL 4.0 to fill out details. Parents assisted children 5–7 years of age in filling the questionnaires. Children younger than 5 years had only parent-reported HRQOL and those above 5 years had both self-reported and parent-reported HRQOL.

Results The median (IQR) total generic HRQOL from self-reports for CHD subjects and controls were 71.7 (62.0, 84.8) and 91.3 (82.6, 95.7), respectively. The corresponding figures for parent-reports were 78.3 (63.0, 90.5) and 92.4 (87.0, 95.7) respectively. The adjusted median difference was −20.6 (99% CI −24.9 to −16.3, p<0.001) for self-reported and −14.1 (99% CI −16.7 to −11.6, p<0.001) for parent-reported total HRQOL between patients with CHD and controls. Cardiac-specific HRQOL by self-reports was 75.0 (53.6, 92.9) for heart problems, 95.0 (73.8, 100.0) for treatment barriers, 83.3 (66.7, 100.0) for physical appearance, 87.5 (62.5, 100.0) for treatment-related anxiety, 91.7 (68.8, 100.0) for cognitive problems and 83.3 (66.7, 100.0) for communication. The values for parent-reports were 71.4 (53.6, 85.7), 100.0 (75.0, 100.0), 100.0 (75.0, 100.0), 81.3 (50.0, 100.0), 100.0 (81.2, 100.0) and 83.3 (50.0, 100.0), respectively.

Conclusions Children and adolescents with uncorrected CHD reported significant reductions in overall quality of life compared with controls.

What is already known on this topic?

- Measurement of health-related quality of life (HRQOL) is essential for assessing the overall physical, psychological and social well-being of children and adolescents with congenital heart disease (CHD).
- Reduction in HRQOL during childhood and adolescence for those with CHD and attendant comorbidities such as neurodevelopmental issues, may have long-term negative consequences.

What this study hopes to add?

- HRQOL of Indian children and adolescents with uncorrected CHD differs significantly from their control counterparts.
- There is an overall reduction in total HRQOL as well as specific deficits in all scales except social functioning for patients with CHD compared with controls.
- The clinical severity of CHD appears to have minimal impact on overall HRQOL.

INTRODUCTION

Congenital heart disease (CHD) accounts for nearly a third of all major congenital anomalies.[1] Cardiovascular diagnostics and cardiothoracic surgery witnessed tremendous advancements during the past century. These advancements played a significant role in the increased survival of newborns with CHD to adulthood.[1] Accordingly, the focus has shifted from mere survival to better management of the morbidity including poor quality of life, neurodevelopmental problems and issues related to educational as well as employment outcomes. Health-related quality of life (HRQOL) is a quantification of the influence of a known illness, therapy or health policy on the ability of the individual patient to both function in and derive personal satisfaction

from various physical, psychological and social life contexts.[2] There is deficiency of data regarding HRQOL among children/adolescents with chronic illness including CHD from low-income and middle-income countries (LMICs).

HRQOL assessment in CHD is often complicated by multiple disease categories, heterogeneity of disease severity, choice of therapeutic modalities and wide spectrum of possible outcomes.[3] Significant determinants of HRQOL in children/adolescents with CHD come under the domains of neurodevelopmental, psychosocial and physical impairments.[4] All such impairments are known to directly impact the overall clinical outcomes in CHD.[4] Recent studies have documented significant HRQOL deficiencies among infants, children and adolescents with CHD in comparison to their normal counterparts.[5–8] A previous study from Kerala, India have documented that infants/toddlers with uncorrected CHD have significantly reduced HRQOL compared with controls.[5] This HRQOL reduction was seen for both physical and psychosocial domains.[5]

There is a need for HRQOL estimation during childhood among those with CHD due to the probable detrimental effect that its reduction can cause in the long term.[9] The study institution is a tertiary-care teaching hospital in Kerala, India and the paediatric cardiac division caters mainly to patients from southern states of India across all socioeconomic strata from rural and urban areas.

The primary objective of this study was to compare parent-reported generic HRQOL of children/adolescents aged 2–18 years with uncorrected CHD to that of controls using Pediatric Quality of Life Inventory (PedsQL 4.0). The secondary objectives were to (1) Compare self-reported generic HRQOL of children/adolescents with uncorrected CHD to that of controls. (2) Examine the association between functional class categories (FCCs) of CHD and HRQOL. (3) To report cardiac disease-specific HRQOL of children/adolescents with CHD.

METHODS

The study was coordinated by the Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala, India. The period of study was 42 months (January 2013 to June 2016). The study design is a dual-setting cross-sectional survey (hospital setting for CHD subjects and community setting for controls). We used the study by Uzark *et al* to calculate the effect size.[7] Uzark *et al* reported an effect size of 0.6 for HRQOL difference between patients with CHD and controls (2–18 years) via parent-reports.[7] We selected an α of 0.01 and 0.80 of desired power, providing us with a minimum sample size of 67 parent-reports each from both groups. All children/adolescents with CHD along with their parents (n=308) enrolled in a previous study were included in the current study. We recruited 719 controls by means of a community survey, the results of which were published recently.[10] The revised sample size enabled us to pick a mean difference in parent-reported HRQOL of 3.8 (effect size of 0.3) for this comparison (CHD vs controls). We used the parent-reported HRQOL for the primary objective as this was available for the whole sample. Self-reported HRQOL was available only for those aged 5 years and above. The best practice is to report both. We increased the sample size anticipating subgroup differences in HRQOL based on FCCs of CHD.[11]

Children/adolescents with uncorrected CHD were recruited by consecutive sampling from the patients under care at the study institution. The inclusion criteria were (1) Children/adolescents aged 2–18 years visiting the hospital for cardiac evaluation and planned surgery. (2) Those with a confirmed diagnosis of CHD. (3) Children/adolescents from families who can comprehend local languages (Malayalam/Tamil). The exclusion criteria included children/adolescents who present in an acute stage requiring intensive care treatment and/or emergency surgical correction. The controls were selected from 40 randomly selected clusters within a circular geographical area having a radius of 10 km from the study institution. The method of control selection was stratified random cluster sampling. The cluster size was 18. Controls were enrolled sequentially from a random start point within each cluster. The inclusion criteria for controls were (1) Children aged 2–18 years. (2) Children/adolescents from families who can comprehend local languages (Malayalam/Tamil). (3) Those residing in the selected clusters for more than 1 year. Children with ongoing acute illness or chronic illness in the preceding 6 months were excluded. The controls were not matched for age, gender, domicile or socioeconomic class. Other details of sample selection are available in an earlier publication.[10]

The tool administrations were conducted in-hospital for CHD subjects and at home for controls. Written informed consent was obtained from parents/caretakers before collecting data. In addition, assent was obtained from children 7 years or older. The PedsQL 4.0 Generic Core and Cardiac modules for children/adolescents and their parents were used to collect HRQOL data.[12] All enrolled subjects had a parent-reported HRQOL. In addition, all children older than 5 years as well as adolescents filled out the appropriate self-report form of PedsQL 4.0. Parents assisted children aged 5–7 years in filling the questionnaires. We used the modified Kuppuswamy's Socioeconomic Scale (2012) to report socioeconomic class (SEC).[13] We used the functional class classification (FCC) of CHD to classify CHD subjects.[11] The acyanotic CHDs were classified into two groups: (1) Left to right shunts (LRS). (2) Left-sided obstructive lesions (LSOL). The cyanotic CHDs were classified into three groups: (1) Lesions with decreased pulmonary blood flow (DPB). (2) Lesions with increased pulmonary blood flow (IPB). (3) Single ventricle physiology (SVP). We defined adolescents as those aged between 13 years and 18 years.

Table 1 Baseline characteristics of the study sample

	CHD		Controls	
	Parent proxy report	Child report	Parent proxy report	Child report
Demographics	N (%)	N (%)	N (%)	N (%)
All	308	155	719	585
Age group				
2–4 years	147 (47.7)	–	133 (18.5)	–
5–7 years	67 (21.8)	64 (41.3)	121 (16.8)	121 (20.7)
8–12 years	52 (16.9)	50 (32.3)	244 (34.0)	244 (41.7)
13–18 years	42 (13.6)	41 (26.5)	221 (30.7)	220 (37.6)
Gender				
Male	166 (53.9)	90 (58.1)	344 (47.8)	280 (47.9)
Female	142 (46.1)	65 (41.9)	375 (52.2)	305 (52.1)
Domicile				
Urban	71 (23.1)	34 (21.9)	504 (70.1)	416 (71.1)
Rural	237 (76.9)	121 (78.1)	215 (29.9)	169 (28.9)
Socioeconomic class*				
Upper	16 (5.2)	9 (5.8)	19 (2.6)	11 (1.9)
Upper middle	138 (44.8)	63 (40.6)	320 (44.5)	266 (45.5)
Lower middle	103 (33.4)	55 (35.5)	252 (35.0)	204 (34.9)
Upper lower	51 (16.6)	28 (18.1)	128 (17.8)	104 (17.8)
Functional class categories				
Acyanotic CHD 1	1	151 (49.0)	64 (41.3)	
	2	5 (1.6)	3 (1.9)	
Cyanotic CHD	1	77 (25.0)	36 (23.2)	
	2	13 (4.2)	10 (6.5)	
	3	52 (16.9)	38 (24.5)	
	Others	10 (3.2)	4 (2.6)	

*Socioeconomic class was defined by the modified Kuppuswamy's Scale 2012.[13]
CHD, congenital heart disease.

Study tool: PedsQL 4.0

The PedsQL 4.0 generic module for 2–18 years consists of 23 items in four scales—Physical Functioning, Emotional Functioning, Social Functioning and School Functioning.[12] The PedsQL 3.0 cardiac module has 22 items under five scales—symptoms, perceived physical appearance, treatment anxiety, cognitive problems and communication.[7] In addition, a treatment barriers scale is included for patients on medications. The study tool was available in English and was translated to two local languages (Malayalam and Tamil) by the study team. The local language versions were then back translated to English by another team not exposed to the English version. The original and back translated versions were checked for content validity and concurrence by an expert team. The tool was then provided in Malayalam and Tamil. A 5-point Likert response scale (0–4) was employed for scoring responses from subjects. All items were reverse-scored and linearly transformed to a 0–100 scale (0=100, 1=75, 2=50, 3=25, 4=0) for better interpretation. Component scale scores were then calculated as the sum of the items divided by the number of items answered. Higher scores on scale signify better HRQOL.

Statistical analysis

Statistical analyses were conducted using SAS V.9.4 for Windows (SAS Institute, Cary, North Carolina, USA). All continuous variables are presented as median (IQR) and categorical variables as number (percentage). Adjusted median differences in HRQOL between the two main groups (CHD and controls) and between subgroups were estimated by quantile regression models and 99% CIs computed using the Markov chain marginal bootstrap algorithm. Subgroup analyses were examined for statistical significance and Bonferroni corrected p values were reported to account for multiple comparisons. All missing data were treated as per instructions in the reference paper.[12]

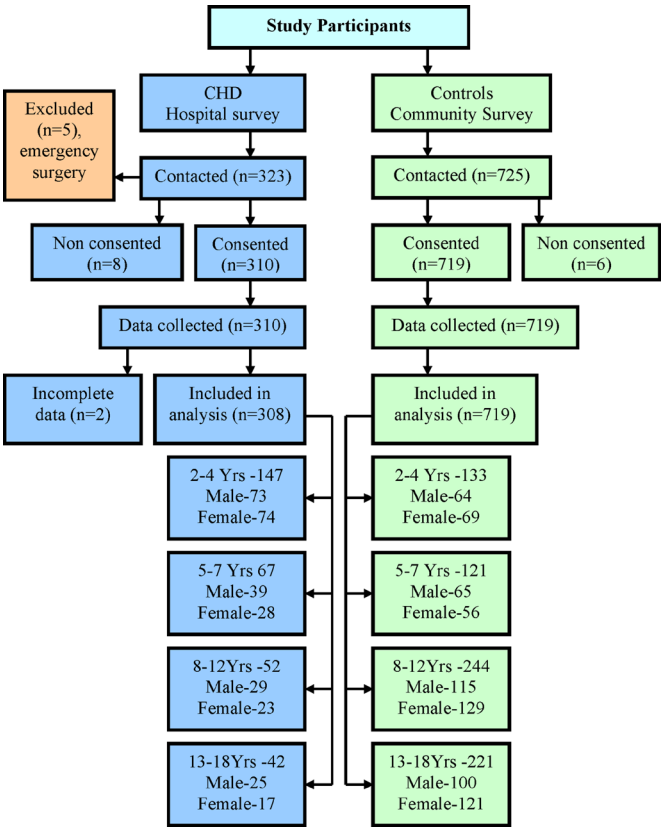

Figure 1 Study flow chart. CHD, congenital heart disease.

Patient involvement

The study concept was largely the consequence of cumulative patient and family experiences over the last 15 years that were shared with the treating team (study investigators). Patients and their parents were involved at the initial stages of questionnaire development. The study questionnaires were designed, translated and contextualised through dedicated patient/parent meetings. We plan to share a plain language summary of results with our CHD patient support group and Non-governmental organizations(NGOs) that work with us and other paediatric heart programmes in LMICs.

RESULTS

Baseline data

We enrolled 764 children (266 with CHD, 498 controls) and 263 adolescents (42 with CHD, 221 controls) along with their parents/caretakers providing us with a total sample of 1027 subjects. All controls and 281 subjects with CHD (91.2%) were from the state of Kerala and the remaining from the neighbouring state of Tamil Nadu. The details of the study population are presented in table 1. Among subjects with CHD, 67 (21.8%) had a history of prior cardiac surgical intervention and 166 subjects (53.9%) reported taking cardiac medications. Among the 67 subjects who reported a history of prior cardiac surgical intervention, 50 were on cardiac medications. A total of 183 subjects with CHD (59.4%) had some form of cardiac disease-related treatment at the time of enrolment.

The overall response to the hospital and community surveys were 97.5% and 99.17%, respectively. The recruitment details and response rates are graphically presented as figure 1. Among generic HRQOL measurements, 98.67% of the self-reports and 97.9% of parent-reports had complete data from among reports where domain-specific response was applicable. We excluded calculating domain values where more than half of the questions under each domain were left unanswered to comply with recommendations.[12]

Generic HRQOL in children and adolescents with CHD and their controls

The median parent-reported generic total HRQOL was 78.3 (63.0, 90.5) for CHD subjects and 92.4 (87.0, 95.7) for controls. The corresponding figures for self-reports were 71.7 (62.0, 84.8) and 91.3 (82.6, 95.7), respectively. The age-stratified values are presented in table 2.

Comparison of generic HRQOL between controls and patients with CHD

We compared generic total HRQOL and component scales between patients with CHD and controls (tables 2 and 3). The median differences were adjusted for age, gender, socioeconomic status and domicile. The adjusted median difference in total parent-reported generic HRQOL between patients with CHD and controls was −14.1 (99% CI −16.7 to −11.6, p<0.001). The corresponding figure for self-reports was −20.6 (99% CI −24.9 to −16.3, p<0.001).

All HRQOL scale medians were significantly lower for patients with CHD compared with controls except for social functioning by parent-reports (tables 2 and 3). Physical health summary, psychosocial summary and school functioning showed significant differences across all age-stratified comparisons. Social functioning showed significant differences across all age-stratified comparisons except for parent-reports from 2 years to 4 years. Comparisons for emotional functioning showed mixed results (tables 2 and 3).

Cardiac disease-specific HRQOL in children and adolescents with CHD

The disease-specific HRQOL of patients with CHD were examined by the PedsQL cardiac module. The values were 71.4 (53.6, 85.7) for heart problems and treatment, 100.0 (75.0, 100.0) for treatment barriers, 100.0 (75.0, 100.0) for perceived physical appearance, 81.3 (50.0, 100.0) for treatment anxiety, 100 (81.2, 100.0) for cognitive problems and 83.3 (50.0, 100.0) for communication from parent-reports. The corresponding values for self-reports were 75.0 (53.6, 92.9), 95.0 (73.8, 100.0), 83.3 (66.7, 100.0), 87.5 (62.5, 100.0), 91.7 (68.8, 100.0) and 83.3 (66.7, 100.0), respectively. The details are presented as table 4 below.

Table 2 Comparison of total and component scores of self-reported HRQOL: controls versus CHD subjects

	Controls		CHD		Adjusted median	
Scale	N	Median (IQR)	N	Median (IQR)	Difference (99% CI)	P values
5–7 years						
Total scale score	121	91.3 (87.0–95.7)	64	80.4 (67.4–89.1)	−12.0 (−18.0 to −5.9)	<0.001
Physical health summary	121	100.0 (93.8–100.0)	64	81.3 (64.1–92.2)	−18.8 (−22.2 to −15.3)	<0.001
Psychosocial health summary	121	90.0 (83.3–93.3)	64	78.9 (67.6–90.0)	−10.0 (−16.0 to −4.0)	<0.001
Emotional functioning	121	80.0 (70.0–90.0)	64	80 (60.9–100.0)	0.0 (−9.5 to 9.5)	1.000
Social functioning	121	100.0 (100.0–100.0)	64	80 (80.0–100.0)	−20.0 (−20.0 to −20.0)	<0.001
School functioning	121	90.0 (80.0–100.0)	61	80 (60.0–95.0)	−10.0 (−19.7 to −0.3)	0.008
8–12 years						
Total scale score	244	91.3 (82.6–95.7)	50	67.1 (54.3–77.2)	−23.9 (−29.1 to −18.7)	<0.001
Physical health summary	244	96.9 (87.5–100.0)	50	67.3 (52.3–82.0)	−31.3 (−41.6 to −20.9)	<0.001
Psychosocial health summary	244	88.3 (80.0–93.3)	50	66.9 (55.0–76.7)	−21.5 (−27.7 to −15.4)	<0.001
Emotional functioning	244	80.0 (70.0–90.0)	50	65.3 (50.2–75.0)	−19.8 (−29.3 to10.3)	<0.001
Social functioning	244	100.0 (95.0–100.0)	50	80 (63.9–100.0)	−20.0 (−20.0 to −20.0)	<0.001
School functioning	244	90.0 (75.0–100.0)	50	65.3 (45.0–80.0)	−24.8 (−35.5 to −14.1)	<0.001
13–18 years						
Total scale score	220	89.1 (80.4–94.6)	41	69.6 (53.7–80.1)	−22.8 (−32.0 to −13.7)	<0.001
Physical health summary	220	93.8 (84.4–100.0)	41	65.6 (44.0–78.1)	−34.1 (−42.0 to −26.3)	<0.001
Psychosocial health summary	220	86.7 (78.3–93.3)	41	70.1 (61.7–85.8)	−18.3 (−27.7 to −9.0)	<0.001
Emotional functioning	220	80.0 (65.0–90.0)	41	70 (50.2–80.0)	−10.0 (−22.6 to −2.6)	0.040
Social functioning	220	100.0 (90.0–100.0)	41	90 (75.0–100.0)	−10.0 (−10.0 to −10.0)	<0.001
School functioning	220	90.0 (70.0–95.0)	40	70 (45.1–80.0)	−22.5 (−35.5 to −10.5)	<0.001
Total						
Total scale score	585	91.3 (82.6–95.7)	155	71.7 (62.0–84.8)	−20.6 (−24.9 to −16.3)	<0.001
Physical health summary	585	96.9 (87.5–100.0)	155	68.8 (53.5–87.5)	−25.0 (−29.0 to −21.1)	<0.001
Psychosocial health summary	585	88.3 (80.0–93.3)	155	73.3 (61.7–86.7)	−18.3 (−22.5 to −14.1)	<0.001
Emotional functioning	585	80.0 (70.0–90.0)	155	70 (60.0–80.4)	−10.0 (−15.3 to −4.7)	<0.001
Social functioning	585	100.0 (95.0–100.0)	155	80 (70.0–100.0)	−20.0 (−20.0 to −20.0)	<0.001
School functioning	585	90.0 (75.0–100.0))	151	70 (55.0–80.0)	−20.0 (−25.8 to −14.2)	<0.001

CHD, congenital heart disease; HRQOL, health-related quality of life.

Subgroup analysis: HRQOL comparison across functional classes of CHD

We compared generic HRQOL scores between controls and four groups of CHD with controls as reference. The four CHD groups were LRS, lesions with DPB, lesions with IPB and SVP.

Similar subgroup comparisons were done for cardiac scales with LRS as reference. We were unable to classify 10 subjects using FCC and they were excluded from analysis (tables 5 and 6). We excluded LSOL from analysis due to low sample size. All four FCC groups showed significant median differences with controls for total score and physical heath summary (table 5). Psychosocial health summary and school functioning showed significant differences for all groups except for IPB (self-reports and parent-reports). Social functioning and emotional functioning showed mixed results (table 5).

Among cardiac module scales, only heart problems and cognitive problems showed significant subgroup differences. In parent-reports, significant differences were seen for cardiac problems in LRS × DBP (−21.4, 99% CI −32.6 to −10.2, p<0.001) and LRS × SVP (−21.4, 99% CI −33.4 to −9.4, p<0.001) comparisons and for cognitive problems in LRS × SVP (−8.3, 99% CI −15.6 to −1.1, p =0.003) comparison (table 6). In self-reports, significant differences were seen for cardiac problems in LRS × DBP (−17.9, 99% CI −33.4 to −2.3, p 0.003) comparison and for cognitive problems in LRS × DBP (−16.7, 99% CI −28.4 to −4.9, p<0.001) and LRS x SVP (−16.7, 99% CI −27.4 to −5.9, p<0.001) comparisons (table 6).

DISCUSSION

The current study is the first to present HRQOL data of children and adolescents with uncorrected CHD and

Table 3 Comparison of total and component scores of parent-reported HRQOL: controls versus CHD subjects

	Controls		CHD		Adjusted median	
Scale	N	Median (IQR)	N	Median (IQR)	Difference (99% CI)	P values
2–4 years						
Total scale score	132	94.2 (90.3–97.4)	147	86.1 (67.9–93.1)	−7.8 (−11.1 to −4.6)	<0.001
Physical health summary	132	100.0 (100.0–100.0)	146	87.5 (65.6–100.0)	−12.5 (−12.5 to −12.5)	<0.001
Psychosocial health summary	132	90.9 (85.0–95.8)	147	82.7 (72.5–94.2)	−7.7 (−12.6 to −2.8)	<0.001
Emotional functioning	132	80.0 (70.0–90.0)	147	80.0 (60.0–90.0)	0.0 (−9.3 to 9.3)	1.000
Social functioning	132	100.0 (100.0–100.0)	147	100.0 (85.0–100.0)	0.0 (0.0 to 0.0)	1.000
School functioning	97	100.0 (83.3–100.0)	57	58.3 (33.3–100.0)	−41.7 (−51.6 to −31.8)	<0.001
5–7 years						
Total scale score	121	92.4 (88.0–95.7)	67	77.2 (60.9–85.9)	−16.2 (−22.3 to −10.0)	<0.001
Physical health summary	121	100.0 (93.8–100.0)	67	71.9 (50.0–90.6)	−28.1 (−32.4 to −23.8)	<0.001
Psychosocial health summary	121	90.0 (85.0–93.3)	67	80.0 (66.7–86.7)	−10.0 (−16.0 to −4.0)	<0.001
Emotional functioning	121	80.0 (70.0–90.0)	67	70.0 (60–85.0)	−10.0 (−19.3 to 0.7)	0.006
Social functioning	121	100.0 (100.0–100.0)	66	90.0 (75.0–100.0)	−10.0 (−10.2 to −9.8)	<0.001
School functioning	121	90.0 (85.0–100.0)	64	80.0 (70.0–90.0)	−12.5 (−18.5 to −6.5)	<0.001
8–12 years						
Total scale score	245	91.3 (87.0–95.7)	50	75.0 (58.4–85.3)	−17.4 (−24.8 to −10.0)	<0.001
Physical health summary	245	100.0 (93.8–100.0)	49	67.9 (45.3–85.9)	−31.3 (−35.2 to −27.3)	<0.001
Psychosocial health summary	245	90.0 (83.3–94.2)	49	78.3 (63.3–89.2)	−11.7 (−19.3 to −4.1)	<0.001
Emotional functioning	245	80.0 (70.0–90.0)	50	75.0 (58.8–90.0)	−5.0 (−16.1 to 6.1)	0.244
Social functioning	245	100.0 (100.0–100.0)	50	90.0 (75.0–100.0)	−10.0 (−10.0 to −10.01)	<0.001
School functioning	245	90.0 (80.0–100.0)	50	75.0 (53.8–90.0)	−15.0 (−23.7 to −6.3)	<0.001
13–18 years						
Total scale score	221	92.4 (85.9–95.7)	42	70.7 (61.6–85.9)	−21.6 (−28.6 to −14.7)	<0.001
Physical health summary	221	96.9 (90.6–100.0)	39	59.4 (40.6–87.5)	−37.5 (−47.1 to −27.9)	<0.001
Psychosocial health summary	221	90.0 (83.3–94.2)	39	78.3 (68.3–95.0)	−11.7 (−20.5 to −2.9)	0.001
Emotional functioning	221	80.0 (70.0–90.0)	42	70.0 (53.8–90.0)	−15.0 (−33.0 to 3.0)	0.032
Social functioning	221	100.0 (100.0–100.0)	42	95.0 (85.0–100.0)	−5.0 (−5.0 to −5.0)	<0.001
School functioning	221	90.0 (80.0–100.0)	40	75.0 (50.0–93.8)	−15.0 (−28.7 to −1.3)	0.005
Total						
Total scale score	719	92.4 (87.0–95.7)	306	78.3 (63.0–90.5)	−14.1 (−16.7 to −11.6)	<0.001
Physical health summary	719	100.0 (93.8–100.0)	301	81.3 (56.3–96.9)	−18.8 (−20.5 to −17.0)	<0.001
Psychosocial health summary	719	90.0 (83.3–95.0)	302	81.7 (68.3–91.9)	−8.9 (−11.6 to −6.1)	<0.001
Emotional functioning	719	80.0 (70.0–90.0)	306	75.0 (60.0–90.0)	−7.3 (−12.6 to −1.9)	<0.001
Social functioning	719	100.0 (100.0–100.0)	305	100.0 (80.0–100.0)	0.0 (0.0 to 0.0)	1.000
School functioning	684	90.0 (80.0–100.0)	211	75.0 (50.0–90.0)	−20.0 (−25.8 to −14.2)	<0.001

CHD, congenital heart disease; HRQOL, health-related quality of life.

their controls from South Asia. Patients with uncorrected CHD reported lower total generic HRQOL when compared with controls. Overall, the largest gradient in generic HRQOL was seen in school functioning and the smallest in social functioning (nil) for parent-reports. By contrast, the largest gradient was reported for physical health summary and the smallest for emotional functioning (nil) as per self-reports. The maximum deficits for physical health were reported by adolescents (parent and self-reports). Among cardiac scales, heart problems and treatment showed maximum deficits (self and parent-reports). Age-stratified comparisons for generic HRQOL showed a consistently deficient pattern across the majority of comparisons. Our results appear to be generalisable to the patients with CHD in Kerala due to the very low exclusion of patients and controls from the list approached for inclusion in the study.

Among the FCC subgroups, the largest gradient for generic HRQOL was reported by the DPB group as per parent-reports and by the IPB group as per

Table 4 Profile of cardiac disease-specific health-related quality of life (HRQOL)

	Child report		Parent report	
Scale	N	Median (IQR)	N	Median (IQR)
Total				
Heart problems and treatment	154	75.0 (53.6–92.9)	302	71.4 (53.6–85.7)
Treatment II	90	95.0 (73.8–100.0)	166	100.0 (75.0–100.0)
Physical appearance	149	83.3 (66.7–100.0)	280	100.0 (75.0–100.0)
Anxiety	154	87.5 (62.5–100.0)	301	81.3 (50.0–100.0)
Cognitive problems	152	91.7 (68.8–100.0)	282	100.0 (81.2–100.0)
Communication	152	83.3 (66.7–100.0)	250	83.3 (50.0–100.0)
2–4 years				
Heart problems and treatment	NA	NA	143	78.6 (60.0–89.3)
Treatment II	NA	NA	76	100.0 (58.3–100.0)
Physical appearance	NA	NA	125	100.0 (83.3–100.0)
Anxiety	NA	NA	142	81.3 (50.0–100)
Cognitive problems	NA	NA	126	100.0 (91.7–100.0)
Communication	NA	NA	94	87.5 (56.2–100.0)
5–7 years				
Heart problems and treatment	64	85.7 (61.1–92.9)	67	75.0 (53.6–85.7)
Treatment II	38	100.0 (66.7–100.0)	37	91.7 (75.0–100.0)
Physical appearance	59	100.0 (83.3–100.0)	64	100.0 (83.3–100.0)
Anxiety	64	87.5 (50.1–100.0)	67	68.8 (50.0–100.0)
Cognitive problems	63	100.0 (83.0–100.0)	65	100.0 (83.3–100.0)
Communication	63	100.0 (66.7–100.0)	65	83.3 (54.2–100.0)
8–12 years				
Heart problems and treatment	51	75.0 (46.4–85.7)	52	66.1 (40.2–83.9)
Treatment II	27	85.0 (70.0–95.0)	27	90.0 (75.0–100.0)
Physical appearance	51	83.3 (66.7–100.0)	52	83.3 (52.1–100.0)
Anxiety	51	81.3 (50.0–100.0)	52	81.3 (50.0–100.0)
Cognitive problems	51	83.3 (59.0–100.0)	52	83.3 (60.4–100.0)
Communication	50	83.3 (50.0–100.0)	52	83.3 (50.0–100.0)
13–18 years				
Heart problems and treatment	39	64.3 (53.4–87.5)	40	64.3 (47.3–85.7)
Treatment II	25	95.0 (80.0–100.0)	26	97.5 (88.8–100.0)
Physical appearance	39	75.0 (50.0–100.0)	39	66.7 (50.0–100.0)
Anxiety	39	93.8 (75.0–100.0)	40	87.5 (59.4–100.0)
Cognitive problems	38	83.3 (64.6–100.0)	39	83.3 (50.0–100.0)
Communication	39	83.3 (66.7–100.0)	39	83.3 (58.3–100.0)

NA, not applicable.

self-reports. The smallest gradient was reported by the LRS group (parent-reports and self-reports). Among cardiac-specific HRQOL, only two scales—heart problems and cognitive problems appear to show some gradient across FCC groups.

The overall results suggest a global reduction of HRQOL in children/adolescents with uncorrected CHD compared with controls. The results also suggest differences in perceptions between patients with CHD and their parents/caretakers regarding individual components of generic HRQOL. The cardiac-specific HRQOL deficits failed to show any consistent pattern across functional CHD subgroups. The generic HRQOL gradients between patients with uncorrected CHD and controls in this study are similar to studies by Mellion *et al* and Uzark *et al* with minor exceptions.[6 7] Mellion *et al* demonstrated reductions for all scales of generic HRQOL among older children (8–12 years) and adolescents (13–18 years)

Table 5 Comparison of HRQOL scores of functional class categories of CHD with controls

	Functional class categories*				
	Acyanotic CHD		Cyanotic CHD		
	LRS (1)	DPB (2)	IPB (3)	SVP (4)	
Scale	AMD (99% CI)	AMD (99% CI)	AMD (99% CI)	AMD (99% CI)	P values
Generic scores scales child report					
Total scale score	−13.1 (−17.9 to −8.2)	−21.7 (−32.9 to −10.6)	−28.3 (−48.6 to −7.9)	−25.3 (−30.7 to −19.9)	(1)<0.001, (2)<0.001 (3)<0.001, (4)<0.001
Physical health summary	−15.6 (−21.9 to −9.3)	−31 (−40.3 to −21.7)	−40.6 (−62.1 to −19.2)	−31.3 (−39.7 to −22.8)	(1)<0.001, (2)<0.001 (3)<0.001, (4)<0.001
Psychosocial health summary	−13.7 (−22.0 to −5.4)	−17.3 (−27.1 to −7.5)	−17.3 (−37.5 to 2.9)	−20.5 (−25.2 to −15.8)	(1)<0.001, (2)<0.001 (3) 0.027, (4)<0.001
Emotional functioning	−9.6 (−16.4 to −2.8)	−7.5 (−22.3 to 7.3)	−10 (−37.4 to 17.4)	−14.4 (−24.2 to −4.6)	(1)<0.001, (2) 0.192 (3) 0.347, (4)<0.001
Social functioning	−20 (−20.0 to −20.0)	−20 (−20.0 to −20.0)	−10 (−10.0 to −10.0)	−20 (−20.0 to −20.0)	(1)<0.001, (2)<0.001 (3)<0.001 (4)<0.001
School functioning	−15 (−24.9 to −5.1)	−20 (−29.0 to −11.0)	−10 (−26.8 to 6.8)	−25 (−37.1 to −12.9)	(1)<0.001, (2)<0.001 (3) 0.125, (4)<0.001
Generic scores scales parent report					
Total scale score	−9.4 (−13.5 to −5.3)	−28.7 (−35.6 to −21.7)	−17.4 (−29.8 to −5.0)	−16.3 (−26.4 to −6.2)	(1)<0.001, (2)<0.001 (3)<0.001, (4)<0.001
Physical health summary	−12.5 (−14.9 to −10.1)	−34.4 (−35.8 to −32.9)	−28.1 (−38.9 to −17.4)	−31.3 (−35.1 to −27.4)	(1)<0.001, (2)<0.001 (3)<0.001, (4)<0.001
Psychosocial health summary	−7.1 (−11.1 to −3.0)	−18.2 (−24.6 to −11.9)	−7.4 (−28.2 to 13.3)	−10.4 (−16.3 to −4.5)	(1)<0.001, (2)<0.001 (3) 0.357, (4)<0.001
Emotional functioning	−2.5 (−9.0 to 4.0)	−13.8 (−20.4 to −7.1)	1.3 (−36.0 to 38.5)	−7.5 (−20.9 to 5.9)	(1) 0.323, (2)<0.001 (3) 0.931, (4) 0.150
Social functioning	0 (0.0 to 0.0)	−10 (−10.0 to −10.0)	0 (0.0 to 0.0)	−10 (−10.0 to −10.0)	(1) 1.000, (2)<0.001 (3) 1.000, (4)<0.001
School functioning	−15 (−21.8 to −8.2)	−33.3 (−44.2 to −22.4)	−10 (−28.4 to 8.4)	−15 (−24.3 to −5.7)	(1)<0.001, (2)<0.001 (3) 0.161, (4)<0.001

*Functional class LSOL (left-sided obstructive lesions) was excluded from the subgroup analysis as the numbers were less in this group.
AMD, adjusted median difference; CHD, congenital heart disease; DPB, decreased pulmonary blood flow; HRQOL, health-related quality of life; IPB, increased pulmonary blood flow; LRS, left to right shunts; SVP, single ventricle physiology.

Table 6 Comparison of cardiac scores between functional class categories of CHD*

	Functional class categories†			
	Acyanotic CHD	Cyanotic CHD		
	DPB (1)	IPB (2)	SVP (3)	
Scale	AMD (99% CI)	AMD (99% CI)	AMD (99% CI)	P values
Cardiac scales child report				
Heart problems	−17.9 (−33.4 to −2.3)	−14.3 (−49.6 to 21.0)	−17.3 (−34.2 to −0.4)	(1) 0.003, (2) 0.293, (3) 0.009
Treatment	0.0 (−11.9 to 11.9)	−15.0 (−54.2 to 24.2)	2.5 (−8.5 to13.5)	(1) 1.000, (2) 0.315, (3) 0.550
Physical appearance	−4.2 (−17.5 to −9.2)	−20.8 (−47.8 to 6.2)	−4.2 (−14.9 to 6.5)	(1) 0.418, (2) 0.046, (3) 0.311
Anxiety	0.0 (−18.1 to 18.1)	−6.3 (−38.6 to 26.1)	−6.3 (−27.2 to 14.7)	(1) 1.000, (2) 0.615, (3) 0.437
Cognitive problems	−16.7 (−28.4 to −4.9)	0.0 (−16.5 to 16.5)	−16.7 (−27.4 to −5.9)	(1)<0.001, (2) 1.000, (3)<0.001
Communication	−2.8 (−19.0 to 13.5)	2.8 (−18.8 to 24.4)	2.8 (−12.2 to 17.8)	(1) 0.657, (2) 0.737, (3) 0.629
Cardiac scales parent report				
Heart problems	−21.4 (−32.6 to −10.2)	−3.5 (−34.7 to 27.5)	−21.4 (−33.4 to −9.4)	(1)<0.001, (2) 0.766, (3)<0.001
Treatment	−4.3 (−22.0 to 13.3)	−7.7 (−39.9 to 24.6)	0.7 (−12.4 to 13.7)	(1) 0.523, (2) 0.536, (3) 0.894
Physical appearance	0.0 (−1.9 to 1.9)	0.0 (−10.8 to 10.8)	0.0 (−3.3 to 3.3)	(1) 1.000, (2) 1.000, (3) 1.000
Anxiety	−12.5 (−26.5 to 1.5)	−12.5 (−48.1 to 23.1)	0.0 (−19.0 to 19.0)	(1) 0.022, (2) 0.363, (3) 1.000
Cognitive problems	0.0 (−3.8 to 3.8)	0.0 (−17.7 to 17.7)	−8.3 (−15.6 to −1.1)	(1) 1.000, (2) 1.000, (3) 0.003
Communication	−10.0 (−27.4 to 7.4)	−10.0 (−36.9 to 16.9)	−16.7 (−34.5 to 1.2)	(1) 0.138, (2) 0.334, (3) 0.016

*With left to right shunts (LRS) as reference.
†Functional class LSOL (left-sided obstructive lesions) was excluded from the subgroup analysis as the numbers were less in this group.
AMD, adjusted median difference; CHD, congenital heart disease; DPB, decreased pulmonary blood flow; IPB, increased pulmonary blood flow; SVP, single ventricle physiology.

compared with controls (parent-reports and self-reports). Our study failed to demonstrate a deficit for emotional functioning in 8–12 years (parent-reports) and in 13–18 years (self-reports and parent-reports). Both Uzark *et al* as well as our study reported similar gradients (lower values in the CHD group) for 10 out of the 12 comparisons available.[7]

When compared with controls after controlling for age, gender, SEC and domicile, the dominant deficits among uncorrected CHD subjects were seen in physical functioning and school functioning. Several types of CHDs can adversely influence haemodynamic adaptations related to physical activity. These include reduced variability of pulmonary blood flow/resistance, abnormal pulmonary vasculature, sinus node dysfunction, ventricular dysfunction, residual shunts and valvular disorders.[14–16] Children with critical CHD are at higher risk for lower scores on intelligence/achievement tests, learning disabilities and abnormalities related to speech, language and behaviour.[17 18] The maximum neurodevelopmental disability is seen in those with SVP and such disabilities can potentially limit educational achievements, scope of employability, eligibility for insurance and quality of life (QOL).[19 20]

The subgroup analysis based on FCC showed mixed results. Significant deficits were seen for total score and physical health summary for all FCC groups compared with controls. School functioning was reduced for all FCC groups compared with controls except IPB (self-reports and parent-reports). Social functioning was reduced for all FCC groups (self-reports). Social functioning (parent-reports) and emotional functioning (self-reports and parent-reports) failed to show any consistent pattern across FCC comparisons.

In the cardiac module subgroup comparison with LRS as reference, no other FCC group showed a significant difference for fourscales which were treatment barriers, physical appearance, treatment-related anxiety and communication. Self-reports showed deficits for cognition (DPB and SVP) and heart problems (DPB). Parent-reports too showed deficits related to cognition (SVP) and heart problems (DPB and SVP).

Our results for FCC-based comparisons of HRQOL are similar to several studies.[5 21–25] Together, these studies suggest that there is either minimal or no congruence between estimated QOL and the severity/type of CHD. Our results as well as those mentioned above are not in agreement with Mellion *et al* that reported a gradient for HRQOL across CHD severity.[6] Knowles *et al* also reported that specific CHD diagnosis was not associated with HRQOL.[25] Detrimental factors for HRQOL among CHD subjects reported earlier are the burden of cardiac interventions, non-cardiac comorbidities, difficulties in vision/hearing, regular medications and school absenteeism.[25] Drakouli *et al* also summarised that frequency and severity of symptoms, physical limitations and restrictions by parents are more important determinants of HRQOL than the clinical complexity of CHD.[4]

The very existence of older children/adolescents with uncorrected CHD in our study points to the late presentation and/or later adoption of corrective treatment in a significant subset of those born with CHD.

Late presentation of CHD is very common in LMICs and suggested reasons include delay in diagnosis/referral, limited resources, poor infrastructure, low levels of awareness and inappropriate medical advice.[26] In addition, the vast majority of patients with CHD do not receive timely attention in LMICs because of several fundamental health system challenges that include limitations in awareness on how to detect CHD early, substantial shortfall in the number of paediatric heart centres and economic barriers with most families having to pay from out of pocket.[27] Currently, cardiovascular services available in LMICs remain severely limited, in contrast to the rapid progress seen in the rest of the world.[28]

In the UK collaborative study of congenital heart defects (UKCSCHD), children/adolescents with serious CHDs were followed up at age 12–14 years after intervention in the first year of life. The reported median differences were much smaller in comparison with our study, suggesting that an early intervention may considerably minimise the HRQOL burden from CHD.[25] The median differences reported by us appear to be larger than the minimum clinically significant difference reported by Varni *et al* (4.36 to 9.67) and Raj *et al* (3.15 to 10.03) for all generic scales except for social functioning (proxy) confirming the clinical relevance of these deficits.[10 29]

The HRQOL burden of CHD needs to be addressed in relation to the economic impact of treatment and the neurodevelopmental issues associated with CHD.[30 31] Together, these three domains present massive challenges to the patients, their families and healthcare providers. The quantification and documentation of HRQOL during treatment of CHD needs to be encouraged in view of the probable benefits.[32 33] They include clinical utility, better patient-physician communication, increased patient/parent satisfaction, identification of hidden morbidities and support in clinical decision-making.[32 33]

Strengths and limitations

The strengths of the current study include a large sample size, high response rate, use of a validated instrument, questionnaires in two languages for ease of use and adjusted analysis to minimise confounding. The study limitations include a single institution sample and residual confounding due to comparison between hospital (patients with CHD) and community (controls) samples.

CONCLUSIONS

There is a significant global reduction in HRQOL among children/adolescents with uncorrected CHD in Kerala, India. Among HRQOL components, deficits in physical functioning and school functioning appeared to be more prominent compared with other scales. The clinical severity of CHD appears to have minimal congruence with HRQOL components. Early identification and appropriate quantification of HRQOL deficits in children/adolescents with uncorrected CHD should be advocated. Initiatives to promote early corrective treatment of CHD may help in reducing the HRQOL burden from CHD.

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