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Predictors of Outcome in Pediatric Medulloblastoma

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ABSTRACT

Background: Medulloblastoma is the most common malignant brain tumor in children, arising in the cerebellum and representing a significant cause of morbidity and mortality in pediatric neuro-oncology. This study was done to evaluate clinical, radiological, and surgical predictors of short-term outcomes in pediatric patients diagnosed with medulloblastoma.

Methods: This retrospective, analytical, observational cohort study was conducted at the Pediatric Neurosurgery Department of the Children's Hospital and the Institute of Child Health, Multan, Pakistan, from January 2022 to March 2025. Data of children aged 1 to 12 years, histologically confirmed medulloblastoma, and underwent surgical intervention, were analysed. Non-probability consecutive sampling technique was adopted. Short-term outcomes were documented in terms of mortality, and postoperative complications at 12 months. Data were analysed using IBM SPSS Statistics version 26.0. Associations with 12-month mortality were assessed using chi-square or Fisher's exact test.

Results: Among 60 children with medulloblastoma, 39 (65.0%) were male, and the mean age was 6.80±2.60 years. Gross-total resection was achieved in 32 (53.3%) cases. Postoperative complications included CSF leak and meningitis in 11 (18.3%) each. Classic histology was most common (63.3%). Radiotherapy and chemotherapy were administered in 88.3% and 85.0% of cases, respectively. Survival analysis estimated a 12-month overall survival of 90.0%. Mortality was significantly associated with younger age (p=0.008), short symptom duration (p=0.039), altered consciousness (p=0.005), metastasis (p=0.004), subtotal resection (p<0.001), meningitis (p=0.005), and anaplastic histology (p=0.008).

Conclusion: Relatively younger age, short symptom duration, altered consciousness at presentation, metastatic disease, subtotal resection, postoperative meningitis, and large cell/anaplastic histology were significantly contributors to 12-month mortality.

Keywords: Altered consciousness, Children, Medulloblastoma, Meningitis, Mortality, Survival.

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INTRODUCTION

Medulloblastoma is the most common malignant brain tumor in children, arising in the cerebellum and representing a significant cause of morbidity and mortality in pediatric neuro-oncology.[1,2] Medulloblastoma represents 15-25% of all pediatric brain tumors.[2,3] The 5-year overall survival rate varies between 60% and 85%, depending on risk stratification.[4,5] Although recent advances in multimodal treatment comprising surgery, craniospinal irradiation, and chemotherapy have improved survival rates, outcomes remain variable.[6,7,8] These outcomes are influenced by a range of clinical, histopathological, radiological, and molecular factors, making early identification of prognostic indicators essential for risk stratification and management.[9]

Medulloblastoma typically presents with signs of raised intracranial pressure (headache, vomiting, papilledema), cerebellar dysfunction (ataxia), or hydrocephalus.[10] Standard therapy includes maximal safe surgical resection followed by craniospinal radiotherapy and adjuvant chemotherapy. Despite these aggressive measures, survival and quality of life differ greatly among patients. Recent research has focused on identifying predictors of outcomes, including age at diagnosis, extent of tumor resection, presence of metastases at presentation, histological subtypes, and emerging molecular classifications, Sonic Hedgehog (SHH), Group 3, and Group 4). Understanding the prognostic value of these variables is the key to individualizing therapy and improving long-term results. The WNT molecular subgroup has the best prognosis (>90% survival), while Group 3 with myelocytomatosis oncogene (MYC) amplification has the poorest (<50%).[11] Metastatic disease at presentation could be present in as high as 50% of patients and is associated with poorer outcomes.[12,13] Gross total resection significantly improves prognosis compared to subtotal resection.

Despite treatment advancements, outcome disparities in pediatric medulloblastoma persist due to clinical and biological heterogeneity. Identifying reliable predictors of outcome can help tailor treatment intensity, guide surveillance strategies, and inform counseling of caregivers. In developing countries like Pakistan, where access to molecular diagnostics is limited, evaluating conventional prognostic indicators such as age, surgical margins, and metastasis becomes even more critical. That is why the current study was planned, aiming to evaluate clinical, radiological, and surgical predictors of short-term outcomes in pediatric patients diagnosed with medulloblastoma. The findings of this study would not be a useful addition to the existing statistics, but it would also help to improve risk stratification and management in resource-limited settings.

METHODS

This retrospective, analytical, observational cohort study was conducted at the Pediatric Neurosurgery Department of the Children's Hospital and the Institute of Child Health, Multan, Pakistan, from January 2022 to March 2025. Using the institutional database, records of pediatric patients diagnosed with medulloblastoma were reviewed. Approval from the ethical review committee was obtained (Letter no. 776). Being a retrospective study, this did not require approval prior to the start of study period as per institutional protocols.

A non-probability consecutive sampling technique was adopted for sample selection. No specific sample size was calculated as data were corrected retrospectively and this study included all eligible children fulfilling the inclusion and exclusion criteria. The inclusion criteria were children of any gender, aged 1 to 12 years, with histologically confirmed medulloblastoma, and who underwent surgical intervention. Only those patients whose complete medical records, radiological reports, operative notes, histopathology results, and follow-up data of 12-months, were available were included in this study. The exclusion criteria were patients with incomplete records or who were lost to follow-up within the first three months post-treatment. As this was a retrospective study, no formal sample size calculation was performed. Instead, all 60 consecutive cases that fulfilled the eligibility criteria and had complete 12-month follow-up data were included in the analysis. Data variables included demographic information (age, gender), duration of symptoms, clinical features, imaging findings, and surgical details. Histopathological subtypes were documented. Short-term outcomes were assessed in terms of postoperative complications (including cerebrospinal fluid (CSF) leak, meningitis, cerebellar mutism, or shunt dependency), and mortality within the first 12 months.

Data were entered and analyzed using "IBM-SPSS Statistics" version 26.0. Quantitative variables, including age at diagnosis, duration of symptoms, and tumor size, were summarized as means and standard deviations (SD). Categorical variables, such as gender, clinical features, tumor location, extent of resection, histological subtype, and postoperative complications, were described using frequencies and percentages. Kaplan–Meier survival analysis was performed to estimate overall survival, and the survival function was plotted to visualize temporal trends in mortality. The chi-square test or Fisher's exact test was applied, as appropriate, to examine associations between categorical variables and 12-month mortality. The primary outcome was all-cause mortality within 12 months of diagnosis. P-value < 0.05 was considered statistically significant.

RESULTS

In a total of 60 children, 39 (65.0%) were males, and 21 (35.0%) females. The mean age, and weight were 6.80±2.60 years, and 20.42±8.44 kg, respectively. The mean duration of symptoms was 5.87±3.38 weeks. The mean tumor size was 4.71±0.97 cm. Extent of resection was gross total, near total, and sub-total in 32 (53.3%), 21 (35.0%), and 7 (11.7%) cases. Post-surgery complications included CSF leak, meningitis, and cerebellar mutism, observed among 11 (18.3%), 11 (18.3%), and 9 (15.0%) cases, respectively. Histology revealed classic, desmoplastic, and anaplastic medulloblastoma among 38 (63.3%), 14 (23.3%), and 8 (13.3%) cases, respectively. Radiotherapy, and chemotherapy were required by 53 (88.3%), and 51 (85.0%) children, respectively. At 12-month follow-up evaluation, 50 (83.3%) children were alive and disease-free, whereas recurrence was reported in 4 (6.7%) cases. Overall, mortality was documented in 6 (10.0%) children. The Kaplan-Meier survival analysis demonstrated an estimated 12-month overall survival of 90.0% (95% CI: 82.0-97.0%). The survival curve showed an initial plateau in the early months post-treatment, followed by stepwise declines between months 6 and 12, consistent with the timing of tumor

recurrence or treatment-related complications (**Figure 1**). These findings reflect a relatively favorable early survival trend in this cohort, with the majority of deaths occurring in children with advanced metastasis or subtotal resection.

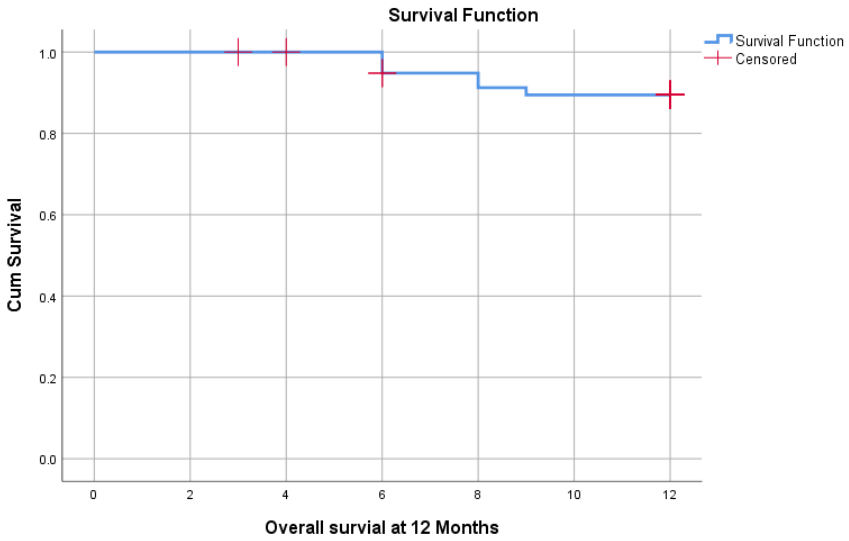

Figure 1: Survival Function for Overall Survival within 12 Months of Diagnosis in Children with Medulloblastoma

Table 1: Association of demographic, clinical and tumour-related characteristics with 12-month mortality in children with medulloblastoma (n=60)

Characteristics		Total (%)	Mortality		P-value
			No (n=54)	Yes (n=6)	
Gender	Male	39 (65.0)	36 (66.7%)	3 (50.0%)	0.417
	Female	21 (35.0)	18 (33.3%)	3 (50.0%)	
Age (years)	1-5	18 (30.0)	10 (18.5%)	4 (66.7%)	0.008
	>5 to 12	42 (70.0)	44 (81.5%)	2 (33.3%)	
Duration of symptoms (weeks)	<4	21 (35.0)	14 (25.9%)	4 (66.7%)	0.039
	≥4	39 (65.0)	40 (74.1%)	2 (33.3%)	
Presenting features/complaints	Headache	50 (83.3)	44 (81.5%)	6 (100%)	0.248
	Vomiting	44 (73.3)	38 (70.4%)	6 (100%)	0.119
	Ataxia	34 (56.7)	32 (59.3%)	2 (33.3%)	0.224
	Visual changes	32 (53.3)	28 (51.9%)	4 (66.7%)	0.490

	Seizures	16 (26.7)	15 (27.8%)	1 (16.7%)	0.559
	Irritability	12 (20.0)	10 (18.5%)	2 (33.3%)	0.389
	Altered consciousness	7 (11.7)	5 (9.3%)	3 (50.0%)	0.005
Tumor location	Lateral	21 (35.0)	20 (37.0%)	1 (16.7%)	0.321
	Midline	39 (65.0)	34 (63.0%)	5 (83.3%)	
Metastasis stage	M0	37 (61.7)	36 (66.7%)	1 (16.7%)	0.004
	M1	10 (16.7)	8 (14.8%)	2 (33.3%)	
	M2	5 (8.3)	5 (9.3%)	-	
	M3	7 (11.7)	5 (9.3%)	2 (33.3%)	
	M4	1 (1.7)	-	1 (16.7%)	

No significant association was observed between gender and 12-month mortality (p=0.417). Children aged 1–5 years had a significantly higher mortality rate (p=0.008). A shorter symptom duration (<4 weeks) was associated with increased mortality (p=0.039). Among presenting features, altered consciousness was significantly associated with mortality (p=0.005). Midline tumors were more common overall (n=39, 65.0%) and more frequent among non-survivors (5/6, 83.3%), though this was not statistically significant (p=0.321). Metastatic staging showed a significant association with mortality (p=0.004); 5 of 6 deaths (83.3%) occurred in patients with metastasis at diagnosis (M1–M4), whereas only 1 of 37 children with M0 disease (2.7%) died. **Table 1** shows details about the association of demographic, clinical and tumour-related characteristics with 12-month mortality among children with medulloblastoma.

Table 2: Association of surgical, histopathological, and treatment variables with 12-month mortality in pediatric medulloblastoma (N=60)

Characteristics		Total (%)	Mortality		P-value
			No (n=54)	Yes (n=6)	
Extent of resection	Gross-total	32 (53.3)	32 (59.3%)	-	<0.001
	Near total	21 (35.0)	19 (35.2%)	2 (33.3%)	
	Sub-total	7 (11.7)	3 (5.6%)	4 (66.7%)	

Complications	Cerebrospinal fluid leak	11 (18.3)	11 (20.4%)	-	0.221
	Meningitis	8 (13.3)	5 (9.3%)	3 (50.0%)	0.005
	Cerebellar mutism	11 (18.3)	9 (16.7%)	2 (33.2%)	0.317
	Shunt placement	11 (18.3)	10 (18.5%)	1 (16.7%)	0.911
Histological findings	Large cell / anaplastic	7 (11.7)	4 (7.4%)	3 (50.0%)	0.008
	Classic	40 (66.7)	38 (70.4%)	2 (33.3%)	
	Desmoplastic	3 (21.7)	12 (22.2%)	1 (16.7%)	
Radiotherapy		51 (85.0)	47 (87.0%)	4 (66.7%)	0.185
Chemotherapy		49 (81.7)	45 (83.3%)	4 (66.7%)	0.317

A significant association was observed between the extent of resection and 12-month mortality ($p<0.001$). Subtotal resection was performed in 7 (11.7%) patients, of whom 4 (66.7%) died, compared to no deaths in the gross-total resection group (n=32, 53.3%). Postoperative meningitis was significantly associated with mortality, occurring in 3 of 6 non-survivors (50.0%) versus 5 of 54 survivors (9.3%; $p=0.005$). Other complications such as CSF leak, cerebellar mutism, and shunt placement, were not significantly associated with mortality. Histopathological subtype also showed a significant relationship with mortality (50.0% vs. 7.4%, $p=0.008$). **Table 2** shows details about the association of surgical, histopathological, and treatment variables with 12-month mortality in children with medulloblastoma.

DISCUSSION

In the present study, the 12-month overall survival rate among children with medulloblastoma was 90.0% (95% CI: 82.0–97.0%). This finding reflects a relatively favorable early outcome and aligns with the survival rates reported in several contemporary studies employing multimodal treatment strategies. A study reported 5-year progression-free survival rate of 85% in children treated with craniospinal radiotherapy and adjuvant chemotherapy, emphasizing that early mortality in their cohort was minimal and disease control in the initial post-treatment phase was largely sustained[12]. In a multicenter study conducted by the Korean Society of Pediatric Neuro-Oncology (KSPNO),[13] 5-year overall survival in the standard-risk group approached 95.8% (95% CI: 88.2–100), further confirming that early survival in children receiving risk-adapted therapies is promising when optimal

surgical and adjuvant treatment is delivered. Retrospective review from a Southeast Asian cohort, reported a 49.1% mortality rate over a median follow-up of 68.8 months, with a 5-year survival of 53.8% (95% CI: 38.7–66.7), indicating substantial attrition in the early years post-treatment, often due to lack of radiotherapy or delayed diagnosis[14]. A local study documented a 12-month mortality of 21% in a cohort of children with primary brain tumors, although their study included mixed histologies[15]. These finding emphasizes that early mortality remains considerable in settings with fragmented pediatric neuro-oncology infrastructure. Other studies emphasize the prognostic value of specific subtypes and stratification. Data analysis from National Cancer Database, reported a 5-year survival rate of 79% across 1300 pediatric patients, with histology and geographic location influencing outcome[16]. The difference in survival rates is attributable to variations in treatment accessibility, risk-adapted therapy, and surgical expertise.

Age was a significant predictor of mortality, with children aged 1–5 years experiencing a 66.7% mortality rate compared to only 33.3% in those older than 5 years (p=0.008). These findings are consistent with the contemporary literature which demonstrates that younger age, particularly 3 to 5 years, is associated with worse outcomes[12,14,17]. This could be due to more aggressive tumor biology and the frequent use of less intensive radiotherapy regimens in younger children to minimize neurocognitive harm, resulting in suboptimal tumor control. Shorter symptom duration before diagnosis (<4 weeks) was associated with higher mortality (66.7% vs. 33.3%; p=0.039), indicating more aggressive tumor behavior. This observation correlates with another study where rapid symptom progression was linked to poorer outcomes[18]. These observations underscore the need for urgent evaluation and intervention in children presenting with rapidly progressive cerebellar signs or symptoms of raised intracranial pressure. Among presenting features, altered consciousness was the only clinical symptom significantly associated with mortality (50.0% vs. 9.3%; p=0.005). This suggests the presence of advanced disease or brainstem involvement at the time of presentation, which is known to worsen prognosis, while neurological deterioration at diagnosis is a predictor of increased mortality and long-term morbidity[19,20].

Midline tumors were more frequent (65.0% of cases) and more common among non-survivors (83.3%), but this difference did not reach statistical significance (p=0.321). This contrasts with a study from Thailand that reported that hemispheric tumor locations had worse survival, possibly due to greater association with group-3 molecular subtype[14]. Some others highlighted the risk of postoperative complications and cerebellar mutism with midline tumors, which can negatively influence outcomes through treatment delays[21]. Metastatic disease at diagnosis was a strong predictor of mortality (p=0.004), with 5 of 6 deaths (83.3%) occurring in patients staged M1 or higher. These finding are in agreement with some other studies where it has been identified that advanced M stage

is a significant independent risk factor for both early and long-term mortality [16,22]. These revelations reinforce the necessity of comprehensive spinal imaging and CSF analysis in staging and risk stratification.

Surgical extent of resection had a strong impact on survival ($p<0.001$). Among children undergoing subtotal resection, 4 out of 7 (66.7%) died, compared to zero deaths among those receiving gross-total resection. These observations emphasize the prognostic importance of maximal safe resection in improving survival outcomes[18,23]. Postoperative meningitis was significantly associated with mortality ($p=0.005$), highlighting the detrimental impact of infectious complications. Similar to this study, it has been previously emphasized that postoperative infections contribute to treatment delays, prolonged hospitalization, and increased risk of neurological morbidity, which may ultimately compromise survival [18,24]. Histopathological subtype was significantly associated with outcome ($p=0.008$). Large cell/anaplastic histology was seen in 50.0% of non-survivors versus only 7.4% of survivors, consistent with the existing evidence that reported higher mortality and recurrence rates in patients with large cell variants [16,17]. Classic and desmoplastic histologies were associated with better outcomes, in line with the findings of others[19,23]. Although radiotherapy and chemotherapy were administered in 88.3% and 85.0% of children, respectively, these treatments were less frequent among non-survivors (66.7% each), though the differences were not statistically significant ($p=0.185$ and $p=0.317$). The absence of statistical significance might be due to the small number of deaths, but the trend aligns with the existing literature that shows improved outcomes with multimodal adjuvant treatment[12,13,16]. Children who could not receive radiotherapy often belonged to the younger age group or experienced treatment interruptions due to complications.

From a clinical perspective, the findings emphasize the prognostic value of early diagnosis, maximal safe resection, and prevention of postoperative infections[25]. The association of younger age, altered consciousness, metastatic stage, subtotal resection, and large cell/anaplastic histology with higher mortality underscores the need for risk-adapted treatment strategies. These may include early referral, enhanced perioperative care, and prioritization of radiotherapy and chemotherapy for high-risk patients. The study has several limitations. The retrospective design is inherently subject to information and selection bias. Molecular subtype data were not available, limiting prognostic precision. The single-center design and relatively modest sample size may restrict generalizability. The short 12-month follow-up does not capture late recurrences or long-term complications such as neurocognitive decline. Future prospective multicenter studies with extended follow-up and integration of molecular profiling are warranted to build upon these findings.

CONCLUSION

Relatively younger age, short symptom duration, altered consciousness at presentation, metastatic disease, subtotal resection, postoperative meningitis, and large cell/anaplastic histology were significant contributors to 12-month mortality. Early identification of high-risk features can guide treatment intensity, improve survival, and ultimately inform national protocols tailored to local resource settings.

LIST OF ABBREVIATIONS

None

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CONFLICT OF INTEREST

None

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Ethical Committee of The Children's Hospital and Institute of Child Health, Multan, through letter no. 776.

AUTHORS' CONTRIBUTION

SA: Design and conception, data collection, proofreading, approved for publication. SSK: Data synthesis, drafting, proofreading, critical revisions, approved for publication. **SZHS**: Conception and design, proofreading, critical revisions, approved for publication. **MAW**: Data collection, responsible for data's integrity, proofreading, and approved for publication. **UU**: Literature review, drafting, proofreading, approved for publication. **ZK**: Conception and design, data analysis, critical revisions, approved for publication

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