



Original Article

Quality of life of pediatric patients with craniopharyngioma: A retrospective series from a low-middle-income country with more than 4 years follow-up

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ABSTRACT

Background: Craniopharyngiomas (CPs) are rare, low-grade tumors characterized by a range of debilitating symptoms. Most of the existing literature reports postoperative outcomes of the different treatment modalities of childhood CP. However, few studies have reported the impact of these different treatment methods on the quality of life (QoL) of survivors of childhood CP. Therefore, we aim to assess the correlation between different surgical modalities on the QoL of patients with childhood CP from a lower-middle-income country.

Methods: Twenty-nine survivors who underwent treatment for CP were included in the study. The selected patients had either been managed with complete resection, debulking, or placement of an Ommaya reservoir. QoL was assessed by the pediatric quality of life (PedsQL) questionnaire. The effect of the different treatment modalities on the QoL was assessed.

Results: Mean follow-up was 4.4 ± 2.19 years. The type of surgery was significantly related to the mean PedsQL scores for the total score as well as each of the individual domain scores ($P < 0.001$). Complete resection of the tumor resulted in the lowest mean (standard deviation) PedsQL total score of 56.6 ± 7.12 compared to the Ommaya reservoir with biopsy (83.3 ± 5.69) and debulking (93.8 ± 3.37) ($P < 0.001$).

Conclusion: There was a significant effect of the type of surgical treatment on the QoL of the survivors of childhood CP. It is important to consider the long-term outcomes in addition to immediate postoperative outcomes when deciding on a treatment strategy while managing children with CP.

Keywords: Craniopharyngioma, Debulking, Ommaya, Quality-of-life

INTRODUCTION

Craniopharyngiomas (CPs) are rare, low-grade (World Health Organization grade I) embryonic malformations arising in the sellar, suprasellar, and parasellar regions.^[11,14] The two clinicopathological variants, adamantinomatous CP (ACP) and papillary CP (PCP), differ in

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pathogenesis and age distribution. Childhood CP is almost exclusively the ACP type whereas the squamous PCP type is exclusively seen in adults.^[1] Childhood CP can present with a clinical presentation characterized by symptoms of increased intracranial pressure (ICP) (e.g., headache and nausea), endocrine deficits, and visual impairment.^[18] As CP is a slow-growing tumor, diagnosis of childhood CP is often made late as symptoms usually appear a year before the diagnosis is established.^[2,6] There has been a persistent debate over the benefits and disadvantages of attempted gross total resection (GTR) as compared to subtotal resection (STR) or biopsy followed by adjuvant therapies.^[3] In addition, an alternative choice of management, that is, repeated, intermittent aspiration of fluid from the cyst through an Ommaya reservoir can be opted for by neurosurgeons as well.^[23]

The anatomical proximity of CP to vascular and visual structures presents an obstacle while planning its surgical management. The debate arises when considering the quality of life (QoL) of these patients as some cases may lead to unfavorable outcomes and long-term neurological and hormonal problems after tumor removal.^[13] While many studies report the postoperative complications of CP excision, little data highlight the impact of the type of surgery performed on the QoL of children undergoing CP excision. QoL should be regarded as a benchmark for the long-term success of treatment. Merchant *et al.* compared the QoL of CP patients managed with a combined modality of surgery and radiotherapy with patients treated with only surgery and concluded that the mean Health Utility Index was higher for the combined-modality group ($P < 0.063$).^[16] Similarly, Poretti *et al.* reported that radical surgery has a considerable impact on QoL as the authors assessed health-related QoL (HRQoL) in CP children who underwent radical resection and reported social functioning was the most impaired dimension of HRQoL.^[19] However, in a study by Hidalgo *et al.*, adults treated with primary GTR for childhood CP reported a similar QoL compared to the general population.^[10] The modified Ketz scale was utilized to compare the level of function of CP patients managed through different treatment modalities by Fischer *et al.* The authors reported that patients with conservative surgery were clustered in the highest level of function on the scale whereas those who had radical surgery were equally distributed among the first three functional categories.^[5] Interestingly, Yano *et al.* did not find a statistically significant correlation between the type of initial treatment done in CP patients and their QoL.^[21]

There is a dearth of data reporting the long-term outcomes of childhood CP in Pakistan, with only one case series reporting the outcomes at a 3-month follow-up of CP patients who underwent GTR.^[15] To fill in the gap of knowledge, our study aimed to measure the QoL of CP children and the impact of different treatment modalities on the QoL. Our goal is to

better understand the best possible treatment modality for childhood CP to help improve the long-term outcomes in these patients. To the best of our knowledge, we present one of the largest studies to report the QoL of patients diagnosed and managed for childhood CP from a low-middle-income country (LMIC).

MATERIALS AND METHODS

This retrospective study, approved by the Institutional Review Board, consists of consecutive patients who were diagnosed and managed for CP at Aga Khan University Hospital, Karachi, Pakistan between January 2003, and January 2020. These patients included those who were aged 2–18 years old and diagnosed and managed with CP and were identified using the International Classification of Diseases, Tenth Revision (ICD-10) codes. Ethical approval was obtained from the Ethical Review Committee at the University before initiating the study. Medical records of these patients were reviewed for collecting information regarding the radiological location of the tumor and its size, histopathology of the tumor, type of surgical procedure and extent of tumor resection, postoperative radiology (complete excision or debulking surgery), re-do craniotomy for recurrence, development of postoperative diabetes insipidus, hydrocephalus, and postoperative radiotherapy. Patients with incomplete or missing medical records, with other congenital malformations, and those with investigations or surgical management done from elsewhere were excluded from the study. Contact information of parents was obtained from the hospital records, and phone calls were made to collect the information on the QoL of these patients at the time of data collection. Verbal consent was obtained over the phone. According to the preference of the interviewee, the interview was conducted in either English or Urdu. In cases where parents did not consent to be part of the study, the patients were excluded from the QoL analysis.

We used the pediatric quality of life (PedsQL) for calculating the QoL of these patients. PedsQL is a comprehensive, validated tool consisting of four domains for measuring QoL in children and adolescents aged 2–18 years. The 23-item PedsQL 4.0 Generic Core Scales consists of eight items addressing physical functioning and five items addressing emotional functioning, social functioning, and school functioning. Parents of the patients were asked to complete the PedsQL 4.0 Generic Core Scales instrument. The questionnaire was offered in either English or a validated Urdu version after permission was granted.

Statistical analysis was done using the Statistical Package for the Social Sciences version 25.0. For categorical variables, frequencies and proportions were calculated, whereas means and standard deviation or median and interquartile ranges were calculated for continuous variables. Each PedsQL

item was reverse scored and linearly transformed to a scale of 0–100; therefore, higher scores reflected better HRQoL. The mean score was computed as the sum of the items divided by the number of items answered. The PedsQL total score was composed of the physical, emotional, social, and school functioning scores. If more than 50% of the items in the instrument were missing, the scale scores were not computed. Mean differences (standard error) were reported to determine the relationship between the type of surgical procedure with QoL using a one-way analysis of variance and *post hoc* Bonferroni test. Pearson correlation coefficient (*r*) was reported by correlation analysis to assess the correlation between the QoL domains. A cutoff of $P < 0.05$ was taken as significant.

RESULTS

Table 1 shows the demographics and clinical characteristics of the patients presenting with CP. Based on the inclusion criteria, 150 patients were identified; however, 29 of the 150 patients could be contacted to complete the survey (response rate: 19.3%). Seventeen out of 29 (58.6%) of the patients were male, and the mean age of the patients was 13.5 years (standard deviation [SD] \pm 4.2). The majority of the patients (19/29, 65.5%) initially presented with symptoms of raised ICP, including headache and vomiting. Other presenting complaints included loss of vision/visual field defect (5/29, 17.2%), endocrinal disorders (4/29, 13.8%), and seizures (1/29, 3.4%). Radiological imaging revealed that in 25 (86.2%) patients, the tumor was located in the suprasellar region, whereas in 4 (13.8%) patients, it was located in the sellar region. In addition, the tumor was a mixed solid-cystic lesion in 14 (48.3%) patients, compared to cystic in 13 (44.8%) and solid in 2 (6.9%) patients. Three (10.3%) of the patients presented with hydrocephalus. An external ventricular drain was placed in 4 (13.8%) patients, whereas 3 (10.3%) patients had a ventriculoperitoneal shunt. The tumor was completely resected in 15 (51.7%) patients compared to 11 (37.9%) patients who underwent debulking surgery and 3 (10.3%) of the patients in whom an Ommaya reservoir was placed. Twelve (41.4%) patients had to undergo a re-do surgery, out of which craniotomies were performed in 7 (24.1%) patients. Only 1 (3.4%) patient received postoperative radiotherapy. Postoperatively, 11 (37.9%) patients developed diabetes insipidus. There were no cases of intra and postoperative mortality.

The mean follow-up time of the demonstration of the QoL survey from the time of surgery was 4.4 (\pm 2.19) years. The mean (SD) PedsQL scores were 73.48 (\pm 18.92) for the total score, 68.86 (\pm 19.38) for physical health, 67.41 (\pm 26.57) for emotional functioning, 78.45 (\pm 20.23) for social functioning, and 81.55 (\pm 17.58) for school functioning for all the patients.

Table 2 represents the correlation of PedsQL domains. We

Table 1: Demographics and clinical characteristics.

Characteristics	Frequency (n=29)	Percent
Age at diagnosis (in years)		
Mean \pm SD	13.5 \pm 4.2	
Gender		
Male	17	58.6
Female	12	41.4
Presenting complaint		
Headache, blurred vision, and vomiting	19	65.5
Loss of vision, visual field defect	5	17.2
Endocrinal disorders	4	13.8
Seizures	1	3.4
Location of tumor		
Sellar	4	13.8
Suprasellar	25	86.2
Characteristics of tumor		
Cystic	13	44.8
Solid cum cystic	14	48.3
Solid	2	6.9
Hydrocephalus		
No	26	89.7
Yes	3	10.3
EVD		
No	25	86.2
Yes	4	13.8
VP shunt		
No	26	89.7
Yes	3	10.3
Type of surgery		
Debulking	11	37.9
Complete excision	15	51.7
Ommaya reservoir	3	10.3
Redo surgery		
No	17	58.6
Yes	12	41.4
Type of redo-surgery		
None	17	58.6
Craniotomy	7	24.1
Trans-sphenoidal excision	3	10.3
Others	2	6.9
Radiotherapy		
No	28	96.6
Yes	1	3.4
Post op diabetes		
No	18	62.1
Yes	11	37.9
Intraoperative mortality		
Yes	0	0.0
Postoperative mortality		
Yes	0	0.0
Length of hospital stay (days)		
Median (IQR)	6.5 (4.25–8)	
Mean follow-up (years)		
Mean \pm SD	4.4 (\pm 2.19)	

EVD: External ventricular drain, VP: Ventriculoperitoneal, SD: Standard deviation, IQR: Interquartile range

Table 2: Correlation of PedsQL domains.

QoL domains	Physical	Emotional	Social	Schooling	Total
Physical					
Pearson correlation	1	0.759**	0.667**	0.827**	0.932**
Emotional					
Pearson correlation	0.759**	1	0.818**	0.777**	0.912**
Social					
Pearson correlation	0.667**	0.818**	1	0.677**	0.841**
Schooling					
Pearson correlation	0.827**	0.777**	0.677**	1	0.891**

**significant at $P < 0.001$ using Pearson correlation analysis. PedsQL: Pediatric quality of life, QoL: Quality of life

observed a significant strong positive correlation between total QL with physical, emotional, social, and schooling domains ($P < 0.001$). Similarly, a significant strong positive correlation between the physical domain and with emotional, social, and schooling domains was also observed ($P < 0.001$). In addition, a significant strong positive correlation was also observed between emotional, social, and schooling domains ($P < 0.001$).

Figure 1 indicates the mean QoL scores of patients with CP. The total mean PedQL score of CP patients was 73.48 ± 18.92 , with the highest mean PedQL scores in the school domain (81.55 ± 17.58), followed by the social domain (78.45 ± 20.23), physical domain (68.86 ± 19.38), and emotional domain (67.41 ± 26.57).

Figure 2 indicates the mean PedQL scores based on the type of surgery. We observed a significant mean difference in total PedQL scores between debulking and complete excision (37.21 ± 2.34). Similarly, a significant mean difference was also observed in the mean total PedQL scores between the Ommaya reservoir and complete excision (26.73 ± 3.72). High mean PedsQL scores were also observed in the physical health domain among patients who underwent debulking versus complete excision with a mean difference of $36.55 (\pm 3.12)$. In addition, a high mean PedQL score in the physical health domain was also observed in the Ommaya reservoir versus complete excision with a mean difference of $28.12 (\pm 4.97)$.

Significantly, high mean PedQL scores were also observed in the emotional functioning domain in patients who underwent debulking versus complete excision and Ommaya reservoir versus complete excision with a mean difference of $45.81 (\pm 5.73)$ and $39.00 (\pm 9.13)$, respectively. Similarly, significantly high mean PedQL scores were also observed in the social functioning domains in patients who underwent debulking versus complete excision and Ommaya reservoir versus complete excision with a mean difference of $33.39 (\pm 5.15)$ and $14.00 (\pm 8.2)$, respectively. The PedQL scores were significantly high in the school functioning domain in patients who underwent debulking versus complete excision and Ommaya reservoir versus complete excision ($P < 0.001$).

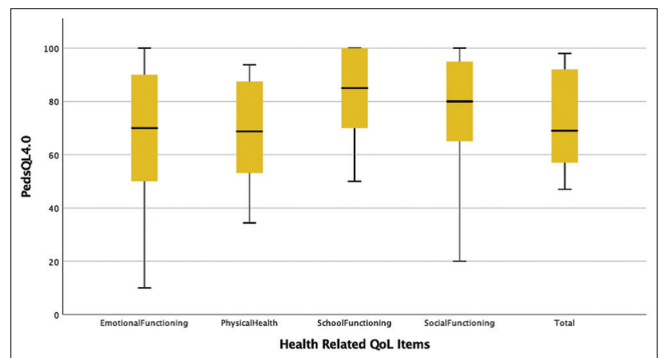


Figure 1: Mean quality of life scores.

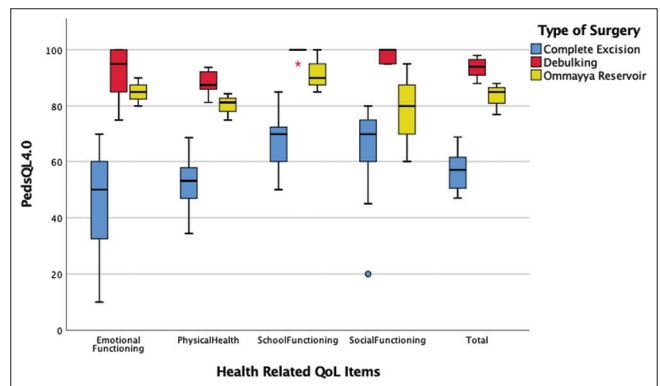


Figure 2: Mean pediatric quality of life scores based on the type of surgery.

DISCUSSION

This is the largest study to report the QoL of patients diagnosed and managed for childhood CP from an LMIC. Twenty-nine patients were included in the study with a mean age of $13.5 (\pm 4.2)$ years. We found a statistically significant relationship between the QoL and the type of initial surgery performed for the management of CP ($P < 0.05$). Complete resection of the tumor resulted in poor QoL with the lowest total mean scores as well as the lowest scores in individual domains of the PedsQL compared to debulking and placement of an Ommaya reservoir with

biopsy. However, patients who underwent debulking reported significantly better QoL with the highest mean total scores and highest mean scores across the individual domains of the PedsQL.

The true incidence of CP in Pakistan is unknown as there is a lack of data exploring the pathology in the country.^[12] At present, only a few studies have reported data on CP from Pakistan with the largest study retrospectively reviewing 207 cases.^[9,12,15,20] In addition, there is a dearth of data reporting QoL of survivors of childhood CP from LMICs. QoL in CP patients is significantly impaired even after surgical resection, which results in not only the need for a close endocrine follow-up but also requires physical, psychological, and psychosocial rehabilitation.^[7] Treatment strategies for pediatric CP are a matter of controversy.^[4] Compared to STR, GTR is associated with lower recurrence rates; however, it is associated with more postoperative morbidity.^[8] Although most of the existing literature reports the postoperative complications of GTR and STR, a few studies report the long-term outcomes and the impact of the treatment modalities on QoL. Merchant *et al.* compared the QoL of 29 CP patients who had been treated with aggressive surgery with those treated with limited surgery and radiation. The authors reported a trend toward a statistically significant difference between the mean health utility scores of the two treatment groups as the mean score for the group receiving limited surgery and RT was 0.85, and that of patients initially treated with surgery alone was 0.716 ($P < 0.063$).^[16] Poretti *et al.* compared HRQoL through PedsQL of 21 CP patients who underwent GTR with healthy individuals. Compared to healthy controls, the patients with CP rated their HRQoL to be lower.^[19] We used PedsQL to assess the QoL in our patients and found similar findings as the patients managed with GTR rated their QoL significantly lower than the patients treated with STR and Ommaya reservoir ($P < 0.05$).

Interestingly, some authors have also reported no significant impact of the type of treatment on the QoL of patients with childhood CP. Hidalgo *et al.* measured the QoL using the Short Form 36 Health Survey Questionnaire Version 2 of 22 patients who underwent GTR for childhood CP. The patients notably reported a similar QoL compared to the general population. Similarly, Yano *et al.* investigated the QoL of 26 patients treated for childhood CP and concluded that there was no significant correlation between QoL and the initial treatment ($P = 0.063$). Although most of the studies report radiation with partial resection of CP as a treatment modality, none of our patients underwent radiation, which can be explained by the reluctance to offer radiation to children due to its adverse effects. However, three of our patients were managed with an Ommaya reservoir, which is a less

aggressive and safe management option.^[17] These patients rated their QoL significantly higher than those who underwent GTR with higher mean total scores as well as individual scores across each of the domains, highlighting it as a reasonable alternative when aggressive surgery is impossible.

Patients treated for childhood CP demonstrate a high prevalence of long-term neurobehavioral, social, and emotional impairment in addition to somatic concerns. Zada *et al.* suggested that between one-third and one-half of patients with treated childhood CP have impairments in social function, school, and maintaining relationships.^[22] Poretti *et al.* reported that in their study, the domains with the greatest difference between the two groups were social functioning (patient median 70; control mean 87.4) and emotional functioning (patient median 70; control mean 80.9), whereas psychosocial health was the lowest rated domain by the patients (patient median 68.3; control mean 84.4).^[19] In our cohort of 29 patients, the collective score of the patients for school functioning and social functioning was the highest, but it significantly varied between the three treatment groups. Emotional functioning was the lowest rated domain as a combined score of all the patients (mean 67.41, SD \pm 26.58); however, there was a statistical difference between the different management groups, with the patients managed with STR rating it the lowest. Although we cannot explain the difference between the different management groups and their reported QoL, comorbid conditions related to CP management, including hypothalamic and frontal lobe dysfunction, endocrine deficiencies, hydrocephalus, and somatic concerns relating to hypothalamic obesity, should be considered.^[22]

There were some limitations of this study. In addition to a small study sample and the retrospective design, we report patients from a single tertiary care private medical center. There is a high probability of patients belonging to middle and high socioeconomic backgrounds, which means better health and social determinants, which lead to better health outcomes. Hence, our patients might not represent pediatric CP patients from across Pakistan.

CONCLUSION

There is an ongoing debate on the best treatment modality for pediatric CP when considering long-term outcomes and QoL. The study highlights the impact of different surgical techniques on the management of childhood CP and their impact on QoL in an LMIC. Studies with larger study samples are needed to understand the most favorable surgical management better while considering long-term outcomes in survivors of childhood CP.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

Conceptualization Muhammad Waqas Saeed Baqai and Muhammad Shahzad Shamim. Data Collection Muhammad Jawad Amin Malik and Noreen Zia. Writing original draft preparation Muhamad Jawad Amin Malik, Nida Zahid, Shameel Shafqat, Zara Shah. Review and Editing Muhammad Waqas Saeed Baqai, Zara Shah, Shameel Shafqat. Supervision Muhammad Shahzad Shamim.

All authors have read and approved the final version of the manuscript.

Ethics approval

Approval was obtained from the Institutional Ethics Review Committee, ERC # 2021–5593–17436. All methods were carried out per the relevant institutional guidelines and regulations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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