

A study analyzing the health-related quality of life of retinoblastoma survivors in India

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Purpose: Retinoblastoma (RB) is the commonest intraocular tumor in children. Despite high cure rates, data on health-related quality of life (HRQoL) of RB survivors are limited. This study aimed to analyze parent's perspective and self-report of HRQoL of RB survivors, using healthy siblings as controls. It also evaluated the impact of socio-economic status (SES), gender, disease laterality, treatment modality, duration since diagnosis, and visual outcomes, on HRQoL. **Methods:** Ninety-two RB survivors were enrolled in this observational, cross-sectional questionnaire-based study conducted at a tertiary care center. QoL was analyzed in four dimensions: physical, emotional, social, and school, using both self-report (for children >6 years) and parent proxy report (for children 2–18 years) using Pediatric Quality of Life Inventory™ (PedsQL™) 4.0 Generic Core Scale. Seventy-seven healthy siblings served as controls. **Results:** The mean age of both cohorts was 5.7 years. Thirty-six (39%) patients had bilateral RB. Of the 92 survivors, 43 (47%) had undergone enucleation. The HRQoL of RB survivors was significantly lower compared to sibling controls ($P < 0.01$) in all four domains, the physical domain being most affected followed by social domain. Parents reported an inferior QoL than patient's self-report. Vision <6/18 in the best eye and enucleation had a negative impact on HRQoL whilst gender, disease laterality, duration since diagnosis and SES had no impact. **Conclusion:** QoL assessment is often neglected but an important aspect of survivorship. Results of our study will help in formulating awareness of the domains affected and allow timely advocacy of initiatives for addressing each issue individually. Remedial measures aimed at optimizing QoL should be incorporated as part of their rehabilitation.

Key words: Health-related quality of life, pediatric quality of life, retinoblastoma, survivors

Retinoblastoma (RB) is an aggressive malignant tumor affecting the retina and is the most common intraocular malignancy in children. It accounts for 2–4% of pediatric cancers.^[1,2] The greatest disease burden has been recorded in populations that have higher birth rates, such as in Asians and Africans.^[3] RB can either affect one or both eyes, with the hereditary form being usually bilateral (B/L). The primary goals of treatment are saving life, ocular salvage, and preserving vision while minimizing the risk of late sequelae.

HRQoL is a multidimensional concept that focuses on the perception of impact, health status has on the physical, psychological, and social domains of QoL. RB predominantly affects very young children and considering the high survival rate with the currently available multimodality treatment, it is imperative to evaluate the HRQoL of RB survivors. Both, the disease itself and the treatment modalities used, can adversely affect the QoL of RB survivors. Functional or cosmetic deformities due to enucleation or external beam radiotherapy (EBRT), visual impairment, enhanced risk of

second primary tumors, and the potential risk for offspring developing RB may all potentially contribute to impaired QoL. Treatment abandonment continues to be the major cause of treatment failure in low-middle income countries, at least partly because of perceived poor HRQoL despite successful treatment.

A few studies have explored QoL and participation in activities of daily living in RB survivors.^[4,5] Data from developing countries are scarce. Advanced disease at presentation, lower rates of ocular salvage, and poor acceptance of enucleation may impact the HRQoL differently in low-middle income countries. In this study, we report both the parent's proxy and self-reported QoL of RB survivors from a tertiary care center in India. The study also evaluated the effects of SES, gender, disease laterality, treatment modality used, duration since diagnosis, and visual outcomes, on HRQoL.

Methods

This was a cross-sectional, observational study conducted for 1 year (August 2018–2019) in a tertiary care hospital of North India. RB survivors, aged 2–18 years having completed

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Received: 31-Jul-2020

Revision: 18-Sep-2020

Accepted: 20-Dec-2020

Published: 21-May-2021

Access this article online

Website:

www.ijo.in

DOI:

10.4103/ijo.IJO_2428_20

Quick Response Code:



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Cite this article as: Dhingra H, Arya D, Taluja A, Das S, Mahajan A. A study analyzing the health-related quality of life of retinoblastoma survivors in India. Indian J Ophthalmol 2021;69:1482-6.

treatment for over 12 months were eligible for enrolment in the study. The time gap of 1-year posttreatment completion was selected so that any treatment-related morbidities during therapy do not influence the questionnaire responses. One healthy sibling per family was enrolled as control. If there were more than 1 sibling, the sibling closest in age, as the survivor was enrolled. For patients with no sibling, only cases meeting the inclusion criteria were included. Informed consent was taken from parents. Either parent was offered participation in the study. Subjects outside the defined age range, those unable to comprehend the study questionnaire, and whose parents were not willing for study participation were excluded from the study. Approval was taken from institutional ethics committee.

The standardized PedsQL™ (version 17) 4.0 Generic Core Scale for scaling and scoring of QoL was used. The parent reports for toddlers (age 2–4 years) composed of 21 items whereas the child and parent reports for ages 5–18 years had 23 items covering 4 core dimensions- Physical (8 items), Emotional (5 items), Social (5 items) and School functioning (3 items for toddlers and 5 items for older children). The items were scored on a 5-point Likert scale from 0 (Never) to 4 (Almost always). For young children's (aged 5–7 years) self-report, items were scored on a 3-point Likert scale from 0 (Not at all), 2 (Sometimes), and 4 (A lot). Scores were initially transformed on a scale from 0 to 100 and following this, items were reverse scored and linearly transformed to a 0-100 scale as [0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0]. Higher scores indicated better HRQoL. Mean scores were calculated for each dimension in both cases and controls. The mean of emotional, social, and school functioning scales formed the Psychosocial Health Summary score. The questionnaire required answers for at least 50% of the items in each dimension for calculation of the mean score and nonfulfillment of these criteria led to exclusion from the study.

The standard Hindi version (local language) of the questionnaire was administered and responses were recorded. Children and their parents were interviewed separately to avoid any influence on individual responses. Privacy and confidentiality were maintained throughout the study. The mean time taken for completion of each questionnaire for children (5–12 years) was 22 min, for teenagers (13–18 years) and parents, it was 13 min.

Data were analyzed by using SPSS version 25.0. Mean scores and standard deviations (SD) were calculated for physical, social, emotional, and school functioning dimensions. Data in survivors and control groups were compared using the Student's *t* test. Effect of the demographical profile, SES, disease laterality, duration since diagnosis, treatment modality used and final visual outcomes were assessed for predicting QoL using Chi-square and Student's *t* test.

Results

Of the total 174 study participants (95 cases and 79 controls), 3 cases and 2 controls were excluded due to incomplete filling of the questionnaire. A total of 169 study participants (92 cases and 77 controls) were eligible for analysis and data compilation. The mean age at the time of interview for both cases and controls was 5.7 ± 3.4 years. The male to female (M:F) ratio in cases vs control arm was 1.4 and 1, respectively. The mean duration since treatment completion was 2.16 ± 0.9 years. Seventy-three

percent participants belonged to upper-lower SES followed by 25% in lower-middle, according to the modified Kuppusswamy scale. None of the study subjects belonged to upper middle or upper class.

The overall HRQoL of the RB survivors was inferior as compared to healthy siblings in all four dimensions ($P < 0.01$) as shown in Fig. 1. However, the mean score of the physical functioning was least among the survivors indicating it to be the most compromised dimension. RB survivors almost always had problems with walking, running and lifting heavy weight. They required more assistance than their siblings in self-care like bathing and doing household chores. Survivors more often complained of aches and low energy levels [Table 1].

RB survivors more frequently reported trouble getting along with other kids, doing things as peers and keeping up with other kids while playing. There was increased perception of dejection among the survivors, for example, other kids not wanting to play with them. There was increased bullying among RB survivors than the siblings [Table 2].

Feeling of sadness, anger and fear were more frequent in RB survivors as compared to the controls [Table 3]. No significant difference was observed in future worries and sleep issues among the two groups but it needs to be borne in mind that this was a very young cohort.

At the time of our study, 66 toddlers (37 cases and 29 controls) were not eligible for enrolment in school. Only 2 survivors were not enrolled despite being in 5–7 years age group. There was higher school absenteeism among RB survivors, mostly attributed to hospital visits. No difference was observed in missed school days due to feeling unwell in the two groups. The survivors reported a higher forgetfulness and increased trouble keeping up with the school work [Table 4]. No difference was observed in attentiveness in class. However, the school drop-out rate among survivors was 13% (none among controls), which was significantly high. The reasons enlisted by parents for school drop-out, were visual impairment, social stigma of disease, lack of resources and illiteracy of the parents themselves. Survivors had an overall poor psychosocial health summary in comparison to controls ($P < 0.01$).

Among 5-18 years of age, parents perceived lower QoL than patients' self-reports. The QoL reported by parents in physical ($P = 0.024$), emotional ($P = 0.001$) and

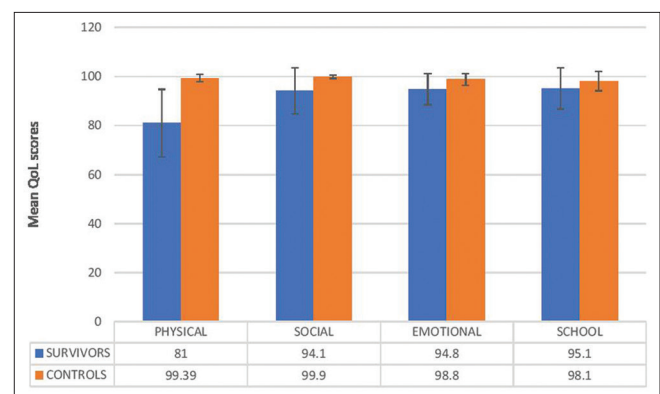


Figure 1: Health-related quality of life (HRQoL) scores of various dimensions in RB survivors and controls

Table 1: Physical health items of HRQoL

| Items | Survivors (n=92) Mean score±SD | Controls (n=77) Mean score±SD | P |
|-----------------------------|--------------------------------|-------------------------------|-------|
| Walking | 73.6±17.4 | 97.6±7.0 | <0.01 |
| Running | 68.6±23 | 99.5±3.2 | <0.01 |
| Lifting heavy objects | 85.7±17.2 | 99.5±2.4 | <0.01 |
| Bathing by self | 83±18.3 | 99.8±1.4 | <0.01 |
| Household chores | 87.9±18.2 | 100±0 | <0.01 |
| Hurt or ache | 96.2±7.6 | 100±0 | <0.01 |
| Low energy | 90.4±16.8 | 99.7±2 | <0.01 |
| Sports activity or exercise | 62.9±29.8 | 99.5±2.4 | <0.01 |

Table 2: Social health items of HRQoL

| Items | Survivors (n=92) | Controls (n=77) | P |
|--|------------------|-----------------|-------|
| Trouble getting along with other kids | 87.0±18.2 | 99.4±3.5 | <0.01 |
| Unwillingness of other kids for friendship | 98.4±6.5 | 100±0 | 0.03 |
| Teasing by others | 99.3±2.8 | 100±0 | 0.04 |
| Ability to do things as peers | 91.7±16.8 | 100±0 | <0.01 |
| Keep up with other kids while playing | 94.3±13.2 | 100±0 | <0.01 |

Table 3: Emotional Health items of HRQoL

| Items | Survivors | Controls | P |
|-----------------------|-----------|----------|-------|
| Afraid or scared | 96.5±8.4 | 100±0 | <0.01 |
| Sad or blue | 98±7 | 100±0 | 0.01 |
| Angry | 81.8±22.3 | 95±11.2 | <0.01 |
| Sleep issues | 98.4±5.9 | 99±4.9 | 0.4 |
| Worrying about future | 99.5±3.2 | 100±0 | 0.1 |

Table 4: School Health items of HRQoL

| Items | Survivors | Controls | P |
|--|-----------|-----------|-------|
| Attentiveness in class | 96.1±7.9 | 98.0±5.2 | 0.14 |
| Forgetfulness | 97±9.6 | 99.8±1.7 | 0.037 |
| Trouble keeping up with school | 93.2±10.5 | 99.3±3.7 | 0.001 |
| Missing school because unwell | 94.2±12 | 94.3±12.4 | 0.96 |
| Missing school because of doctor visit | 93.5±12.4 | 98.2±4.8 | 0.02 |

school ($P < 0.001$) dimensions were significantly lower than patients' self-report. However, no difference was observed in the social dimension ($P = 0.12$). The self-versus parent report is summarized in Table 5.

In our study 39.1% cases had B/L RB and rest had unilateral (U/L) disease. However, disease laterality did not significantly affect the QoL. This could be attributed to lesser degree of visual impairment even in patients with B/L disease. The average HRQoL scores of the three patients who underwent B/L enucleation were 78.3, 72.8, respectively, which were substantially lower than others. One patient was a toddler so self-reported HRQoL score was not available for the same. However, the corresponding parental proxy score was 66.7. The other two parental scores were 68.5 and 59.8,

respectively. Almost 93.5% cases received chemotherapy either as neoadjuvant or as adjuvant therapy. Forty-three (46.7%) cases underwent enucleation. Of these, 3 underwent B/L enucleation. None underwent orbital exenteration. Those undergoing enucleation reported an inferior QoL ($P < 0.05$). Radiation was rarely (1.08%) used as a treatment modality in our cohort.

Visual impairment is also considered one of the major causes limiting the activities of daily living of RB survivors. This was reiterated in our study. Patients with best corrected visual acuity (BCVA) in better eye $< 6/18$ reported an inferior QoL. Around 73% patients had good visual outcome despite B/L disease with BCVA in better eye being $> 6/18$. Only 8.7% patients had BCVA of 3/60 or worse in the better eye.

There was no impact of gender, duration since diagnosis, and SES on HRQoL [Table 6].

Discussion

HRQoL is a multidomain concept that characterizes the survivor's general perception of the effect of disease and treatment on physical, psychological, and social domains of life.^[6,7] It is increasingly accepted as a useful tool to evaluate outcomes in survivors of cancer. Given the excellent cure rates of RB in children, and a number of factors that could potentially impact HRQoL, it is essential to evaluate this outcome measure in RB survivors. This could assist us further, in identifying the aspects where remedial measures may be needed to optimize the HRQoL. Data on the HRQoL in this cohort are limited and conflicting. This could be attributed to the different assessment tools used, parent's perspective of QoL vs the child's self-report, heterogenous demographic profile of the study population. In a recent review of literature by Belson *et al.*,^[8] only 5 of 15 eligible studies reported a compromised HRQoL in RB survivors as compared to controls or general population. They also emphasized on the need for further research in this area, so that factors affecting the

long-term outcomes of these survivors could be identified and addressed timely.

In the current study, RB survivors reported an inferior psychosocial and physical health summary scores as compared to sibling controls. This was consistent with the study from China^[9] evaluating the QoL in children with RB following enucleation. However, Batra *et al.*^[10] have reported preservation of physical functioning of RB survivors same as controls without any significant limitation. In contrast, a study by Dijk *et al.*^[4] from Netherlands have reported better HRQoL of RB survivors as compared to Dutch reference group. Interestingly, in this study children and adolescent survivors of RB reported better “moods and emotions” and considered themselves more autonomous than the healthy controls. The possible reasons for these contradictory results could be early disease presentation requiring less mutilating therapies, preserved body image, better cultural acceptance, multidisciplinary management with involvement of counselors and psychologists improving the coping skills of patients undergoing treatment for cancer in the Dutch cohort. The author also reported negative association of age with “psychosocial well-being”, “self-perception” and other dimensions.

The physical dimension was the most affected in our study. The survivors reported a limitation in performing most of the day to day tasks. This could be linked to the visual impairment caused by the disease. With the exception of sleep issues and future worries, RB survivors reported an inferior emotional

dimension. This was in concordance to the population-based Italian study^[9] which also reported emotional disabilities in the childhood cancer survivors.

RB survivors experienced difficulty in getting along with peers, making friends, and playing with other kids, and increased teasing by others. Perceived low self-esteem and impaired body image could be one of the reasons leading to increased bullying and disappointment among the survivors. Similar findings were also noted by Batra *et al.*,^[10] wherein they reported a significantly hampered social domain in RB survivors. Dijk *et al.*^[11] analyzed QoL of adult RB survivors and have reported an overall good QoL with exception of increased mental problems like anxiety, loss of control and depression, which have been attributed to childhood bullying and increased sense of subjective impairment in the past. Hence, it is imperative to address these issues timely so that survivors can develop appropriate coping skills.

Very few studies have examined the perception of QoL at school of RB survivors. In the present study, RB survivors reported higher school absenteeism due to doctor visits, impaired memory, and trouble keeping up with school work. Despite a similar overall HRQoL in RB survivors as the age normative population control group, Weintraub *et al.*,^[12] reported a lower QoL at school for RB survivors. This did not correlate with the cognitive, psychological, and sensory-motor problems of the survivors. A noteworthy finding in our study was that 13% survivors dropped out of school. Lack of social support, low SES, limited access to special schools are some of the unique challenges of resource-limited countries compared to the west.

In children above 5 years, self-report is chosen over parent’s proxy report of child’s QoL.^[13] Children are able to reliably report on their own well-being and functioning if the questionnaire is appropriate to the child’s age and cognitive level. In our study, we analyzed both the parent and the child reported QoL. Parents reported an overall compromised HRQoL in comparison to the self-report. This was in concordance with the other studies^[8,13,14] with parents

Table 5: Parents vs self-report of the four dimensions of HRQoL

| Dimension | Parents mean score±SD | Child’s self-report mean score±SD | P |
|-----------|-----------------------|-----------------------------------|--------|
| Physical | 88.3±16.6 | 90.5±13.0 | 0.024 |
| Emotional | 95.2±7.3 | 97.45±5 | 0.001 |
| Social | 95.6±9.6 | 97.2±7.3 | 0.12 |
| School | 92±11.5 | 97.8±9.6 | <0.001 |

Table 6: Factors affecting HRQoL

| Factors | No. of Cases (n=92) | Mean HRQoL Score | P |
|-------------------------------------|---------------------|------------------|-------|
| Disease Laterality | Unilateral=56 | 96.2±4.8 | >0.8 |
| | Bilateral=36 | 96.3±4.2 | |
| Socioeconomic status | Lower middle=27 | 95.8 | >0.05 |
| | Upper lower=63 | 96.4 | |
| | Lower=2 | 100 | |
| Gender | Male=54 | 96.8±4.6 | >0.05 |
| | Female=38 | 95.6±4.4 | |
| Enucleation | Yes=43 | 94.2±4 | <0.05 |
| | No=49 | 98.2±4.2 | |
| BCVA in better eye | 6/18 or better 67 | 96.4±4.7 | <0.05 |
| | 6/18-6/60 17 | 95.6±5 | |
| | 3/60 or worse 8 | 96.8±2.2 | |
| Duration since diagnosis (in years) | 1=27 | 96.6±4 | >0.05 |
| | 2=13 | 94.5±4.2 | |
| | 3=25 | 95.8±6.4 | |
| | 4=16 | 97.7±2.7 | |
| | 5=9 | 97.1±2.1 | |
| | >5=2 | 95.0 | |

consistently reporting inferior outcomes in comparison to survivor's self-report.

Batra *et al.* reported no significant difference in HRQoL of metastatic vs localized disease,^[15] B/L vs U/L disease^[10] or enucleated survivors vs not enucleated survivors.^[15] In our study visual impairment and enucleation negatively affected the HRQoL of the survivors. This could be attributed to the psychological trauma due to loss of an eye, cosmetic, and functional defect. Lack of access to appropriate customized prosthetic implants, fear of repeat surgeries, and difficulties in maintenance of prosthesis are some of the factors responsible for facial disfigurement after enucleation. Rehabilitation of such patients warrants multidisciplinary team approach to provide optimal aesthetic outcomes.

Care providers must be appropriately apprised of the impact of disease and treatment on HRQoL of survivors. Sensitization of teachers and peers regarding challenges faced by survivors could potentially assist in better adaptation to the school environment. Remedial measures such as aids/teaching material for the visually impaired could also go a long way to help the patients improve their HRQoL. Finally, ongoing assessment of HRQoL as these survivors grow older and identifying and guiding them through the challenges they face in education, seeking suitable employment and negotiating relationships should be added as a treatment goal during continuing follow-up.

Study limitations

Selection bias cannot be ruled out in our study as the participants deemed unable to answer the questionnaire were excluded. Siblings were used as controls, since they share the same socio-economic and cultural environment as the survivor. However, they may not be exactly representative of the normative age-matched population. As young siblings of cancer patients might suffer from emotional issues due to undue attention of parents towards the diseased child, ignorance of health needs of healthy siblings by parents, financial constraints, and social ostracism of the family due to cancer diagnosis. Although siblings are not the ideal choice of controls; however, they were the most practical choice in the given setting of this study. In our study, the impact of SES on the HRQoL was not statistically significant. However, as patients included in the study were not the exact representative of the socio-economic classes in the society this conclusion might be biased because of lack of patients in the upper middle and upper class. Our study included more younger patients; therefore, special adolescent problems, beyond the questionnaire, could not be studied.

Conclusion

RB survivors reported a compromised HRQoL in comparison to sibling controls. The physical health summary score was significantly lower among the survivors. Parent proxy reported an inferior QoL score compared to the self-report. Visual impairment and enucleation negatively impacted HRQoL.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Broaddus E, Topham A, Singh AD. Incidence of retinoblastoma in the USA: 1975–2004. *Br J Ophthalmol* 2009;93:21-3.
2. Seregard S, Lundell G, Svedberg H, Kivelä T. Incidence of retinoblastoma from 1958 to 1998 in Northern Europe: Advantages of birth cohort analysis. *Ophthalmology* 2004;111:1228-32.
3. Kivela T. The epidemiological challenge of the most frequent eye cancer: Retinoblastoma, an issue of birth and death. *Br J Ophthalmol* 2009;93:1129-31.
4. Van Dijk J, Huisman J, Moll AC, Schouten-van Meeteren AY, Bezemer PD, Ringens PJ, *et al.* Health-related quality of life of child and adolescent of retinoblastoma survivors in the Netherlands. *Health Qual Life Outcomes* 2007;5:65.
5. Alessi D, Dama E, Barr R, Mosso ML, Maule M, Magnani C, *et al.* Health related quality of life of long-term childhood cancer survivors: A population-based study from the Childhood Cancer Registry of Piedmont, Italy. *Eur J Cancer* 2007;43:2545-52.
6. Varni JW, Burwinkle TM, Lane MM. Health-related quality of life measurement in pediatric clinical practice: An appraisal and precept for future research and application. *Health Qual Life Outcomes* 2005;3:34.
7. Langeveld NE, Stam H, Grootenhuis MA, Last BF. Quality of life in young adult survivors of childhood cancer. *Support Care Cancer* 2002;10:579-600.
8. Belson PJ, Eastwood JA, Brecht ML, Hays RD, Pike NA. A review of literature on health-related quality of life of retinoblastoma survivors. *J Pediatr Oncol Nurs* 2020;37:116-27.
9. Zhang L, Gao T, Shen Y. Quality of life in children with retinoblastoma after enucleation in China. *Pediatr Blood Cancer* 2018;65:e27024.
10. Batra A, Kumari M, Paul R, Patekar M, Dhawan D, Bakhshi S. Quality of life assessment in retinoblastoma: A cross-sectional study of 122 survivors from India. *Pediatr Blood Cancer* 2016;63:313-7.
11. Van Dijk J, Imhof SM, Moll AC, Ringens PJ, Cohen-Kettenis PT, Rijmen F, *et al.* Quality of life of adult retinoblastoma survivors in the Netherlands. *Health Qual Life Outcomes* 2007;5:30.
12. Weintraub N, Rot I, Shoshani N, Pe'er J, Weintraub M. Participation in daily activities and quality of life in survivors of retinoblastoma. *Pediatr Blood Cancer* 2011;56:590-4.
13. Yeh CH, Chang CW, Chang PC. Evaluating quality of life in children with cancer using children's self-reports and parent-proxy reports. *Nurs Res* 2005;54:354-62.
14. Sheppard L, Eiser C, Kingston J. Mothers' perceptions of children's quality of life following early diagnosis and treatment for retinoblastoma (Rb). *Child Care Health Dev* 2005;31:137-42.
15. Batra A, Kain R, Kumari M, Paul R, Dhawan D, Bakhshi S. Parents' perspective of quality of life of retinoblastoma survivors. *Pediatr Blood Cancer* 2016;63:1287-9.