The Health-Related Quality of Life of Children with Hereditary Retinal Disorders and the Psychosocial Impact on Their Families

Esther Louise Hamblion,[1,2] *Anthony Thomas Moore,*[1,3] *and Jugnoo Sangeeta Rahi*[1,2,3]

Purpose. Childhood-onset hereditary retinal disorders comprise a group of visually disabling conditions with variable onset and progression of visual impairment. Their impact on the health-related quality of life (HRQoL) of affected individuals, as well as the broader impact on their families has not been investigated previously.

Methods. In a cross-sectional study, a generic age-appropriate instrument, the PedsQL, was used to assess self-reported HRQoL in a subsample of a representative group of children with hereditary retinal disorders and their siblings as well as parental (proxy) assessment of HRQoL of their affected children. In addition, parents reported the broader impact and effect on functioning of the family using the PedsQL Family Impact Module.

Results. Affected children ($n = 44$) reported worse HRQoL than their unaffected siblings ($n = 34$) and notably, also worse scores than those reported by children with various serious chronic systemic disorders. On average, parents assessed their child's HRQoL to be worse than that self-reported by the child. There was an overall adverse impact on the family and its functioning, although siblings did not report impaired HRQoL themselves.

Conclusions. This study demonstrates the significant impact, on both affected children and their families, of living with an untreatable, often progressive, and sometimes blinding ophthalmic disorder. It highlights the importance of support for affected individuals and their families, which may be targeted through use of generic or vision-related quality-of-life instruments for children as the latter become more widely available. Assessment of HRQoL would also be an important outcome measure in clinical trials of novel therapies for hereditary retinal disorders. (*Invest Ophthalmol Vis Sci.* 2011;52: 7981–7986) DOI:10.1167/iovs.11-7890

There is an increasing emphasis in health care systems on assessing the impact of chronic disorders on quality of life from the perspective of affected individuals and the effect on this impact of treatment and other interventions.[1,2] Measuring quality of life is a particular focus of assessment of patient-reported experience and outcome measures in health care.[3] An individual's health-related quality of life (HRQoL) is considered to be the degree to which individuals perceive themselves able to function physically, emotionally, and socially, with particular reference to their aspirations in these domains.[4] There are several instruments that have been used to assess vision-related quality of life in adults. However, until very recently (postdating the present study), there have been no instruments specifically for children that assess either vision-related quality of life or vision-dependent functioning in terms of activities of daily living,[5–8] partly because of the significant methodological challenges to instrument development in this area.

Childhood-onset hereditary retinal disorders comprise several rare disorders that result in retinal dysfunction and visual impairment in infancy and childhood. These disorders affect development as well as education, social life, and employment prospects. The care of affected children has an additional impact on their families.[9,10] Childhood retinal dystrophies are currently not amenable to treatment, but clinical trials of novel therapies are under way, and it is likely that treatments to slow retinal degeneration will be developed within the next decade. Evaluation of the effectiveness of such therapies requires that we be able to measure the impact of retinal disease on the quality of life of affected children and their families, as well as any improvement that may come from such treatments. We report an investigation of the HRQoL of children with hereditary retinal disorders and an assessment of the impact on their families.

Methods

Our study population was drawn from a previously established cohort of patients with a childhood-onset hereditary retinal dystrophy and recruited at the time of diagnosis to participate in ongoing clinical and molecular genetics research at Moorfields Eye Hospital and Great Ormond Street Hospital. As most of the children with these disorders in the United Kingdom are managed at these two hospitals,[11] this is a representative cohort. All 151 children (aged <16 years) in this existing cohort were invited to participate in the present study (i.e., irrespective of level of visual function and whether the condition was isolated or part of a systemic disorder). Their parents or guardians and unaffected siblings were also invited to take part in the study.

Materials

The parents or guardians were sent a summary of the study, a consent/assent form and a family background questionnaire to obtain informa-

From the [1]UCL Institute of Ophthalmology, London, United Kingdom; and the [2]MRC Centre of Paediatric Epidemiology for Child Health and the [3]Ulverscroft Vision Research Group, UCL Institute of Child Health, London, United Kingdom.

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Corresponding author: Jugnoo Sangeeta Rahi, MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health, 30 Guilford Street, London, WC1N 1EH, UK; j.rahi@ich.ucl.ac.uk.

TABLE 1. PedsQL Scores

Subjects	Total Score	Physical Health Score	Psychosocial Health Score
Retinal Disorder (Present Study)			
Child with retinal disorder self report, $n = 38$*	65.5 (16.7)	65.1 (20.3)	65.7 (16.4)
CI for mean	60.0–71.0	58.4–71.8	60.3–71.1
Ceiling effects, %	0	2.6	0
Healthy sibling self report, $n = 34$†	87.2 (10.4)	90.9 (10.6)	86.4 (11.3)
CI for mean	83.6–91.0	87.2–94.7	82.5–90.4
Ceiling effects, %	17.7	44.1	17.7
P‡	<0.001	<0.001	<0.001
Proxy report by parent, $n = 44$	60.6 (17.9)	59.4 (21.6)	62.0 (17.0)
CI for mean	55.2–66.1	52.9–66.0	56.8–67.1
Ceiling effects, %	0	2.3	0
Other Disorders Self-report by Affected Children			
Inflammatory bowel disease,[21] $n = 76$	74.2 (14.7)	75.1 (18.2)	73.6 (14.4)
P‡	0.005	0.009	0.009
Asthma,[21] $n = 99$	75.3 (16.9)	76.1 (19.1)	74.9 (17.5)
P‡	0.003	0.003	0.006
Cancer (various, in remission),[21] $n = 66$	75.7 (15.4)	78.1 (17.6)	74.4 (15.9)
P‡	0.002	<0.001	0.01
Congenital cataract,[16] $n = 33$	75.9 (15.6)	80.8 (8.6)	72.9 (16.1)
P‡	0.008	<0.001	0.07
Diabetes,[21] $n = 124$	82.5 (12.8)	84.8 (13.7)	81.2 (13.8)
P‡	<0.001	<0.001	<0.001
Healthy Children			
Healthy children,[21] $n = 665$	83.9 (11.8)	88.5 (11.6)	81.8 (13.2)
P‡	0.001	<0.001	<0.001

Data are expressed as the mean (SD).

* Six children aged 2–4 years therefore unable to self-report.

† Paired *t*-test.

‡ Reference population self reporting children with retinal disorders (present study). All are statistically significant at $P < 0.05$.

tion on the family's ethnic and socioeconomic background, the latter comprising the parents' education attainment and current occupation, as well as postal code, for derivation of the Index of Multiple Deprivation (IMD)[12] score (grouped into quintiles), which is used in the United Kingdom to categorize socioeconomic status at family level. Clinical information comprising visual acuity (VA) and diagnosis was obtained from the clinical database. We used (with copyright permission) the Pediatric Quality of Life Inventory (PedsQL), using large print/font versions for affected subjects. This generic HRQoL instrument has been used extensively in pediatric studies: It has age-appropriate versions for self-completion by children, as well as parallel parent-proxy forms. It is known to be applicable across disorders and has been widely validated including in general "healthy " child populations.[13,14] The PedsQL employs a modular approach using four scales: physical, emotional, social, and school functioning, with five to eight questions in each scale answered by circling a score from 0 to 4 corresponding with "never," "almost never," "sometimes," "often," and "almost always." Three summary scores are produced: total scale score, physical health summary score, and psychosocial health summary score, on a scale of 0 to 100, where higher scores indicate better HRQoL. The PedsQL was produced in large scale font suitable for visually impaired children. In addition, there is a PedsQL Family Impact Module[15] that measures the overall impact on the family of having a child with a chronic disorder by measuring both family functioning and parent quality of life. The PedsQL has also been successfully when used as a measure in the assessment of children with other ophthalmic disorders.[16,17] It is therefore a particularly useful instrument for comparing HRQoL across diverse groups of children, including "benchmarking" against general-population children.

Families who consented to participate were sent age group–appropriate versions of the PedsQL for the affected child and one unaffected sibling to self-complete, in addition to parent-proxy versions for one parent to complete reporting on the affected child's quality of life (with parental report only for children aged 2–4 years). The same

TABLE 2. Variation of PedsQL HRQoL Scores of Affected Children by VA in the Better Eye

	Better than 0.50 ($n = 8$)	≥0.51–≤1 ($n = 11$)	Worse than 1.01 ($n = 19$)
Total score			
Mean (SD)	65.8 (20.6)	74.9 (10.0)	59.9 (16.5)
Range	29.3–92.4	63–90.2	19.6–87.0
Physical health score			
Mean (SD)	65.6 (22.8)	74.4 (9.85)	60.5 (21.7)
Range	25.0–93.8	62.5–93.8	6.3–100.0
Psychosocial health score			
Mean (SD)	66.3 (20.0)	74.3 (11.4)	60.5 (15.9)
Range	31.7–91.7	60.0–90.0	26.7–93.3

parent also completed the PedsQL Family Impact Module. Nonresponding families were sent one reminder after a month.

Ethics approval was obtained from the local research ethics committee (LREC) and the research complied with the Declaration of Helsinki.

Statistical Analysis

Patterns of participation by sociodemographic and clinical characteristics in the study were examined to assess the degree and nature of any bias.[18] The internal reliability of the PedsQL was assessed with Cronbach's α,[19] and the distribution of the scores was analyzed using Shapiro-Wilk test of normal distribution.[20] PedsQL scores were calculated in accordance with the standard approach.[21] Descriptive analysis was undertaken of scores according to clinical variables and using *t*-tests scores were compared with prior reports of HRQoL of children with other chronic disorders as well as healthy siblings. The degree of agreement between parent's assessment of their child's quality of life and the child's own assessment was examined by using the Bland and Altman method.[22]

Results

Participation

Of the families who were invited, 29% participated in the study, resulting in a study population of 44 affected children, 44 unaffected parents, and 34 unaffected siblings. Participants did not differ from nonparticipants by age, sex, or VA ($P > 0.05$). However, there was some underrepresentation of children of Asian ethnicity ($P = 0.02$) and some overrepresentation of those from the least socioeconomically deprived group ($P = 0.03$) in the study sample, compared with the cohort from which it was drawn.

HRQoL of Children with Retinal Disorders

The PedsQL scores self-reported by affected children and their unaffected siblings as well as parental reports for their affected children are shown in Table 1. No floor effects were seen; however, some ceiling effects were apparent. A high degree of internal consistency was seen in all completed questionnaires, Cronbach's α correlation co-efficient >0.76.

Of interest, the scores of affected children were significantly lower across all PedsQL HRQoL scores than those reported previously by children with other chronic systemic disorders and ophthalmic disorders, with the exception of the psychosocial health scores previously reported by children with congenital cataract (Table 1).

As shown in Table 2, there was an inverted U pattern of variation in scores by VA among children with retinal disorders, although the small sample size limited the power to detect differences with confidence. Those with the worst vision (logMAR 1.01 or worse) reported the lowest PedsQL HRQoL scores, but the second lowest scores were reported by those with only mildly or moderately reduced vision (0.50 logMAR or better),

On average, parents assessed the HRQoL of their child with a retinal disorder to be worse than as self-assessed by the child (Table 1, Figs. 1, 2). Scores were most similar for the psychosocial health scale and least similar for the child's physical health; however, there was a wide range of agreement[22] between child–parent pairs (Figs. 1, 2).

Unaffected siblings reported HRQoL scores that were in keeping with those of healthy children from the general population.[21] They reported significantly better HRQoL scores than did their affected siblings (Table 1).

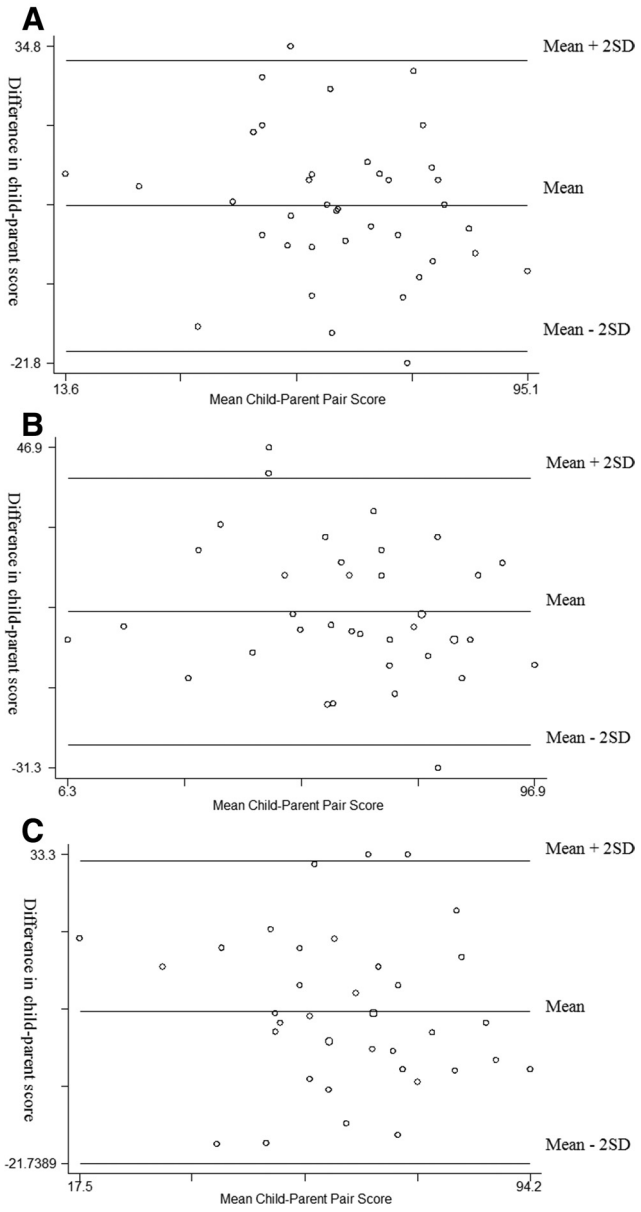

Figure 1. Bland-Altman plots of (**A**) overall scores (**B**) physical health subscores, and (**C**) psychosocial health subscores for PedsQL scores for child–parent pairs.

There were no variations in the HRQoL scores, according to ethnicity or deprivation score, although the sample size may have precluded the ability to detect true differences.

The parent-reported family impact score decreased with decreasing VA of the affected child (i.e., there was greater impact on the family in those with a child with more severe visual loss). The family functioning score followed the same pattern, with families with a more severely visually affected child reporting worse family functioning (Table 3). The lowest (worst) family impact scores were seen in those in the lowest two quintiles of deprivation, and the lowest (worst) family functioning scores were seen in those in the lowest three quintiles of deprivation (Table 3). The overall family impact module mean score of 60.7 was considerably lower than that reported in the only other published study to use the PedsQL family impact module with parents of children with an ophthalmic disorder.[23]

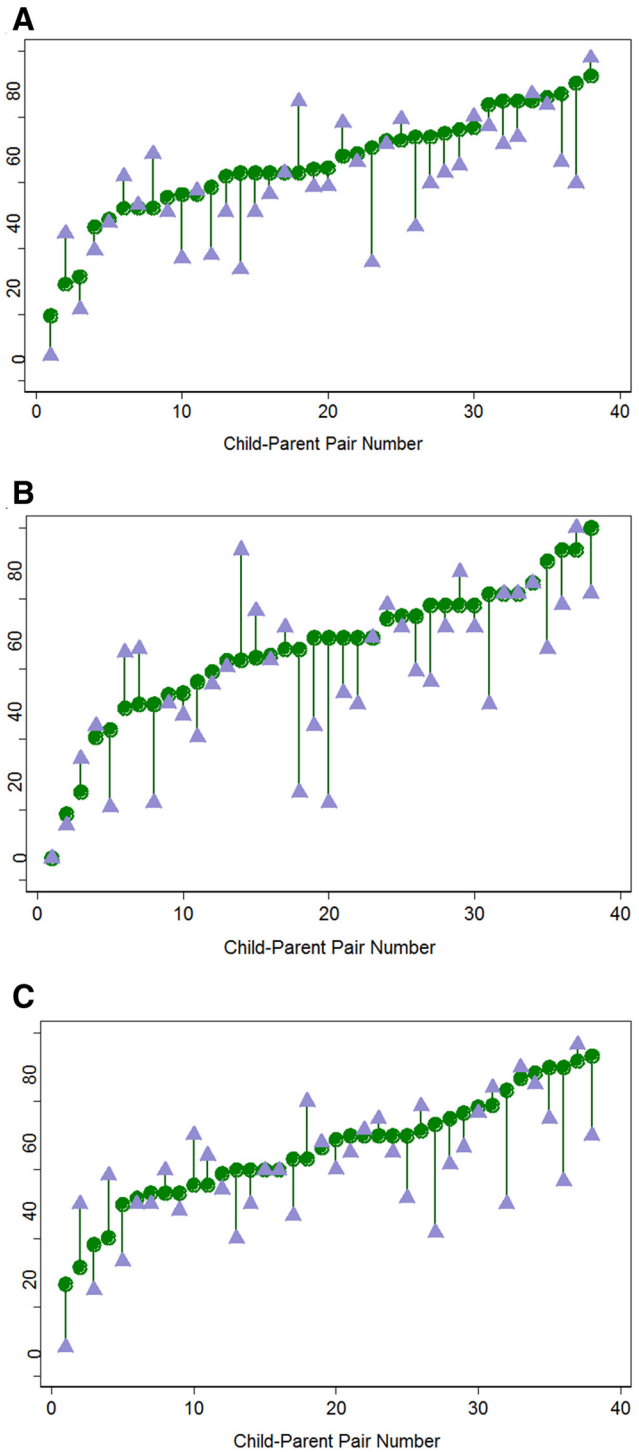

Figure 2. Distribution of child–parent proxy pair scores for (**A**) overall scores, (**B**) physical health subscores, and (**C**) psychosocial health subscores.

Discussion

Our findings show that having a hereditary retinal disorder has a significant adverse effect on the self-perceived and -reported HRQoL life of affected children. The degree of impact on HRQoL is not predictable from the level of acuity of affected children. Of note, it is, on average, of a magnitude that is comparable to that of serious systemic chronic disorders. On average, parents tend to rate the HRQoL of their affected children to be worse than that self-reported by their children, and the disparity is, on average, greater than the level of disagreement seen in other chronic disorders.[16,21] Unaffected siblings do not report their own HRQoL to be impaired; however, a significantly broader impact on the family and its functioning is reported by parents.

Ours is the first study of HRQoL in children with hereditary retinal disorders. We used a generic instrument that allows both self- and proxy-reporting of HRQoL to enable comparisons to be made with other chronic disorders[21] and with published findings relating to other ophthalmic disorders causing visual impairment.[16,17] However, the use of a generic instrument (rather than one of the very recently reported vision-specific instruments,[6–8] which were not available at the time of our study, does limit the ability to delineate the direct impact of visual impairment itself. Only 29% of invited subjects participated, which potentially raises questions of selection bias and power and the generalizability of our findings to the wider population of children with inherited retinal disorders. There is limited literature on participation rates and biases in research of this type by children with visual impairment and their families. Participation patterns are often not reported,[18,24] but there is some evidence that there has been a general decline in participation in health care research[25,26] and that those from ethnic minority groups or socioeconomically deprived groups are less likely to participate.[18,27] This finding is consistent with variations in participation by ethnicity and deprivation score observed in our study. It is relevant because hereditary retinal disorders are more prevalent in ethnic minority populations.[18,28,29] However, the direction of the effect of the sociodemographic biases in our sample are most likely to mean that our study has, in effect, elicited a minimum estimate of the impact of hereditary retinal disorders rather than presenting an exaggerated view. Because of the constraints of our study resources, we used a postal survey, which is likely to have affected participation, per se. It also means that it is not possible to be certain that parents did not influence the self-completion of the instrument by their child, even though the study information sheets made it clear that we were seeking independent completion. Nevertheless, the range of discrep-

Table 3. Variation in Family Impact and Functioning PedsQL HRQoL Scores by Acuity of Affected Child and Socioeconomic Status

	Family Impact Score	Family Functioning Score
Acuity in Better Eye of Affected Child		
Better than 0.51, $n = 8$	68.2 (15.7)	72.1 (23.4)
	48.6–91.7	34.4–100.0
≥0.51–<1, $n = 13$	64.3 (22.5)	68.0 (22.9)
	19.4–94.4	12.5–100.0
Worse than 1.01, $n = 23$	58.1 (17.0)	57.1 (23.5)
	24.3–92.4	12.5–96.9
Socioeconomic Status*		
1 (least deprived), $n = 12$	69.77 (18.7)	69.03 (23.1)
	33.3–94.4	31.3–100
2, $n = 10$	67.62 (14.1)	70.03 (20.5)
	42.4–86.8	43.8–100
3, $n = 5$	58.06 (21.6)	60 (29.5)
	30.6–88.9	34.4–93.8
4, $n = 7$	51.67 (18.4)	49.94 (27.3)
	24.3–72.2	12.5–78.1
5 (most deprived), $n = 7$	57.17 (14.9)	64.31 (16.2)
	44.4–90	46.9–98.8

Data are the mean (SD) and range.

* Excluding three families from Wales, where IMD score cannot be applied.

ancy between self- and parent-proxy–reported scores provides some reassurance regarding parental influence on form completion.

We found that children with retinal disorders self-reported lower HRQoL than children with congenital cataracts.[16] This result may reflect the impact of having a treatable versus untreatable disorder. Notably, they also reported worse HRQoL than children with various chronic systemic disorders such as asthma, diabetes, inflammatory bowel disease, and even some children in remission from cancer.[21] Although the reasons for this are unclear, it does emphasize the importance of capturing children's perceptions of their own HRQoL. Children with retinal disorders rated their psychosocial and physical health as being comparable, unlike children with congenital cataract and nonophthalmic disorders who have tended to report better physical than psychosocial health.[16,21] The reasons for this are unclear and may simply reflect the relatively small sample size of our study or the limitations of a generic instrument[30] in ascertaining the specific impact of visual impairment in this group.

The children with the most severe visual impairment (worse than 1.01 LogMAR) had the lowest HRQoL scores, but the second worst scores were reported by those with vision that, although reduced, is considered to be in the "normal" range (i.e., better than 0.50 logMAR), This inverted U-shaped relationship between objective function and quality of life, rather than a gradient across acuity range, has been recognized in other disorders. In the present study it may reflect that knowledge of the progressive nature of the disorders affected HRQoL, even when vision is not yet severely affected. Irrespective of the underlying reasons, the finding in itself serves to underline the added value of HRQoL assessment in understanding the impact of disorders, in particular in the context of therapeutic trials. Our finding that the HRQoL of unaffected siblings of children with hereditary retinal disorders is similar to the general healthy child population is unexpected. Prior studies of siblings of children with chronic systemic conditions have suggested that they can have lower quality of life due to the effect on the home environment.[31] It may be that other disorder-specific factors, such as treatment or prognosis, are important in this situation, and this area would be interesting for future research.

By contrast, the discordance, also found in our study between parent-proxy report and child self-report of HRQoL, is well recognized[32,33] and underlines the importance of self-reporting whenever possible. The level of discordance we found is more marked than that reported for other ophthalmic (congenital cataracts[16]) and nonophthalmic[21] chronic disorders, but the reasons for the difference are unclear. The parents' perspectives remain valuable in their own right, as the parents are the main decision makers in regard to the child's utilization of health care services.[2,34] Hence, the reported family-level impact in the present study is of interest. The positive association between impact on family and severity of visual loss in the present study agrees with previous research on families of children with other chronic illnesses.[35,36] The tendency toward an inverse relationship between socioeconomic status and impact on the family is also consistent with prior reports.[37] Taken together, these findings serve to highlight the broader impact on families of having a member affected by a hereditary retinal disorder and the need for easy access to relevant support services.[34]

Our study demonstrates the considerable impact that hereditary retinal disorders can have on affected individuals and their families. Better understanding of the impact on HRQoL and family functioning is particularly relevant in the current context of rapid development of novel therapies. The use of a generic HRQoL instrument enables the impact of hereditary retinal disorders in the present study to be compared with the impact of other disorders or health states. However, there are several pediatric vision-specific instruments in development,[5–8] which will offer the prospect of more detailed assessment of vision-specific aspects of quality of life or functioning. Their use in future research should help to deepen our understanding of the real-life impact of these disorders. Furthermore, we suggest that the use of generic and vision-specific instruments to assess child (patient)-reported outcome and experience should be key outcome measures in future treatment trials.

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