



RESEARCH

Open Access



Factors associated with changes in the quality of life and family functioning scores of primary caregivers of children and young people with primary brain tumors in Karachi, Pakistan: a prospective cohort study

Nida Zahid^{1,2*} , Syed Ather Enam¹, Thomas Mårtensson², Iqbal Azam³, Naureen Mushtaq⁴, Mariya Moochhala⁵, Faiza Kausar¹, Aneesa Hassan¹, Saqib Kamran Bakhshi¹, Farrukh Javed⁶, Lal Rehman⁶, Muhammad Nouman Mughal¹, Sadaf Altaf⁴, Salman Kirmani⁷ and Nick Brown^{2,8*} 

Abstract

Background There are limited data available, particularly in low- and middle-income countries (LMICs), on the long-term quality of life (QoL) and family functioning of primary caregivers of children and young people (CYPs) affected by primary brain tumors (PBTs). This study aimed to assess the factors associated with the mean change in QoL and family functioning scores of primary caregivers of CYP patients with PBTs 12 months posttreatment.

Methods This prospective cohort study enrolled CYPs aged 5–21 years with newly diagnosed PBTs and their primary caregivers. The study was carried out between November 2020 and July 2023. The primary caregivers of CYPs were recruited from two major tertiary care centers in Karachi, Pakistan. The primary caregivers QoL were assessed by the Pediatric Quality of Life Inventory (PedsQL) Family Impact Module. The assessment was undertaken by a psychologist at the time of diagnosis and 12 months posttreatment. The data were analyzed with STATA version 12.

Results Forty-eight CYPs with newly diagnosed PBTs and their primary caregivers (46 mothers and 2 fathers) were enrolled. At 12 months posttreatment, 25 (52%) CYPs and their primary caregivers (mothers) were reassessed, and 23 (48%) were lost to follow-up. On multivariable analysis, a significant decrease in mothers' mean 12-month posttreatment QoL and family functioning scores was associated with CYP having posttreatment seizures (beta = -10.2; 95% CI: -18.4 to -2.0) and with the financial burden associated with the CYP's illness (beta = -0.3; 95% CI: -0.4 to -0.1). However, in those cases where CYP had higher posttreatment quality of life scores (beta = 0.4; 95% CI = 0.1, 0.6) and posttreatment higher verbal intelligence scores (beta = 0.1; 95% CI = 0.01, 0.3), the mothers' QoL and family functioning scores were significantly greater.

*Correspondence:

Nida Zahid

nida.zahid@aku.edu; nida.zahid@kbh.uu.se

Nick Brown

nick.brown@kbh.uu.se; nickjwbrown@gmail.com

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Conclusion We found a significant decrease in QoL of mothers who had a high financial burden and whose CYP had posttreatment seizures. However, those whose CYPs had higher posttreatment verbal intelligence scores and quality of life scores had significantly greater QoL scores. Identification of the factors that influence primary caregivers QoL has the potential to aid in the development of targeted strategies to alleviate stressors and improve the overall quality of life for primary caregivers and their children who are at high risk.

Keywords Quality of life, Family functioning, Primary caregivers, Mothers, Children and young people, Primary brain tumor, Cohort study, Pakistan

Background

Cancer in children and young people (CYPs) is a stressful event that affects the entire family and has long-lasting psychosocial effects on survivors and their caregivers. Due to improvements in treatment, a greater fraction of CYPs, including those with primary brain tumors (PBTs), survive cancer of all types [1]. The behavioral science literature shows that stress and coping prove challenging for all parents to some extent [2]. Parents of cancer patients endure continuous uncertainty and long-term concerns about the future health of CYP, and the risk of cancer recurrence and care for these patients can be very demanding [3, 4]. However, caring for PBT survivors involves numerous challenges that may differ from caring for survivors of other cancer types. These challenges are due to the need for additional neurotoxic treatments, differing prognoses, and increased risk of late effects [5].

The long-term consequences of PBT have been reported to predict parental quality of life (QoL) and family functioning. Klassen AF et al. reported that these patients experience higher stress levels and a diminished QoL [6]. Other studies have shown that parental QoL can be influenced by their CYP disease status, psychological factors [7–12] and parental characteristics [6, 7, 12–14]. The high levels of distress experienced by parents underscore the importance of early intervention, such as cognitive behavioral therapy and psychoeducation, for high-risk individuals [11, 15]. Screening of primary caregivers and referral of those at high risk to mental health services may improve their psychological outcomes [16]. Targeted support and coping therapies have been proven to increase well-being in parents in the hospital setting [17].

Although there are some studies on QoL in CYP patients with PBTs, there are very few longitudinal data available for their caregivers [7, 18, 19]. There is currently limited research from low- and middle-income countries (LMICs) on the assessment of parental caregiver QoL and family functioning. A single qualitative study in Pakistan assessing the factors affecting the well-being of adult brain tumors suggested that the role of the family, particularly in the Pakistani context, is pivotal [20].

Our prospective cohort study aimed to determine the factors associated with the mean change in QoL and family functioning scores for primary caregivers of CYP

patients diagnosed with PBTs 12 months posttreatment at two tertiary care hospitals in Karachi, Pakistan.

Methods

Study design and setting

A prospective cohort study was chosen because it allows the examination of changes over time within the same group of individuals. The study was conducted in Karachi, Pakistan, at two tertiary care centers: the private tertiary care hospital Aga Khan University Hospital (AKUH) and the public tertiary care hospital Jinnah Postgraduate Medical Center (JPMC). The data were collected over 33 months from November 2020 to July 2023.

Study population and eligibility criteria

The CYPs aged 5 to 21 years with a diagnosis of PBTs and their primary caregivers of all the patients living in Pakistan, presenting at any tumor stage, without previous treatment and pre-existing debilitating diseases, were included. Those who were unable to communicate in English or Urdu were excluded. The details of the eligibility criteria of the CYP with PBTs are given in the study conducted by our research group [21].

Sample size

The sample size estimation was based on parallel studies conducted by our research group with the primary objectives of evaluating 12-month posttreatment changes in neurocognition [21] and QoL scores (the results of the study are under review) in CYPs with PBTs. A standard estimation formula was used, where $n = 8(CV^2)/(PC^2) [1 + (1-PC)^2]$, with PC representing the proportionate change in means ($PC = (\mu_0 - \mu_1)/\mu_0$) and CV indicating the coefficient of variation ($CV = \sigma_0/\mu_0 = \sigma_1/\mu_1$) [22]. A minimum of 48 CYPs with PBTs were required to achieve 80% statistical power and to detect a minimum 10% change in mean neurocognition and QoL scores, as well as a 20% or less change in the coefficient of variation [23–25] at a two-sided 5% level of significance. The sample size was inflated by 65% to account for potential loss to follow-up or nonresponse, figure based on prior research that aimed to assess the epidemiology, treatment, and outcomes of children with brain tumors in a single tertiary care center in Pakistan. Nearly half of the patients were lost to follow-up [26].

Data collection

A nonprobability purposive sampling method was employed to select the study participants. A research assistant screened the potential CYPs with PBTs during scheduled appointments at surgical/oncology clinics at AKUH and JPMC. Forty-eight CYP with PBTs were eligible and were recruited along with their primary caregivers (46 mothers and 2 fathers). The same research assistant (RA) was responsible for collecting data at both study sites. For screening and recruitment of the participants, the research assistant followed the processes rigorously outlined in the standard operating procedures (SOPs). Training sessions for the RA were conducted by the principal investigator (PI) at both the centers to ensure proficiency in executing procedures accurately. The PI had regular meetings with the RA to discuss issues and ensure alignment on procedures. The RA maintained detailed documentation of activities at each center. The PI conducted periodic onsite visits to observe the processes and provide feedback to the RA. The assessment of CYP and their primary caregiver took place at two points: pretreatment, i.e., at the time of PBT diagnosis, and subsequently, at 12 months posttreatment. For those CYP whose first intervention was surgery, reassessment was performed post-surgery, while for those whose primary treatment was adjuvant therapy, reassessment took place after the completion of adjuvant therapy. However, for CYP patients who underwent no intervention, the assessment was conducted 12 months after the time of diagnosis.

Independent variables

CYP Sociodemographic, tumor and treatment factors

The following data were collected from the CYPs: (1) demographic data and (2) tumor and treatment information, which included tumor histopathology, tumor location (supratentorial, infratentorial, suprasellar and sellar), history of pretreatment seizures, presence or absence of hydrocephalus at diagnosis confirmed radiologically by magnetic resonance imaging (MRI), posttreatment seizures, and type of treatment (surgical resection, chemotherapy, radiotherapy, and shunt placement). Surgical tumor resection types were determined by institutionally established cut-offs, assessed post-MRI, and categorized as total resection (100% removal), maximum safe resection (>90% removal prioritizing safety), or subtotal resection (<90% removal). This information was extracted by the RA from the surgeons' notes in the patients' files and further confirmed by the surgeon.

Parental sociodemographic factors and financial burden

The data were also collected on the parents' sociodemographic and financial burden. The financial burden was assessed by a visual analog scale (VAS), which ranged

from 0 (representing no financial burden) to 100 (representing high financial burden). There is substantial literature demonstrating the reliability of visual analog scale (VAS) assessments, specifically in terms of interrater reliability and test-retest reliability, as described by Brazier et al. [27]. Parents were also asked about receiving financial aid for CYP treatment, which could come in the form of assistance from AKUH for poor patients, zakat (a form of almsgiving or charity in Islam), insurance coverage, or support from their extended families. Additionally, parents were surveyed about any unforeseen hospitalizations for CYP, admissions to the intensive care unit, or any instances of parents losing their jobs or having to quit their job [28].

Quality of life of CYP patients

The QoL for CYP patients was evaluated with the PedsQL 4.0, a validated generic core scale and brain tumor module that is applicable both internationally and in the local language of Pakistan, Urdu [29, 30]. A parallel study by our research group examining the QoL of CYP is under review.

Neurocognition of CYP

The verbal and nonverbal neurocognition outcomes of CYP patients were assessed using validated tools. Verbal intelligence was determined with the Slosson Intelligence tool, Revised 3rd edition (SIT-R3) [31]. Perceptual reasoning was assessed by Raven's Progressive Matrices (RPM) tool [32, 33]. Processing speed was assessed using the Wechsler Intelligence Scale for Children (WISC-V) [34–36] and Wechsler Adult Intelligence Scale (WAIS-IV) [37]. For consistency reasons only one research assistant (assessor), a trained junior psychologist who was well versed with the tools, was responsible for conducting neurocognitive assessments. She conducted the assessments in a separate room, each lasting for 1 to 1.5 h. The details of the study conducted by our research group, assessed the predictors of neurocognition outcomes in children and young people with primary brain tumors are given in the following publication [21].

Outcome variable

Parental health-related quality of life and family functioning

Health-related QoL and family functioning of the primary caregivers were evaluated using an internationally validated tool, the Pediatric Quality of Life Inventory (PedsQL)[™] Family Impact Module. This tool consists of 36 items distributed across 6 scales measuring parental self-reported functioning, including physical functioning (6 items), emotional functioning (5 items), social functioning (4 items), cognitive functioning (5 items), communication (3 items), and worry (5 items). Additionally, there are 2 scales measuring parent-reported family

functioning: Daily Activities (3 items) and Family Relationships (5 items) [38]. It is a 5-point response scale with (0=never a problem; 4=always a problem). Items are reverse-scored and linearly transformed to a 0–100 scale (0=100, 1=75, 2=50, 3=25, 4=0), so that higher scores indicate better functioning (less negative impact). Scale Scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). If more than 50% of the items in the scale are missing, the Scale Score is not computed [39].

The PedsQL Family Impact Module Total Scale Score is the sum of all 36 items divided by the number of items answered. The Parent HRQOL Summary Score (20 items) is computed as the sum of the items divided by the number of items answered in the Physical, Emotional, Social, and Cognitive Functioning Scales. The Family Functioning Summary Score (8 items) is computed as the sum of the items divided by the number of items answered in the Daily Activities and Family Relationships Scales [39].

As the tool has not previously been validated in Urdu, content validation was conducted with the input of a panel of experts, including neurosurgeons, psychologists, mental health nurses, pediatricians and neurologists. Each expert rated the tool for relevance and clarity. Based on these ratings, the content validation index (CVI) was determined, resulting in a CVI of 0.7 for clarity and 0.9 for relevance indicating acceptable to excellent agreement on both clarity and relevance, respectively. The internal consistency (reliability) of the total score, which included 36 items, as well as parental health-related QoL (28 items) and family summary score (8 items), was excellent, with Cronbach's alpha values ranging from 0.91 to 0.93. The internal consistency of the individual modules ranged from acceptable to excellent, with Cronbach's alpha values varying from 0.52 to 0.94. The greatest floor effects were observed for emotional functioning, while the greatest ceiling effect was observed for family relationships (Supplemental Table 1).

Ethical considerations

The study received ethical and institutional review committee approval from the relevant sites AKUH-ERC (ERC#2020-4859-11855) and JPMC (F2-81/2021-GENL/65,706/JPMC). Informed consent was obtained from the parents. For CYPs aged 18 years and older, informed consent was directly obtained. For those under 18 years of age, informed assent and parental consent were obtained in both English and Urdu based on the participants' understanding. The interviews were conducted in a private room to ensure confidentiality. Since this was an observational study, no intervention was given to the participants. However, those participants with a significant decline in QoL were guided by the psychologist towards a treatment plan.

Statistical analysis

The analysis was performed with STATA version 12 software (STATA Corp., Texas). Quantitative variables are presented as mean and standard deviation (SD) or median with interquartile range (IQR) for normal and nonnormal data, respectively. The mean differences between mothers' QoL and family functioning scores before treatment and 12 months after treatment were assessed using paired *t* tests. Categorical variables are expressed as frequencies and percentages. To explore the correlation between the QoL scores of primary caregivers and their CYPs, Pearson and Spearman correlation coefficients were estimated. To determine the relationships of various independent factors, including tumor factors, treatment factors, psychological factors, and parental characteristics, with mothers' QoL and family functioning scores, generalized estimating equations were employed while adjusting for covariates. Unadjusted and adjusted beta coefficients with 95% confidence intervals are reported. Additionally, potential interactions were examined. *P* values less than 0.2 for univariate analysis and *p* values less than 0.05 for multivariable analysis were considered statistically significant. We assessed the confounding factors such as socioeconomic status (SES), tumor grade and age in regression analysis. The cutoff criteria for determining the significance of confounding variables were > 15% to see the change in beta coefficient.

Results

Forty-eight CYP with PBTs were eligible and were recruited along with their primary caregivers (46 mothers and 2 fathers). However, at 12 months post-treatment 23 CYP and their primary caregivers were loss to follow-up and we were able to assess only 25 CYP and their primary caregivers, who were the mothers.

CYP demographic, tumor and treatment factors

A total of 48 CYPs with PBTs were enrolled. The mean age was 12.8 ± 4.6 years, and 60% of the patients were males. Seventeen (35%) patients had an infratentorial tumor. Pilocytic astrocytoma was the predominant type of astrocytoma in 12 (25%) patients. Hydrocephalous and shunt placement was performed in 23 (48%) of the CYPs. Posttreatment seizures occurred in 4/25 (16%) patients. A total of 26 (54%) patients underwent surgical resection only, 12 (25%) underwent surgical resection with adjuvant therapy (chemotherapy and/or radiotherapy), 1 (2%) had only radiotherapy, and 9 (19%) had no intervention. Among those who underwent surgical resection, 25 (66%) had maximum safe resection, 10 (26%) had total resection, 2 (5%) had subtotal resection, and 1 (3%) had only biopsy. Within 12 months, 10 (21%) of the CYPs expired. Further details are available in a previous study by our research group [21].

Sociodemographic parental factors and financial burden of the disease

Eighteen (72%) mothers and 21 (84%) fathers were aged older than 35 years. The educational status of 11 (44%) mothers and 18 (72%) fathers was higher than or equal to secondary. Twenty one (84%) of the parents were married, while the remaining 4 (16%) were either widowed or divorced. In 19 (76%) of the households, fathers were the sole bread earners. The median household monthly income was 141 (71–442) USD. (Table 1)

When parents were asked about the financial impact of their CYP illness, only 1 out of 25 reported an unexpected hospitalization, and similarly, only 1 out of 25 reported quitting their job. Approximately 11 (44%) of the patients covered the CYP treatment expenses out of pocket, while 14 (56%) received financial assistance through AKUH welfare, Zakat, or insurance.

Mean difference in quality of life and family functioning scores of mothers (pre-treatment versus post-treatment)

An increase in daily activity scores was found at 12 months posttreatment (mean difference=10.3; 95% CI=0.3, 20.3). However, there was no statistically significant difference in the remaining QoL domains (Table 2).

Regression analysis

On univariate analysis, there was a statistically significant decline in mothers' mean 12-month QoL and family functioning scores in those whose CYPs had posttreatment seizures, had hydrocephalous and shunt placement, and had a high financial burden associated with CYP illness. However, there was a statistically significant improvement in the mean 12-month QoL and family functioning scores among those whose CYPs had high QoL scores, high verbal intelligence scores, high processing speed scores and high perceptual reasoning scores. However, there was no significant association of maternal QoL and family functioning with parental factors

Table 1 Sociodemographic parental factors of children and young people (5–21 years) with primary brain tumor ($n = 25$)

Characteristics	n (%)
Age of Mothers' (in year)	
25–34	7 (28)
≥ 35	18 (72)
Mean age of Mothers' (SD)	38.7 (6.5)
Age of Fathers (in years)	
25–34	4 (16)
≥ 35	21 (84)
Mean age of Fathers (SD)	42.8 (8.3)
Marital status	
Married	21 (84)
Others (Widower, Widow, Divorce)	4 (16)
Educational status of Mothers'	
No formal education	6 (24)
Primary	3 (12)
Secondary	5 (20)
Higher Secondary and above	11 (44)
Median Years of Mothers' education (IQR)	10 (0.5–14)
Education status of Fathers	
No formal education	4 (16)
Primary	0 (0)
Secondary	3 (12)
Higher Secondary and above	18 (72)
Median Years of Fathers education (IQR)	12 (10–15)
Working status of the Parents	
Only Father Working	19 (76)
Only Mothers' Working	2 (8)
Both Father and Mothers' Working	1 (4)
Both Father and Mothers' Not Working	3 (12)
Household Monthly Income (in USD/PKR)	
≤ 53/14,999	5 (20)
53–159/14,999–44997	9 (36)
159–318/44,997–89,994	4 (16)
318–3600/89994–1018800	7 (28)
Median Household Monthly Income (IQR)	141 (71–442)/39,903 (20,093–125,086)

Current conversion rate of USD is 283 PKR

Table 2 Mean difference in quality of life and family functioning scores of mothers' of children and young people (5–21 years old) with primary brain tumors 12 months post-treatment ($n = 25$)

Quality of Life domains	Mean Pre-treatment Scores (SD)	Mean Post-treatment Scores (SD)	Mean difference of QoL Scores (95% CI)
Parent Functioning			
Total Score	81.6 (13.3)	79.4 (17.3)	-2.2 (-8.6,4.2)
Parent HRQOL Summary Score	80.0 (13.9)	78.9 (17.5)	-1.1 (-7.8,5.7)
Physical Functioning	79.8 (13.4)	81.7 (16.5)	1.8 (-5.2,8.9)
Emotional Functioning	74.2 (19.1)	71.8 (23.0)	-2.4 (-11.9,7.2)
Social Functioning	86.0 (13.9)	81.5 (20.5)	-4.5 (-14.6,5.6)
Cognitive Functioning	81.2 (21.6)	80.8 (25.9)	-0.4 (-11.6,10.8)
Communication	94.3 (17.3)	96.3 (11.3)	2.0 (-3.2,7.2)
Worry	72.6 (23.8)	56.6 (34.4)	-16.0 (-33.4,1.4)
Family Functioning			
Family Summary Score	86.5 (17.5)	88.4 (22.4)	1.9 (-5.3,9.1)
Daily Activities*	74.7 (22.6)	85.0 (25.6)	10.3 (0.3, 20.3)
Family Relationships	93.6 (18.1)	90.5 (25.1)	-3.1 (-11.6, 5.4)

*Significant at p value < 0.05 based on paired t test

i.e., educational status, household monthly income and child's factors i.e., age of the child, type of treatment, grade of tumor, tumor location and tumor size.

On multivariable analysis, a significant decrease in mothers' mean 12-month QoL and family functioning scores was associated with CYP having posttreatment seizures (beta= -10.2; 95% CI: -18.4 to -2.0), and financial burden associated with the CYP's illness (beta= -0.3; 95% CI: -0.4 to -0.1). However, in those patients in whom CYPs had higher posttreatment quality of life scores (beta=0.4; 95% CI=0.1, 0.6) and higher posttreatment verbal intelligence scores (beta=0.1; 95% CI=0.01, 0.3), the mothers' QoL and family functioning scores were significantly greater (Table 3). No significant confounders were found.

Discussion

Our prospective cohort study aimed to determine the factors associated with the mean change in QoL and family functioning of the primary caregivers of CYP patients with PBTs at 12 months posttreatment.

The findings of our study showed that the QoL and family functioning of mothers were predicted by the cognition status of CYPs. These findings were consistent with those of Hocking et al., who indicated that survivors' neurocognitive functioning across all cognitive domains was related to mothers' reported family functioning [8]. Peterson and Drotar's model of childhood cancer survivorship depicts a significant correlation between the neurocognitive functioning of cancer survivors and family functioning support [40]. The intensity of neurocognitive deficits in CYP plays a crucial role in caregivers' lives, placing increased demands on them and potentially straining parental and family resources. This strain may impede effective support for the neurocognitive and developmental needs of the child [8]. Strengthening

initiatives focused on improving the cognitive functioning of CYP could play a pivotal role in enhancing the QoL of their caregivers and alleviating the overall burden on their families [41, 42].

Our study also revealed a significant association between the QoL of mothers and the QoL of their CYPs. Our findings were consistent with the results of Buchbinder et al., who highlighted a link between adverse physical and mental health outcomes in parents and the mental health of their children [7]. Prolonged treatment, recovery, and rehabilitation pose challenges to patients' reintegration into normal life, contributing to an overall low QoL [43, 44]. Moreover, PBT survivors have a greater incidence of physical limitations than do those with other types of cancer [45]. Fuemmeler et al. and Chien et al. further support our observations, indicating that caregivers of children with PBT experience elevated levels of distress and lower QoL in both the physical and psychological domains [46, 47]. Assessment and treatment of caregiver needs are now standard of care in pediatric oncology [48], and tailoring support services to caregivers can enhance the overall functioning of the family, in turn empowering a PBT survivor to attain her/his maximum developmental potential [49].

We found a significant decrease in the QoL and family functioning scores of mothers whose CYPs had post-treatment seizures. Our findings are consistent with those of Thurman et al., who identified seizures among children as potential contributors to parental anxiety [50]. Cognition and behavioral changes in individuals with epilepsy have a multifactorial etiology, including epilepsy itself, treatment of epilepsy (with antiepileptic drugs or surgery), response to epilepsy (such as stigma, social marginalization, and familial dynamics), and any concurrent brain dysfunction and/or damage [51, 52], causing a substantial impact on the health-related quality

Table 3 Factors associated with change in mean total quality of life scores for mothers' of children and young people (5–21 years) with primary brain tumors ($n=25$)

Characteristics	Unadjusted β coefficient (95% CI)	Adjusted β coefficient (95% CI)
Surgery intervention		
No intervention	(Reference)	-
Biopsy	-17.6 (-43.9,8.7)	
Total Resection	9.2 (-0.7,19.2)	
Subtotal resection	-15.7 (-32.1,0.8)	
Maximum safe Resection	3.6 (-4.9,12.1)	
Post-treatment Seizures		
Yes	-12.4 (-25.6,0.7)	-10.1 (-18.4, -2.0)
No	(Reference)	
Hydrocephalous		
Yes	-7.0 (-14.2,0.2)	-
No	(Reference)	
Shunt Placement		
Yes	-6.8 (-14.0,0.5)	-
No	(Reference)	
Household Monthly Income (in USD/PKR)		
$\leq 53/14,999$	-13.4 (-24.5, -2.3)	-
53–159/14,999–44997	-9.8 (-18.7, -0.8)	
159–318/44,997–89,994	-1.8 (-13.5,9.7)	
318–3600/89994–1018800	(Reference)	
Pre-treatment financial burden of the CYP's disease	-0.2 (-0.3, -0.1)	-
Post-treatment financial burden of the CYP's disease	-6.5 (-13.8, 0.8)	-0.2 (-0.4, -0.1)
Pre-treatment QoL scores of CYP	0.4 (0.1, 0.8)	-
Post-treatment QoL scores of CYP	0.7 (0.4, 1.0)	0.4 (0.1, 0.6)
Pre-treatment verbal intelligence scores of CYP	0.2 (-0.01, 0.3)	-
Post-treatment verbal intelligence scores of CYP	0.3 (0.2, 0.5)	0.1 (0.01, 0.3)
Pre-treatment processing speed scores of CYP	0.2 (-0.1, 0.5)	-
Post-treatment processing speed scores of CYP	0.3 (-0.02, 0.6)	-
Post-treatment perceptual reasoning scores of CYP	0.3 (0.1, 0.5)	-

CI: confidence interval

QoL: Quality of life

USD: United states dollar

PKR: Pakistani rupee

of life (HRQoL) of parents [53, 54]. Furthermore, Fastenau et al. reported that seizures may result in academic difficulties [55], and attendance problems at school [56]. A systematic review meta-synthesis by Zhichao et al. [57] included 13 studies that explored the experiences and needs of caregivers of children with seizures. Over 50% of family members caring for children with seizures experience stigma, which negatively impacts caregivers' mental health, as indicated by shame, low self-esteem, anger, and disorder disclosure [58]. The majority of caregivers reported a high burden of their child's disease, socially, emotionally, functionally, and economically [59]. Yu Z et al. showed that the prevalence of anxiety and depression in caregivers of children who experienced seizures was 25% and 23.5%, respectively, suggesting that healthcare providers should pay attention to the psychological and emotional symptoms of caregivers [57]. Healthcare workers need to develop interventions to reduce the burden of caregivers, improve their mental health status, provide

them with disease-related information and enhance their caring capacity [57].

The QoL and family functioning of mothers significantly declined at the 12-month reassessment due to the high costs associated with CYP treatment in our study. A similar finding was reported by Innasimuthu et al. from India [60]. Comparing stress levels across health systems with diverse financial models poses inherent challenges. Andersen et al. from the USA drew similar conclusions to ours, highlighting that different treatment modalities, including surgery, chemotherapy, or radiation therapy, not only increase the risk of side effects but also impose a significant financial burden on parents of children with PBTs [12]. The financial burden on parents plays a crucial role, with a significant proportion bearing the treatment costs out of their own pockets [61]. Similarly, in our study, 48% of the parents had to cover the expenses for CYP treatment out of pocket. Financial constraints pose a significant burden for many families in Pakistan.

The average monthly income of middle-class households is approximately \$230 [62]. The mean monthly cost per patient for cancer care at a private tertiary care hospital exceeds this amount by more than five times. The majority of these expenses are shouldered by the patient's family [63]. In a study from Pakistan on adult brain tumors, the patients reported financial constraints attributable to treatment costs. Few mentioned becoming "hand-to-mouth" since the start of treatment, and well-to-do patients expressed their concern about exorbitant expenses [20]. To address financial burdens, the implementation of proactive measures such as patient assistance programmes at the institutional level can be effective. These programs, which attract support from multiple sponsors, offer tailored assistance based on each patient's specific financial needs [64]. Within AKU, there is a charitable society responsible for collecting and disbursing zakat. It provides assistance to the most underprivileged members of society without any discrimination or compromise on the quality of care [65]. Moreover, government-led initiatives, such as Punjab's health card system in Pakistan, provides a swift and dignified means to reduce out-of-pocket expenses for underprivileged people, enhancing healthcare access [20]. Similar programs should be initiated across the country.

Limitations

This study has several limitations. First, the relatively small sample size due to loss to follow-up. However, the study retained adequate statistical power even though loss to follow-up was observed in 23/48 CYPs and their primary caregivers because sample size was inflated by 65% to account for potential loss to follow-up. Therefore, none of the characteristics were underpowered.

Second, the primary caregivers QoL and family functioning were assessed only before treatment and at 12 months after treatment. However, certain cognitive deficits of CYP may not have been apparent during the 12-month follow-up, and could potentially emerge beyond 12 months after the start of treatment [66]. Thus, it is plausible that a more extended follow-up duration might have unveiled significant shifts in neurocognitive outcomes.

Finally, the use of nonprobability purposive sampling technique introduces selection bias and limits the generalizability. In our study, patients who did not seek medical attention or treatment at the hospital might have been excluded from the study. Furthermore, individuals with more severe symptoms or advanced stages of brain tumors are more likely to seek treatment at the hospital, potentially leading to an overrepresentation of such cases in the sample. Moreover, by exclusively recruiting participants from two hospitals, our sample might not

adequately represent those seeking care at other health-care settings.

Conclusions and future recommendations

We found a significant decrease in maternal QoL in mothers who had a high financial burden and whose CYP had posttreatment seizures. However, those whose CYPs had higher posttreatment verbal intelligence scores and quality of life scores had significantly greater QoL scores. Identification of the factors that influence parental QoL could enable the development of targeted strategies to alleviate stressors and improve the overall quality of life for mothers and their children who are at high risk. However, the limited size of our sample restricts the generalizability of our study findings. The next step would be ensuring internal consistency with a new cohort of CYP patients with PBTs and testing it in studies outside the country.

Study implications

The identification of factors influencing the quality of life (QoL) of primary caregivers in the context of primary brain tumors in children and young people has significant implications for healthcare and support services. By determining these factors, the study facilitates the development of tailored support services, such as enhanced mental health support, interventions addressing financial stress, and coping strategies. This research contributes to education and awareness programs for healthcare providers and the public, emphasizing the challenges faced by primary caregivers. Future research priorities can be shaped to guide a focus on important factors in primary caregivers' QoL outcomes. The emphasis on family-centered care, consideration of long-term implications, and the development of social support initiatives can collectively contribute to more comprehensive and empathetic care for families navigating life.

Abbreviations

AKUH	Aga khan university hospital
CI	Confidence Interval
CV	Coefficient of variation
CVI	Content validation index
CYP	Children and young people
IQR	Inter quartile range
JPMC	Jinnah postgraduate medical center
LMICs	Low-and middle-income countries
MRI	Magnetic resonance imaging
PBTs	Primary brain tumor
PC	Proportionate change in means
PedsQL	Pediatric quality of life inventory
QoL	Quality of Life
RA	Research Assistant
RPM	Raven's progressive matrices
SITS R3	Slosson Intelligence tool, Revised 3rd edition
SD	Standard deviation
SES	Socioeconomic Status
USD	United states dollar
VAS	Visual analog scale

WISC-V Wechsler Intelligence Scale for Children
 WAIS-IV Wechsler Adult Intelligence Scale

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12887-024-04867-z>.

Supplementary Material 1

Author contributions

Nida Zahid conceived the study, analyzed the data, and critically reviewed the manuscript. Nick Brown and Thomas Mårtensson overlooked the study and critically reviewed the manuscript. Iqbal Azam critically reviewed the results section of the manuscript. Syed Ather Enam, Naureen Mushtaq and Saqib Bakhshi were the subject experts. Faiza Kausar and Aneesa Hassan collected the data. Farrukh Javed and Lal Rehman were the collaborators of the study. Mariya Moochhala, Muhammad Nouman Mughal, Sadaf Altaf and Salman Kirmani critically reviewed the manuscript. All the authors contributed intellectually to this manuscript and read and approved the final manuscript.

Funding

The study was funded by the Faculty Development Award (FDA), Aga Khan University Karachi, Pakistan. The funders had no role in the preparation of the data or the manuscript.

Open access funding provided by Uppsala University.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent of the participants

The study received ethical and institutional review committee approval from the relevant sites, Aga Khan University Hospital Ethics Review Committee, AKUH-ERC (ERC#2020-4859-11855) and Jinnah Postgraduate Medical Centre, JPMC (F2-81/2021-GENL/65706/JPMC). Informed consent was obtained from the parents. For CYPs aged 18 years and older, informed consent was directly obtained. For those under 18 years of age, informed assent and parental consent were obtained in both English and Urdu based on the participants' understanding.

Consent for publication

Not applicable.

Competing interests

The authors have no conflicts of interest to declare.

ClinicalTrials.gov identifier

NCT05709522.

Author details

- ¹Department of Surgery, Aga Khan University, Karachi, Pakistan
- ²Global Health and Migration Unit Department of Women's and Children's Health, Uppsala University, Box 256, Uppsala 751 05, Sweden
- ³Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan
- ⁴Department of Pediatric Oncology, Aga Khan University, Karachi, Pakistan
- ⁵Department of Psychiatry, Aga Khan University, Karachi, Pakistan
- ⁶Department of Neurosurgery, Jinnah Post graduate Medical Centre, Karachi, Pakistan
- ⁷Division of Women & Child Health, Aga Khan University, Karachi, Pakistan
- ⁸Department of Pediatrics, Aga Khan University, Karachi, Pakistan

Received: 29 March 2024 / Accepted: 31 May 2024

Published online: 08 June 2024

References

1. Ostrom QT, Gittleman H, Truitt G, Boscica A, Kruchko C, Barnholtz-Sloan JS. CBRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011–2015. *Neuro-oncology* 2018, 20(suppl_4):iv1-iv86.
2. Lazarus RS, Folkman S. Stress, appraisal, and coping. Springer publishing company; 1984.
3. Kazak AE, Barakat LP, Meeske K, Christakis D, Meadows AT, Casey R, Penati B, Stuber ML. Posttraumatic stress, family functioning, and social support in survivors of childhood leukemia and their mothers and fathers. *J Consult Clin Psychol.* 1997;65(1):120.
4. Wallander JL, Varni JW. Effects of pediatric chronic physical disorders on child and family adjustment. *J Child Psychol Psychiatry Allied Disciplines.* 1998;39(1):29–46.
5. Gunn ME, Lähdesmäki T, Malila N, Arola M, Grönroos M, Matomäki J, Lähteenmäki PM. Late morbidity in long-term survivors of childhood brain tumors: a nationwide registry-based study in Finland. *Neurooncology.* 2015;17(5):747–56.
6. Klassen AF, Klaassen R, Dix D, Pritchard S, Yanofsky R, O'Donnell M, Scott A, Sung L. Impact of caring for a child with cancer on parents' health-related quality of life. *J Clin Oncol.* 2008;26(36):5884–9.
7. Buchbinder D, Fortier MA, Osann K, Wilford J, Shen V, Torno L, Sender LS, Parsons SK, Wenzel L. Quality of life among parents of adolescent and young adult brain tumor survivors. *Journal of pediatric hematology/oncology* 2017, 39(8):579.
8. Hocking MC, Hobbie WL, Deatrick JA, Hardie TL, Barakat LP. Family functioning mediates the association between neurocognitive functioning and health-related quality of life in young adult survivors of childhood brain tumors. *J Adolesc Young Adult Oncol.* 2015;4(1):18–25.
9. Fotiadou M, Barlow JH, Powell LA, Langton H. Optimism and psychological well-being among parents of children with cancer: an exploratory study. *Psycho-Oncology: J Psychol Social Behav Dimensions Cancer.* 2008;17(4):401–9.
10. Hovén E, Anclair M, Samuelsson U, Kogner P, Boman KK. The influence of pediatric cancer diagnosis and illness complication factors on parental distress. *J Pediatr Hematol Oncol.* 2008;30(11):807–14.
11. Sloper P. Predictors of distress in parents of children with cancer: a prospective study. *J Pediatr Psychol.* 2000;25(2):79–91.
12. Andersen BL, Shapiro CL, Farrar WB, Crespin T, Wells-DiGregorio S. Psychological responses to cancer recurrence: a controlled prospective study. *Cancer.* 2005;104(7):1540–7.
13. Canning RD, Harris ES, Kelleher KJ. Factors predicting distress among caregivers to children with chronic medical conditions. *J Pediatr Psychol.* 1996;21(5):735–49.
14. Arora NK, McHorney CA. Patient preferences for medical decision making: who really wants to participate? *Med Care* 2000;335–41.
15. Boele FW, Hoeben W, Hilverda K, Lenting J, Calis A-L, Sizoo EM, Collette EH, Heimans JJ, Taphoorn MJ, Reijneveld JC. Enhancing quality of life and mastery of informal caregivers of high-grade glioma patients: a randomized controlled trial. *J Neurooncol.* 2013;111:303–11.
16. Olson AL, Dietrich AJ, Prazar G, Hurley J. Brief maternal depression screening at well-child visits. *Pediatrics.* 2006;118(1):207–16.
17. Dellve L, Samuelsson L, Tallborn A, Fasth A, Hallberg LRM. Stress and well-being among parents of children with rare diseases: a prospective intervention study. *J Adv Nurs.* 2006;53(4):392–402.
18. Schulte F, Russell KB, Cullen P, Embry L, Fay-McClymont T, Johnston D, Rosenberg AR, Sung L. Systematic review and meta-analysis of health-related quality of life in pediatric CNS tumor survivors. *Pediatr Blood Cancer.* 2017;64(8):e26442.
19. Litzelman K, Catrine K, Gangnon R, Witt WP. Quality of life among parents of children with cancer or brain tumors: the impact of child characteristics and parental psychosocial factors. *Qual Life Res.* 2011;20:1261–9.
20. Shah NZ, Masroor T, Zahid N, Zahid W, Hassan A, Azam I, Ahmad K, Bhamani SS, Jabbar AA, Asad N. Factors affecting well-being in brain tumor patients: an LMIC perspective. *Front Psychol.* 2023;14:1117967.
21. Zahid N, Enam S, Mårtensson T, Azam I, Mushtaq N, Moochhala M, Javed F, Kausar F, Hasan A, Rehman L. Predictors of neurocognition outcomes in children and young people with primary brain tumor presenting to tertiary care hospitals of Karachi, Pakistan: a prospective cohort study. *Child's Nerv Syst.* 2024;1:1–13.
22. Van Belle G. Statistical rules of thumb. Volume 699. Wiley; 2011.

23. Quast LF, Phillips PC, Li Y, Kazak AE, Barakat LP, Hocking MC. A prospective study of family predictors of health-related quality of life in pediatric brain tumor survivors. *Pediatr Blood Cancer*. 2018;65(6):e26976.
24. Penn A, Shortman RI, Lowis SP, Stevens MC, Hunt LP, McCarter RJ, Curran AL, Sharples PM. Child-related determinants of health-related quality of life in children with brain tumours 1 year after diagnosis. *Pediatr Blood Cancer*. 2010;55(7):1377–85.
25. Shortman RI, Lowis SP, Penn A, McCarter RJ, Hunt LP, Brown CC, Stevens MC, Curran AL, Sharples PM. Cognitive function in children with brain tumors in the first year after diagnosis compared to healthy matched controls. *Pediatr Blood Cancer*. 2014;61(3):464–72.
26. Riaz Q, Naeem E, Fadoo Z, Lohano M, Mushtaq N. Intracranial tumors in children: a 10-year review from a single tertiary health-care center. *Child's Nerv Syst*. 2019;35:2347–53.
27. Brazier J, Ratcliffe J. Measurement and valuation of health for economic evaluation. *International encyclopedia of public health*. edn.: Elsevier Inc.; 2017. pp. 586–93.
28. Warner EL, Kirchoff AC, Nam GE, Fluchel M. Financial burden of pediatric cancer for patients and their families. *J Oncol Pract*. 2015;11(1):12–8.
29. McCarthy ML, MacKenzie EJ, Durbin DR, Aitken ME, Jaffe KM, Paidas CN, Slomine BS, Dorsch AM, Berk RA, Christensen JR. The Pediatric Quality of Life Inventory: an evaluation of its reliability and validity for children with traumatic brain injury. *Arch Phys Med Rehabil*. 2005;86(10):1901–9.
30. Palmer SN, Meeske KA, Katz ER, Burwinkle TM, Varni JW. The PedsQL™ brain tumor module: initial reliability and validity. *Pediatr Blood Cancer*. 2007;49(3):287–93.
31. Slosson RL, Nicholson C, Hibpshman T. Slosson Intelligence Test, Revised (SIT-R3). *Austin, TX: Slosson Education Publications* 1991.
32. Raven J. The Raven progressive matrices tests: their theoretical basis and measurement model. *Uses and abuses of Intelligence Studies advancing Spearman and Raven's quest for non-arbitrary metrics* 2008:17–68.
33. Ahmad R, Khanam SJ, Riaz Z. The Standard Progressive Matrices in Pakistan. *Uses and abuses of intelligence: studies advancing Spearman and Raven's quest for non-arbitrary metrics* 2006:404–412.
34. Wechsler D. WISC-III: Wechsler Intelligence Scale for Children. San Antonio, TX: Psychological Corporation. In.: Harcourt Brace Jovanovich; 1991.
35. Wechsler D. Wechsler intelligence scale for children. 1949.
36. AMBREEN S: Wechsler Intelligence Scale for Children-(WISC-IV): adaptation, translation, and standardization in Pakistan. QUAID-I-AZAM UNIVERSITY ISLAMABAD; 2015.
37. Wechsler D. Wechsler adult intelligence scale. *Arch Clin Neuropsychol* 1955.
38. Varni JW, Sherman SA, Burwinkle TM, Dickinson PE, Dixon P. The PedsQL™ family impact module: preliminary reliability and validity. *Health Qual Life Outcomes*. 2004;2(1):55.
39. Varni JW, Sherman SA, Burwinkle TM, Dickinson PE, Dixon P. The PedsQL™ family impact module: preliminary reliability and validity. *Health Qual Life Outcomes*. 2004;2:1–6.
40. Peterson CC, Drotar D. Family impact of neurodevelopmental late effects in survivors of pediatric cancer: review of research, clinical evidence, and future directions. *Clin Child Psychol Psychiatry*. 2006;11(3):349–66.
41. Butler RW, Copeland DR, Fairclough DL, Mulhern RK, Katz ER, Kazak AE, Noll RB, Patel SK, Sahler OJZ. A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy. *J Consult Clin Psychol*. 2008;76(3):367.
42. Hardy KK, Willard VW, Allen TM, Bonner MJ. Working memory training in survivors of pediatric cancer: a randomized pilot study. *Psycho-oncology*. 2013;22(8):1856–65.
43. Lannering B, Marky I, Lundberg A, Olsson E. Long-term sequelae after pediatric brain tumors: their effect on disability and quality of life. *Med Pediatr Oncol*. 1990;18(4):304–10.
44. Zebrack BJ, Gurney JG, Oeffinger K, Whitton J, Packer RJ, Mertens A, Turk N, Castleberry R, Dreyer Z, Robison LL. Psychological outcomes in long-term survivors of childhood brain cancer: a report from the childhood cancer survivor study. *J Clin Oncol*. 2004;22(6):999–1006.
45. Ness KK, Mertens AC, Hudson MM, Wall MM, Leisenring WM, Oeffinger KC, Sklar CA, Robison LL, Gurney JG. Limitations on physical performance and daily activities among long-term survivors of childhood cancer. *Ann Intern Med*. 2005;143(9):639–47.
46. Fuemmeler BF, Mullins LL, Marx BP. Posttraumatic stress and general distress among parents of children surviving a brain tumor. *Children's Health Care*. 2001;30(3):169–82.
47. Chien L-Y, Lo L-H, Chen C-J, Chen Y-C, Chiang C-C, Chao Y-MY. Quality of life among primary caregivers of Taiwanese children with brain tumor. *Cancer Nurs*. 2003;26(4):305–11.
48. Kearney JA, Salley CG, Muriel AC. Standards of psychosocial care for parents of children with cancer. *Pediatr Blood Cancer*. 2015;62(S5):S632–83.
49. Musiol K, Bulska W, Brożek P, Ośliżło B, Ryzak S, Dubiel J, Sobol-Milejska G. Quality of life in survivors of childhood brain tumour and the association of children's diseases on quality of their parents life. *Psycho-Oncology*. 2019;28(5):1088–95.
50. Thurman DJ, Beghi E, Begley CE, Berg AT, Buchhalter JR, Ding D, Hesdorffer DC, Hauser WA, Kazis L, Kobau R. Standards for epidemiologic studies and surveillance of epilepsy. *Epilepsia*. 2011;52:2–26.
51. Ott D, Siddarth P, Gurbani S, Koh S, Tournay A, Shields WD, Caplan R. Behavioral disorders in pediatric epilepsy: unmet psychiatric need. *Epilepsia*. 2003;44(4):591–7.
52. Reilly C, Atkinson P, Das K, Chin R, Aylett S, Burch V, Gillberg C, Scott R, Neville B. A population-based study of neurobehavioral comorbidities in children with active epilepsy. *Pediatrics*. 2014;133(6):e1586–1593.
53. Baca CB, Vickrey BG, Caplan R, Vassar SD, Berg AT. Psychiatric and medical comorbidity and quality of life outcomes in childhood-onset epilepsy. *Pediatrics*. 2011;128(6):e1532–43.
54. Reilly C, Atkinson P, Das KB, Chin RF, Aylett SE, Burch V, Gillberg C, Scott RC, Neville BG. Factors associated with quality of life in active childhood epilepsy: a population-based study. *Eur J Pediatr Neurol*. 2015;19(3):308–13.
55. Fastenau PS, Shen J, Dunn DW, Austin JK. Academic underachievement among children with epilepsy: proportion exceeding psychometric criteria for learning disability and associated risk factors. *J Learn Disabil*. 2008;41(3):195–207.
56. Aguiar BVK, Guerreiro MM, McBrien D, Montenegro MA. Seizure impact on the school attendance in children with epilepsy. *Seizure*. 2007;16(8):698–702.
57. Yu Z, Shao Q, Hou K, Wang Y, Sun X. The experiences of caregivers of children with epilepsy: a meta-synthesis of qualitative research studies. *Front Psychiatry*. 2022;13:987892.
58. Lee S-A, Han S-H, Cho Y-J, Kim KT, Kim J-E, Shin DJ, Seo J-G, Kim Y-S, Ryu HU, Lee S-Y. Factors associated with stigma and depressive symptoms in family members of patients with epilepsy. *Epilepsy Behav*. 2020;110:107129.
59. King-Stephens D, Wheless J, Krogh C, Bettles M, Niemira J, Stolper R, Benitez A, Fournier M, Spalding W, Lu M. Burden of disease in patients with a history of status epilepticus and their caregivers. *Epilepsy Behav*. 2020;112:107374.
60. Innašimuthu AJ, Jayaraman D, Jeyarani G, Scott JX, Iyengar SK, Subramanian L, Sneha LM, Kovindan BT, Arul J. Quality of life of parents of children with Cancer—Single-Center, prospective cross-sectional study from South India. *Indian J Med Pediatr Oncol*. 2022;43(03):255–61.
61. Siddiqui DF, Ashraf MS, Iftikhar S, Belgaumi AF. Predictors of treatment abandonment for patients with pediatric cancer at Indus Children Cancer Hospital, Karachi, Pakistan. *Pediatr Blood Cancer*. 2018;65(2):e26818.
62. Catt SL, Anderson JL, Chalmers AJ, Fallowfield LJ. A UK-wide survey of follow-up practices for patients with high-grade glioma treated with radical intent. *J Eval Clin Pract*. 2011;17(1):1–6.
63. Giovagnoli A, Silvani A, Colombo E, Boiardi A. Facets and determinants of quality of life in patients with recurrent high grade glioma. *J Neurol Neurosurg Psychiatry*. 2005;76(4):562.
64. Sherman D, Fessele KL. Financial support models: a case for use of financial navigators in the oncology setting. *Clin J Oncol Nurs*. 2019;23(5):14–8.
65. Kline CN, Mueller S. Neurocognitive outcomes in children with brain tumors. *Seminars in Neurology*: 2020. Thieme Medical; 2020. pp. 315–21.
66. Brière ME, Scott JG, McNall-Knapp RY, Adams RL. Cognitive outcome in pediatric brain tumor survivors: delayed attention deficit at long-term follow-up. *Pediatr Blood Cancer*. 2008;50(2):337–40.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.