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GLOBAL ONCOLOGY: RESEARCH ARTICLE

Epidemiological characteristics and survival outcomes of children with medulloblastoma treated at the National Cancer Institute (INCA) in Rio de Janeiro, Brazil

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Abstract

Background: Medulloblastoma (MB),the most common malignant brain tumor of childhood has survival outcomes exceeding 80% for standard-risk and 60% for high-risk patients in high-income countries (HICs). These results have not been replicated in low- and middle-income countries (LMICs), where 80% of children with cancer live.

Methods: This is a retrospective review of 114 children aged 3–18 years diagnosed with MB from 1997 to 2016 at National Cancer Institute (INCA). Sociodemographic, clinical, and treatment data were extracted from the medical records and summarized descriptively. Overall survival (OS) and progression-free survival (PFS) were calculated using the Kaplan–Meier method.

Results: The male-to-female ratio was 1.32 and the median age at diagnosis was 8.2 years. Headache (83%) and nausea/vomiting (78%) were the most common presenting symptoms. Five-year OS was 59.1% and PFS was 58.4%. The OS for standard-risk and high-risk patients was 69% and 53%, respectively. The median time to diagnosis interval was 50.5 days and the median time from surgery to radiation therapy initiation was 50.4 days. Patients who lived >40 km from INCA fared better (OS = 68.2% vs. 51.1%, $p = .032$). Almost 20% of families lived below the Brazilian minimum wage. Forty-five patients (35%) had metastatic disease at admission. Gross total resection was achieved in 57% of the patitents.

Conclusions: Although there are considerable barriers to deliver effective MB treatment in countries like Brazil, the OS seen in the present study demonstrates that good outcomes are not only feasible but can and should be increased with appropriate interventions.

KEYWORDS
childhood cancer, medulloblastoma, survival analysis

Abbreviations: CI, confidence interval; COG, Children's Oncology Group; CSI, craniospinal irradiation; GTR, gross total resection; Gy, Gray; HIC, high-income country; HR, high risk; INCA, National Cancer Institute; LMIC, low- and middle-income country; M+, metastatic disease; M0, localized disease; MB, medulloblastoma; MRI, magnetic resonance imaging; NOS, not otherwise specified; OS, overall survival; PFS, progression-free survival; SR, standard risk; STR, subtotal resection; UMIC, upper middle-income country

1 | INTRODUCTION

Medulloblastoma(MB) is the most common malignant brain tumor that occurs in children.[1] Current therapies in children include maximal safe resection and/or radiation therapy, followed by maintenance chemotherapy. In high-income countries (HICs), the survival outcomes of MB are 80% for standard-risk (SR) and 60% for high-risk (HR) patients.[2] These outcomes are largely due to refined risk stratification, surgical expertise, timely radiation therapy, advancements in imaging technology, and supportive care that are available in HICs. Current strategies are also focused on reducing the long-term sequelae of the available treatment.[3–6] Unfortunately, the same survival outcomes are not seen in patients from low- and middle-income countries (LMICs), where almost 80% of all children with cancer live.[7–9] Most epidemiological studies of MB in LMIC settings are retrospective, descriptive, with few addressing survival, and within these, there is a wide range of treatment outcomes. For example, 5-year overall survival (OS) of 32% in a study from Pakistan with 63 patients; 5-year OS and EFS of 43% and 41%, respectively, in Turkey with 203 patients; 5-year OS of 48% in China, with 173 patients; 5-year OS of 53.8% in a southern Thailand study, with 55 patients; 7-year OS and progression-free survival (PFS) of 59% and 53.8%, respectively, in Iran, with 126 patients; and finally, 3-year OS of 100% for average-risk (12) patients and 81% for HR (37) patients in a Jordanian study.[10–15] In Latin America, we found one study from Mexico with 26 patients and 5-year OS of 69%[16] and one from Argentina, but exclusively with infants, with 29 patients, and a PFS of 70%.[17] A few studies have been performed in Brazil, with different 5-year survival outcomes for SR patients: 50% in a study with 69 patients from Porto Alegre; 81% in study with 106 patients from Campinas; and 53%, for the whole cohort, in a study with 101 patients from Rio de Janeiro.[18–20]

Pediatric brain cancer patients living in LMICs have lower survival rates for a multitude of reasons including barriers to accessing medical services, shortages of primary care professionals, a lack of knowledge regarding brain tumor symptoms leading to delays in diagnosis, difficulty in patient referral to health care settings, and a lack of available subspecialtisty care with appropriate expertise.[21] Data predominantly from HICs have found that delays in care and lack of specialized treatment centers can impact outcomes, specifically in pediatric brain tumors.[22–24] The most common initial presenting symptoms (i.e., headache, nausea, and emesis) can be attributed to many benign childhood conditions, which frequently lead to delayed diagnoses. It may be difficult for patients to obtain diagnostic and timely postoperative magnetic resonance imaging (MRI) due to lack of resources, which can affect tumor staging and risk stratification, and therefore contribute to under- or over-treatment.[24] Surgery is not always performed by a pediatric neurosurgeon, which can affect the quality of the resection. Several reports have indicated that pediatric neurosurgeons achieve better results with fewer postoperative complications, such as cerebellar mutism.[25–27] These same factors that negatively impact survival outcomes in HICs are likely present, if not exacerbated, in LMICs.

According to the World Bank classification in 2018,[28] Brazil is an upper middle-income country (UMIC), with a gross national per capita income of $9140 (United States Dollars [USD]). With a population of more than 209 million, Brazil has vast socio-economical disparities within its five major regions. The National Cancer Institute (INCA) is located in the state of Rio de Janeiro, in southeastern Brazil, and is the branch of the Ministry of Health responsible for leading a country-wide policy for the prevention and control of cancer.[29] The median incidence rate for pediatric CNS tumors in Brazil (2016) was 20.49 cases per million between 0 and 14 years and 17.94 cases per million between 0 and 19 years, according to Brazilian population-based registries.[30] INCA is a tertiary care reference center for the free treament of children and adults with cancer within Brazil's Unified Public Health System (SUS). INCA's pediatric cancer treatment approach includes a multidisciplinary team of pediatric oncologists, neurosurgeons, neuro-radiologists, pathologists, and radiation oncologists, among others. Patients who are identified as HR for abandoning treatment (low socioeconomic status, residence far from the treatment center, intensive treatment, among others) receive additional support including food, lodging, and transportation from both government and nonprofit organizations.[31] On average, 200 new solid tumor pediatric patients are registred annually, 40–50 of which are patients with brain tumors.

The aim of the present study was to describe the epidemiological characteristics of and provide survival outcome data for children treated for MB at a single public, tertiary care referral center in Rio de Janeiro, Brazil.

2 | METHODS

2.1 | Study population

We retrospectively reviewed the medical records of pediatric MB patients at INCA, in Rio de Janeiro, Brazil. The inclusion criteria were as follows: patients 3–18 years old with a histopatologically confirmed diagnosis of MB between January 1997 and December 2016. The sample was limited to patients who received full adjuvant treatment at INCA; therefore, we excluded patients who had previously received chemotherapy or radiation therapy in other facilities. Patients who had surgery at other hospitals were included. Abandonment was defined as ≥4 consecutive weeks for patients who failed to start or complete therapy of a potentially curable disease.

An initial search revealed 134 patients that met the inclusion criteria; five patients were excluded due to missing data, six without an adequate performance status to receive adjuvant treatment after surgery, five patients were treated elsewhere, and four patients were admitted exclusively for radiation therapy, after which they would resume treatment at their original hospital. After these exclusions, a total of 114 patients were included in the analysis. The study was approved by the hospital ethics committee.

2.2 | Patient data

The patient records were examined for relevant demographic and clinical data. Demographic and socioeconomic characteristics were recorded, including age, sex, family income, city of origin, distance from INCA, maternal age, home type, level of maternal education, and presence of household utilities (i.e., water, sewage, and electricity). Racial and ethnic information is captured in a subjective way in Brazil and therefore it was not included in the analysis. Clinical data regarding disease and treatment information included initial symptoms, first radiological evaluation, surgery location (INCA or another hospital), histology report for the tumor and cerebrospinal fluid cytology, risk stratification, surgical report, residual tumor volume, modified Changt's staging criteria (M0: nonmetastatic; M+: seeding to the spinal subarachnoid space, to supratentorial compartment or out of the cerebrospinal axis), craniospinal radiation therapy dose (23.4 or 36 Gy, according to stratification risk), with boost to the posterior fossa in HR patients or to the tumor bed in SR patients, and chemotherapy regimen (pre-irradiation regimen, Children's Oncology Group [COG] A9961, or others).

2.3 | Study definitions and treatment

A higher education level was defined as more than 9 years of education. The patients were separated into two groups based on the median distance from home to the tertiary cancer center: close (≤40 km) and far from INCA (>40 km). The diagnosis date was defined as the date of the primary tumor surgery. The extent of surgical resection was categorized into two major groups based on surgeon's report: gross total resection (GTR) and subtotal resection (STR)/biopsy, in which some of the tumor remained. Patients were classified as HR if they had evidence of metastases and residual tumor >1.5 cm^2 on postoperative MRI. Patients with localized disease, with residual tumor <1.5 cm^2 and >3 years were classified as SR. The histopathologic diagnoses were divided into the following groups: classic, anaplastic/large cell, desmoplastic/extensive nodularity, and not otherwise specified (NOS). Molecular analyses were not performed in this cohort.

Between April 1997 and March 2000, all patients received our institutional pre-irradiation chemotherapy regimen consisting of three cycles of ifosfamide/etoposide and three cycles of cisplatin/vincristine, with radiation therapy starting by week 15 (36 Gy craniospinal irradiation [CSI] plus a boost to the posterior fossa). After March 2000, the COG A9961 regimen became the standard treatment for children aged >3 years.[32] Per this regimen, children were treated with upfront radiation therapy (23.4 Gy CSI for SR and 36 Gy CSI for HR patients) with concomitant vincristine. Until the 3D conformal radiation therapy was implemented in 2002, every patient had a boost of 32.4 Gy to the posterior fossa. After that, SR patients had the boost to the tumor bed. The total radiation dose was 54 Gy. After 6 weeks of termination of the radiation therapy, the treatment was continued with eight cycles of maintenance chemotherapy with cisplatin, vincristine, and lomustine.

2.4 | Statistical analysis

All data were described using standard summary statistics. Survival estimates were obtained using the Kaplan–Meier method, and were presented with corresponding 95% confidence intervals (CIs). PFS was defined as the time from registry at INCA to the date of first relapse or progression of disease, death, secondary malignancy, or the date of last follow-up. OS was measured as the time from registry at INCA to the date of death or last follow-up. Log-rank tests were used to compare survival between patient groups. *p*-Values were two-sided and those less than .05 were considered statistically significant. Statistical analyses were performed using the R statistical package (R Foundation for Statistical Computing, Vienna, Austria) using the *survival* and *survminer* packages.

3 | RESULTS

3.1 | Patient demographic and socioeconomic characteristics

Data on 114 patients aged 3–18 years with histopathologically confirmed MB who were admitted to INCA between 1997 and 2016 were extracted from medical records. The male-to-female ratio was 1.32, and the median age at diagnosis was 8.2 years (range 3–17.7). Almost 75% of the children lived in the city of Rio de Janeiro and surrounding areas. The median distance from the patientt's homes to INCA was 40 km. High maternal education levels were found in 30% ($n = 34$) of the patients; however, this information was only available for 47% ($n = 53$) of the patients. The median maternal age at diagnosis was 35 years (range 20–54 years). Nearly 20% of the families had a household income of less than minimum wage. Eletricity, sewage, and water were available in more than 80% of the homes (Table 1).

There were two patients who abandoned treatment after completing radiation therapy. Both patients resumed follow-up, without chemotherapy.

3.2 | Clinical characteristics

Headache (83%), nausea/vomiting (78%), and visual disturbances (37%) were the most frequently reported initial symptoms described by families. The median time between the onset of symptoms and surgery (time to diagnosis interval) was 50.5 days (range 0–1151 days).

All 114 patients had surgery for their disease, 42% ($n = 48$) of which occurred at INCA. GTR, as described by the neurosurgeon, was achieved in 65 patients (57%). All patients had a postoperative MRI at different time intervals before radiation therapy. On radiological reports 52% of the patients ($n = 59$) showed less than 1.5 cm^2 of residual tumor. The majority of the tumors were found to be MB NOS (86%), followed by desmoplastic/extensive nodularity (4.4%), classic histology (5.3%), and large cell/anaplastic (2.4%). Based on the modified Chang's

TABLE 1 Demographics and socioeconomic information

	N (%)
Male sex	65 (57)
Median age at diagnosis (range)	8.2 years (3–17.7)
City of origin	
Rio de Janeiro (and surrounding)	85 (74.4)
Other cities	25 (21.9)
Unknown	4 (3.7)
Distance from tertiary center	
≤40 km	47 (41.2)
>40 km	49 (42.9)
Unknown	18 (15.7)
Family income (# of min wages)	
<1	21 (18.4)
1–1.9	27 (23.7)
2–2.9	14 (12.3)
≥3	34 (29.8)
Unknown	18 (15.8)
Median paternal age (range)	38 (23–68)
Median maternal age (range)	35 (20–54)
Maternal education	
9 years or less	19 (16.5)
More than 9 years	34 (30)
Unknown	61 (53.5)
Home type	
House	77 (68)
Apartment	9 (8)
Shack	16 (14.2)
Unknown	11 (9.8)
Water availability	90/101
Sewage availability	83/100
Electricity availability	98/99

Abbreviation: km, kilometer.

classification, 35% (n = 40) of the patients were considered to have metastatic disease (M+) at diagnosis. Of the 114 patients, 57% (n = 65) were defined as HR patients, 105 patients received chemotherapy (92%), and 109 received radiation therapy (95%) (Table 2).

The median time to radiation therapy initiation (TTR) for patients treated as per COG A9961 protocol was 50.4 days (range 11.9–259 days), and 33 days (range 12–77 days) for patients who underwent surgery at INCA (n = 38). For patients who had surgery at a facility other than INCA (n = 45), the median TTR was 68 days (range 21–260 days, $p < .0001$). We did not evaluate TTR for the remaining 12 patients because they were treated with pre-irradiation chemotherapy and therefore began radiation therapy after chemotherapy (week 15), and not after surgery.

3.3 | Survival analysis

The median follow-up was 5 years, and 5-year estimated PFS and OS for the entire population were 58.4% (95% CI: 49.4%–69.1%) and 59.1% (95% CI: 50.5%–69.3%), respectively (Figure 1). Patients with localized disease (71.0% [95% CI: 60.3%–83.7%]) had better OS compared to those with metastatic disease (52.9% [95% CI: 38.7%–72.4%]; p = .019) (Figure 2). There was no statistical significance between GTR (63% [95% CI: 53%–77%]) and STR (58% [95% CI: 42%–80%]) nor between SR patients (68.6% [95% CI: 56.1%–83.7%]) and HR patients (53.7% [95% CI: 43.0%–67.0%]). Patients who lived >40 km from INCA (5-year OS: 68.2%) fared better than those who lived closer (5-year OS: 52%; p = .032) and patients with sewage at home fared worse

TABLE 2 Disease and treatment information

Initial symptoms	***N* = 111**
Headache	93 (83.7)
Nausea/vomiting	87 (78.3)
Visual disturbances	42 (37.8)
Ataxia	35 (31.5)
Seizures	6 (5.4)
Facial paralysis	4 (3.6)
Lethargy	2 (1.8)
Somnolence	10 (9)
First radiological exam	
CT	65 (57)
MRI	13 (11.4)
Both CT and MRI	33 (29)
Unknown	3 (2.6)
Median time to diagnosis (range)	50.5 days (0–1151)
Surgery location	
INCA	48 (42)
Other hospital	66 (57)
Ventricularperitoneal shunt	64/100
Histology report	
Classic	6 (5.3)
EN/DM	5 (4.4)
Large cell/anaplastic	3 (2.7)
Not specific	98 (86)
M stage	
M0	62 (54.4)
M+	40 (35)
Unknown	12 (10.6)
Risk stratification	
Standard risk	44 (38.5)
High risk	65 (57)
Unknown	5 (4.5)
Surgery outcome (surgeon report)	
GTR	65 (57)
<GTR (STR or biopsy)	32 (28)
Unknown	17 (15)
Residual tumor	
≥1.5 cm	22 (19.1)
<1.5 cm	59 (52)
Unknown	33 (28.9)
Chemotherapy regimen	
Pre-irradiation regimen	12 (10.5)
COG A9961	82 (72)
Others	7 (6.2)
Unknown	13 (11.3)

Abbreviations: CT, computerized tomography; MRI, magnetic resonance imaging; EN/DN, extensive nodularity/desmoplastic; GTR, gross total resection; STR, subtotal resection.

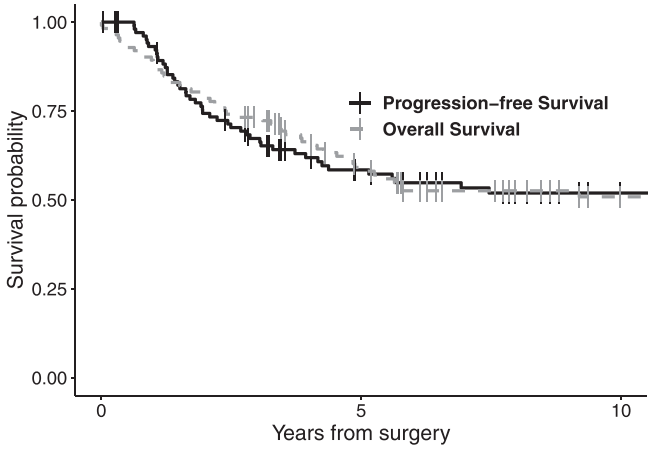

FIGURE 1 Overall survival and progression-free survival of the entire cohort

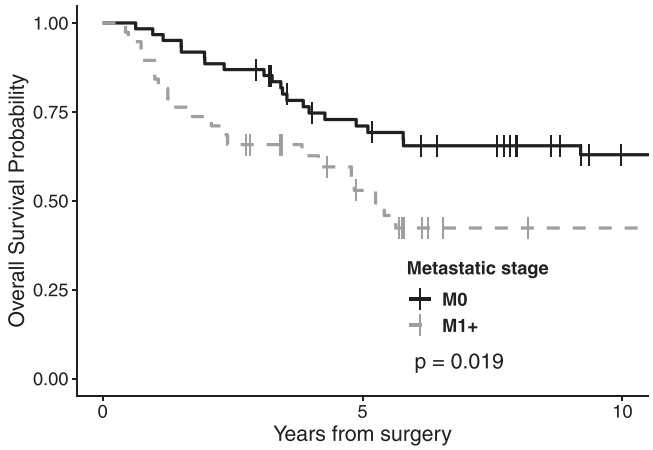

FIGURE 2 Overall survival according to M stage

(HR: 3.02, 95% CI: 1.08–8.46), which means they had a higher chance of dying (Table 3). No other correlations were found between sociodemographic factors and survival in univariable Cox proportional hazard models.

4 | DISCUSSION

The present study aimed to describe the epidemiological characteristics and provide survival outcome data for children with MB, aged 3–18 years, treated in a single public tertiary care referral center located in Rio de Janeiro, Brazil.

In a previous retrospective study from 1983 to 2001 of 101 MB patients under 18 years, at INCA, the 5-year OS was 53% and 5-year disease-free survival (DFS) rate was 40%.[20] The results of the present study showed an increase in the 5-year OS reaching 59.1%. This improved outcome may possibly be due to treatment standardization with international protocols, such as COG A9961 and improvements in diagnosis and clinical support such as the introduction of six beds in the pediatric intensive care unit (2002) and in the pediatric emergency department (2009). Radiation therapy with 3D conformal technique was implemented in 2002.

An evaluation of sociodemographic factors revealed certain characteristics of LMICs that could have contributed to lower survival outcomes, such as low family income and lower maternal education levels; however, no correlation with survival was statistically significant aside from distance from home to the treatment center. Possible explanations for this include missing or incomplete information in the medical records and the small number of patients in the cohort, which may have skewed the results. The impact of socioeconomic factors and disparities in medical access on survival outcomes have been studied in pediatric oncology, specifically in brain tumors, with inconclusive results.[33–41] Previous sociodemographic studies in MB focused largely on long-term survivorship and neuropsychological results,[42–44] but not on survival outcomes.

Patients who lived >40 km from INCA fared better than those who lived closer (5-year OS: 68.2% vs. 52%, respectively; $p = .032$). This unexpected conclusion may be explained by the socioeconomic conditions that Brazilian patients face during their treatment. Almost 43% of patients live more >40 km from INCA, and these patients and their parents, can stay in housing provided by Ronald McDonald House Charities. This housing is near the hospital and provided transportation at any time of day and in case of emergencies such as fever. This ensured that even the poorest patients had prompt access to medical interventions and also decreased the treatment abandonment.[31] Avoiding delays in treatment is crucial when treating infectious events in neutropenic patients, and socioeconomic factors have previously been linked to sepsis and mortality.[45] Patients often complain about a lack of transportation to access the hospital for outpatient consultations or emergencies, and while the government provides some resources for patient transportation, these resources are not easily accessible to all eligible patients.

The results of the study indicated that patients with sewage in the home had a higher chance of dying. This finding is counterintuitive, and we are unable to provide a clinical explanation. It is possible the data are skewed because it was a small number of patients without sewage that were still alive.

The time-to-diagnosis interval (median 50.5 days) was longer than those reported in a previous study from United States whose median interval was 30 days, but shorter than another study from United States and one study from France, whose median interval was 56 and 65 days, respectively, and the latter was not associated to decreased survival.[46–48] In the present study, the wide range for time-to-diagnosis interval (0–1151 days) is due to an outlier result from a patient who had previous rheumatological disease with nonspecific symptoms, which delayed the MB diagnosis. The increased time to diagnosis interval can be explained by low suspicion for brain tumors by primary care and emergency professionals, barriers to neuroimaging, and untimely referrals to INCA. "HeadSmart: Be Brain Tumour Aware" is an initiative from the United Kingdom that provides guidelines for health care professionals regarding symptoms suspicious for a brain tumor.[49] With their program, the total diagnostic interval in the United Kingdom was reduced from 13 weeks in 2011 to 6.7 weeks in 2013.[50] Initiatives such

TABLE 3 Univariate analysis of sociodemographic factors and overall survival

Characteristic	HR	95% CI	*p*-Value
Distance from treatment center			
≤40 km	*Reference*	–	–
>40 km	0.51	0.27–0.95	.0352*
Family income (# of minimum wages)			
<1	*Reference*	–	–
1–1.9	1.11	0.48–2.61	.80
2–2.9	0.81	0.30–2.18	.67
≥3	1.22	0.54–2.74	.63
Water availability	3.55	0.86–14.7	.08
Sewage availability	3.02	1.08–8.46	.0349*
Electricity availability	N/A*		
Maternal education			
≤9 years	*Reference*	–	–
>9 years	1.67	0.69–4.05	.26
Paternal education			
≤9 years	*Reference*	–	–
>9 years	1.10	0.43–2.84	.85
Mother age	1.01	0.96–1.05	.81
Father age	1.00	0.96–1.03	.86

Abbreviations: CI, confidence interval; HR, hazard ratio.

as these could be adopted and have a meaningful impact in the diagnostic interval in our country.

Patients who had surgery in other institutions had significantly longer median TTR than those operated at our hospital (68 vs. 33 days, respectively; $p < .001$). This significant difference highlights the need for specialized centers with multidisciplinary teams that can diagnose and treat cancer patients in a timely manner.

Only 52% of the patients had a postoperative MRI showing less than 1.5 cm^2 of residual disease. We did not perform central review of the images to confirm these findings. GTR was achieved in 57% of patients in the present study, according to the surgeon reports. There was no stastitical significance in the difference in OS and PFS between GTR and STR, which might be explained by not being able to confirm resection status with a postoperative MRI prior to intiating therapy. The small proportion of patients with less than 1.5 cm^2 of residual disease may be accounted to technical aspects such as some patients being operated by neurosurgeons without pediatric expertise, or at emergency hospitals without an MRI prior to surgery, affecting the surgical planning. In some cases, postoperative MRI was only performed after the patient was admitted at INCA. There were a small number of patients with postoperative MRI within 72 hours as recommended by the standard of care. The small proportion of patients with residual disease less than 1.5 cm^2 might have affected the proper risk stratification, with more patients stratified as HR. This might also explain why there was no statistical significance in the difference in OS and PFS between SR and HR patients. Until 2002, the radiation therapy planning was based on either CT or MRI because the technique was 2D conventional radiation therapy. After that the 3D conformal radiation therapy was implemented and MRI became essential for the planning. This issue of timely MRI (within 72 hours postoperatively) is being addressed in order to accurately stratify our patients and enhance radiation treatment plans prior to starting therapy.

The largest histological subtype reported in our study was MB NOS (86%). In our institution in earlier times, the pathologists used to report the classic subtype as "medulloblastoma," hindering the stratification. For proper stratification, it is necessary to determine the accurate histopathological subtype because certain histological subtypes are also important for risk stratification.[51,52] One of our next goals is to improve the quality in the histopathological reports by enhancing the pathologists training.

The use of chemotherapy immediately after surgery with delayed radiation therapy has shown poor outcomes compared to patients who received upfront radiation therapy.[53,54] In our cohort, a small group of patients ($n = 12$) received pre-irradiation chemotherapy by week 15, whereas 83 patients received upfront radiation therapy postoperatively as per the COG A9961 protocol, which was implemented in 2000. There are strategies that recommend upfront radiation therapy, with risk-adapted CSI and adjuvant chemotherapy in children aged 3–5 years,[1] while other regimens for infants and young children recommend treatment with either high-dose chemotherapy and stem cell transplantion[55–57] or intraventricular chemotherapy,[58–61] in order to avoid or delay the use of radiation therapy.

HICs generally have better survival outcomes than LMICs. The COG A9961 protocol, conducted in the United States, had a 5-year OS 87%

for SR patients.[32] Reports from a large study from Canada with 628 patients and from the United Kingdom with 25 patients indicated survival outcomes of 69.2% and 73.4%, respectively.[62,63] There are disparities among HICs, however, with some showing lower survival rates: a multi-institutional Spanish study had a 5-year OS of 55%, a study from Singapore had 51.5%, and from Norway 62%.[64–67] UMICs also reported variable outcomes: Taiwan reported 5-year OS of 65.9% and 50%, and Malaysia reported 58.3%.[68–70]

The survival gap between HICs and LMICs is multifactorial. Late diagnosis with advanced disease presentation, comorbidities (such as malnutrition), treatment abandonment, and inefficient health care systems are some of the barriers to care for pediatric cancer patients in LMICs.[21]

In order to reduce the survival gap, we should focus on raising brain tumor awareness and improving early diagnosis, using strategies such as "HeadSmart," strengthening relations with pediatric neurosurgeons and other services to facilitate referrals to cancer centers, working to improve quality of histopathological diagnosis with incorporation of molecular biology, timely postoperative MRI for appropriate risk stratification, and investing and prioritizing financial support for lodging and transportation for families at risk of abandonment. LMICs should participate in cooperative trials and in twinning programs to improve knowledge and exchange experiences.[15,71–73] These tele-oncology tumor boards are an opportunity to access high-level subspecialists that provide feasible treatment recommendations. Additionally, data collection is enormously important, as it allows for improved epidemiological analysis and decision-making policy.

The limitations of our study are primarily its retrospective nature and the limitations of the information in the medical records, particularly missing data. The strengths of the present study are the relatively large number of patients with MB from a single institution in LMIC, and the homogeneous treatment that most patients received. INCA as a public hospital for pediatric cancer patients admits most pediatric cancer patients in the state.

In short, as LMIC, treating MB in Brazil can be challenging. We found no statistical association between socioeconomic factors and survival, other than when evaluating the distance from home to the cancer treatment center. Although there are considerable barriers to deliver effective MB treatment in countries like Brazil, the PFS and OS seen in our study demonstrated that good outcomes are feasible, but appropriate interventions can and should be implemented to improve upon these outcomes.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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