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Predictive Factors of Postoperative Peritumoral Brain Edema after Meningioma Resection: A Prospective Study

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Abstract

Background: Postoperative peritumoral brain edema (PTBE) significantly impacts the clinical outcomes of patients undergoing meningioma resection.

Objective: This study aimed to identify predictive factors of PTBE by examining various demographic, clinical, and surgical variables.

Methods: A Prospective analysis was conducted on 50 patients who underwent meningioma resection. Data collected included age, sex, chief complaints, duration of symptoms, presence of preoperative seizures, tumor characteristics (location, origin, shape, MRI T2 intensity, maximum diameter, volume), edema volume, edema index, midline shift, and preoperative treatments (mannitol, steroids, anti-epileptic drugs). Surgical details such as tumor consistency, Simpson grade of resection, sinus violation, operative time, intraoperative blood loss, and histopathological features including WHO grade and prominent nucleoli were also analyzed. Postoperative edema was assessed on day 7 after surgery.

Results: Preliminary analysis indicated that 21 patients (42%) diagnosed having postoperative PTBE. Preoperative seizures, Sinus violation during surgery, Prominent nucleoli, mixed tumor consistency (soft+ firm) were the independent risk factors for postoperative PTBE,whereas Preoperative Mannitol use and Steroid usewere independent protective factors for postoperative PTBE. It was also found that sphenoid wing meningioma resection was associated with significant postoperative PTBE as compared to all other tumour locations. Tumor size, Tumor shape, Tumor MRI T2 intensity, midline shift, surgical simpsons grade and histopathological grade did not significantly increase complication rate. Detailed statistical analysis is ongoing to further elucidate these relationships. **Conclusion:** This study identifies several predictive factors of PTBE following meningioma resection. Use of Mannitol and Steroid in preoperative period is protective in developing postoperative PTBE. Factors like preoperative seizures, sinus violation, prominent nucleoli, mixed tumor consistency should warrant surgeon's attention and needs comprehensive perioperative management to mitigate the risks. Further studies with larger sample sizes are necessary to validate these findings.

Keywords: Meningioma Resection, Peritumoral Brain Edema, Predictive Factors.

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INTRODUCTION

Postoperative peritumoral brain edema (PTBE) is a significant complication that can arise following the surgical resection of meningiomas. PTBE not only affects the immediate postoperative recovery and neurological status of patients but also poses long-term management challenges. The incidence and severity of PTBE are influenced by various factors, including the biological behavior of the tumor, surgical techniques, and patient-specific characteristics.[1]

Meningiomas, generally benign intracranial tumors, are the most common primary brain tumors, accounting for approximately 30% of all cases. They originate from the meningeal layers of the brain and spinal cord. Although often benign, their location and growth can lead to serious neurological impairments and life-threatening conditions, especially when associated with significant edema. The development of PTBE can result in increased intracranial pressure, impaired consciousness, and can prolong hospital stay, thereby affecting the overall prognosis and quality of life.[2]

The pathophysiology of PTBE involves both tumor related and iatrogenic factors. Tumor-induced PTBE is thought to result from the secretion of vascular endothelial growth factors (VEGF) and other inflammatory cytokines that increase vascular permeability and lead to fluid accumulation. Surgical intervention can exacerbate this through direct trauma to the brain tissue and disruption of existing tumor-vasculature interfaces.[3]

Given the impact of PTBE, understanding its predictive factors is crucial for improving surgical outcomes. Several studies have suggested that the size, location, and histopathological features of meningiomas, as well as the extent of surgical resection, can influence the likelihood and severity of PTBE. However, comprehensive studies that integrate a wide array of demographic, clinical, surgical, and histopathological parameters are lacking.[4]

Aim

To identify predictive factors of postoperative peritumoral brain edema (PTBE) in patients undergoing meningioma resection.

OBJECTIVES

1. To analyze the relationship between tumor characteristics and the development of PTBE.
2. To explore the role of preoperative treatment in influencing formation of PTBE.

MATERIAL AND METHODOLOGY

The study included a total of 50 patients who underwent surgical resection of meningioma at Sawai Man Singh Medical college and Hospitals, Jaipur between January 2023 to May 2024.

Inclusion Criteria

- Confirmed cases of meningioma via MRI and histopathological examination.

Exclusion Criteria

- Previous cranial surgery or radiation therapy.
- Presence of multiple intracranial tumors.
- Non-surgical management of meningioma.
- comorbid conditions or medication use that could be confounding
- post-operative histology that does not yield the diagnosis of meningioma

Data collection

Data was obtained using a customized proforma from 50 patients who underwent surgical resection of meningioma within the study period. All data were anonymized and stored securely in compliance with data protection regulations. Detailed data including age, sex, chief complaints, seizure history, symptom duration, tumor location, Tumor shape (regular/irregular), midline shift, Tumor MRI T2 intensity, Preoperative Mannitol, Steroid(min. for 3 days) and Anti-epileptics use, Tumor consistency, Surgical Simpsons grade,sinus violation during surgery, operative time and intraoperative blood loss, histopathological tumor grade and Prominent Nucleoli were recorded. Tumor volume was measured using T1 –weighted MRI scans with gadolinium, but PTBE will be evaluated on T2-weight magnetic resonance imaging (MRI). Postoperative edema was measured on postoperative day **7**. Postoperative PTBE was defined if postoperative brain MRI showedan

increase in volume compared to preoperative edema. Volume was be measured by using three maximal diameters in axial, coronal and sagittal scans.

DATA ANALYSIS

MRI images were reviewed by a neuroradiologist, and tumor dimensions were calculated using standard software. Histopathological examinations were performed by a pathologist blinded to the clinical data. Descriptive statistics were used to summarize demographic and clinical variables. Statistical analysis of categorical variables was carried out using Pearson Chi-Square(PCS) test, degree freedom(df) and p-value. Associations between PTBE and potential predictive factors were analyzed using logistic regression. Statistical significance was set at $p < 0.05$.

Observation and Results:

Table 1: Patients demographic and clinical characteristics

		NE(29)	VE(21)	Total (50)	PCS	df	p-value
Sex	Female	17	14	31	0.335	1	0.563
	Male	12	7	19			
Chief complaints	Headache	8	7	15	13.054	14	0.522
	Dizziness	4	1	5			
	Limb weakness	4	3	7			
	Headache with others	23	18	41			
Seizures	None	24	13	37	**0.911**	1	**0.048**
	Yes	5	8	13			
Symptom duration		2 +\- 18	6 +\- 60	50	17.899	16	0.330

NE- no edema, VE-Vasogenic edema

Table illustrates the distribution of a study population (50) and there clinical characteristics. There were 31 females (17 in Group NE and 14 in Group VE) and 19 males (12 in Group NE and 7 in Group VE. The chi-square test did not show a significant difference between sexes (Pearson Chi-Square = 0.335, df = 1, p-value = 0.563), indicating that the distribution of sex between the two groups was similar. Majority patients reported headache as a chief complaint. Chief complaints distribution between the two groups (NE and VE) varied, with the most common complaint being just headache in 15 participants, followed by three months of headache in 6 participants. The chi-square test yielded a Pearson value of 13.054 resulting in a non-significant p-value of 0.522, suggesting no strong association between group and type of chief complaints. Out of the total participants, 37 did not experience preoperative seizures while 13 did. The breakdown between the NE and VE groups shows participants in the VE group (8) experienced more seizures than those in the NE group (5). The Chi-Square test results in a p-value of **0.048**, suggesting a strong association between preoperative seizures and postoperative PTBE.

The data highlights a diverse range of tumor locations with the convexity being the most common site, accounting for 46% of cases. The distribution between the groups showed a significant difference, with Group NE having a higher incidence of tumors at the convexity than Group VE. The chi-square test yielded a p-value of 0.175, indicating that while there was a noticeable distribution pattern, it was not statistically significant. This suggests that tumor origin might not be a robust predictor for the development of brain edema post-meningioma resection.

Analysis of tumor shape revealed that 36 cases had regular shapes while 14 were irregular.

Table 2: Tumor Characteristics

Tumor origin	NE	VE	Total	PCS	df	P-value
Convexity	16 (55.2%)	7 (33.3%)	23 (46.0%)			
Falcine	5 (17.2%)	3 (14.3%)	8 (16.0%)			
Parasaggital	4 (13.8%)	4 (19.0%)	8 (16.0%)			
Sphenoid Wing	3 (10.3%)	1 (4.8%)	4 (8.0%)		8.97160.175	
Tuberculam Sella	0 (0.0%)	1 (4.8%)	1 (2.0%)			
Tentorial	0 (0.0%)	4 (19.0%)	4 (8.0%)			
Ventricular	1 (3.4%)	1 (4.8%)	2 (4.0%)			
Total	29 (100.0%)	21 (100.0%)	50 (100.0%)			
Tumor shape						
Irregular	11	3	14			
Regular	18	18	36		3.37810.066	
Total	29	21	50			
Tumor MRI T2 Intensity						
Heterogenous	10	3	13			
Hyperintense	19	18	37		2.58220.108	
Hypointense	0	0	0			
Total	29	21	50			
Midline shift (cm)						
No shift	13	15	28			
≤0.5 cm	2	2	4		13.54340.140	
0.6-1 cm	6	1	7			
>1 cm	8	3	11			
Total	29	21	50			
Tumor consistancy						
Firm	15	19	34		8.40610.004	
Soft+Firm	14	2	16			
Total	29	21	50			
Tumor grade (WHO)						
I	21	19	40			
II	5	1	6		2.55230.279	
III	0	0	0			
IV	3	1	4			
Prominent Nucleoli						
No	21	19	40		6.33410.03	
Yes	8	2	10			
Total	29	21	50			

The p-value from the chi-square test was **0.066**, nearing significance, suggesting a potential trend where tumor shape could influence postoperative outcomes and PTBE.

The study also examined the MRI T2 signal intensity of the tumors. Most tumors (37) showed hyperintensity, with a more balanced distribution across both groups compared to the heterogeneous intensity (13 cases). The p-value was 0.108, showing no significant correlation between T2 intensity and the development of PTBE.

The study analyzed the degree of midline shift measured in centimeters. A majority of the patients, 28 out of 50, exhibited no midline shift. Notably, the higher instances of significant midline shifts (e.g., >1 cm) were predominantly observed in Group NE. The chi-square analysis resulted in a p-value of 0.140, suggesting no statistically significant association between midline shift and the incidence of brain edema post-surgery.

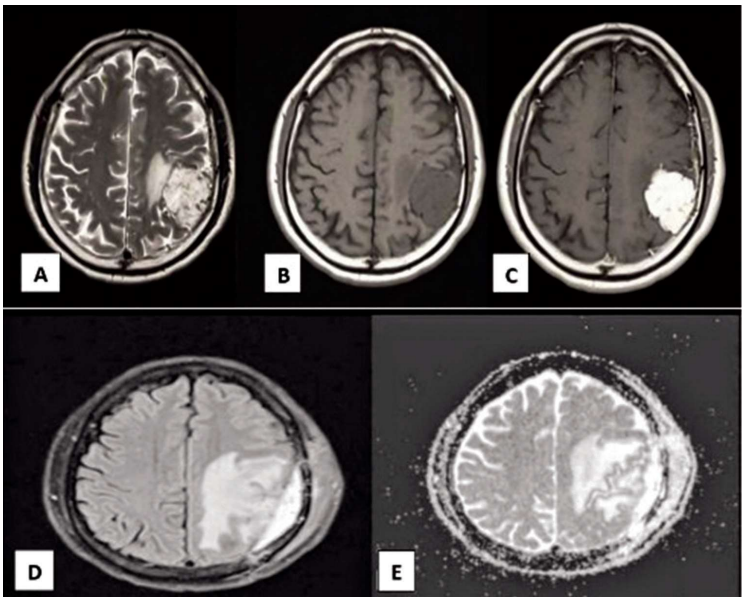
Tumors were graded according to WHO guidelines, with most (40 out of 50) classified as Grade 1, indicating generally benign characteristics. The distribution across groups did not significantly differ (p-value = 0.279), which may support the observation that lower WHO grades are less likely to influence the development of brain edema aggressively

Tumor consistency was categorized as either 'firm' or 'mixed.' The distribution showed a higher prevalence of firm tumors in Group VE and a mixed consistency in Group NE. The chi-square test indicated a significant difference with a p-value of **0.004**, suggesting that tumor consistency might play a role in the surgical approach and potentially influence the development of brain edema.

The presence of prominent nucleoli can be an indicator of cellular activity and potentially aggressive tumor behavior. In this study, 10 cases showed prominent nucleoli. However, the chi-square test resulted in a p-value of 0.03, indicating significant correlation between this histopathological feature and the postoperative incidence of brain edema (PTBE).

Table 3: Preoperative Management

		NE	VE	Total	PCS	Df	P-value
Mannitol	No	4	12	16			
	Yes	25	9	34	**10.519**	**1**	**0.001**
	Total	29	21	50			
Steroids	No	8	15	23			
	Yes	21	6	27	**9.425**	**1**	**0.002**
	Total	29	21	50			
Atiepileptics	No	0	0	0	**Constant variable as used in all cases**		
	Yes	29	21	50			



The administration of Mannitol for a minimum of three days preoperatively was more common in Group NE (25 out of 29) compared to Group VE (9 out of 21). The Pearson Chi-Square test showed a p-value of **0.001**, indicating a significant association between preoperative Mannitol use and the study groups, which might suggest a potential influence on postoperative outcomes.

The use of steroids preoperatively was significantly different between the groups, with Group NE having a higher frequency (21 out of 29) compared to Group VE (6 out of 21). The statistical analysis yielded a p-value of **0.002**, reflecting a significant variance that could correlate with differences in postoperative brain edema.

All participants in the study were administered anti-epileptic drugs, making this variable constant across both groups and thus not applicable for statistical comparison regarding its influence on postoperative brain edema.

Table 4: Operative Information

		NE	VE	Total	PCS	Df	P-value
Surgical Simpsons Grade	1	6	2	8			
	2	6	1	7			
	3	14	13	27	**4.955**	**3**	**0.175**
	4	3	5	8			
	Total	29	21	50			
Sinus violation	No	21	19	40			
	Yes	8	2	10	**6.334**	**1**	**0.03**
	Total	29	21	50			

Surgical Simpsons Grade scale indicates the extent of tumor removal during surgery. Grades range from 1 (complete removal including the dural attachment) to 4 (only partial removal). The majority of cases were classified as Grade 3 (27 out of 50), suggesting a predominant approach of less aggressive resection, potentially to minimize surgical risks or due to tumor characteristics. The chi-square analysis yielded a p-value of 0.175, indicating no significant statistical difference in surgical grades between groups relative to the development of brain edema.

Sinus involvement during meningioma resection can be a critical factor due to potential bleeding and subsequent complications. In this study, 10 out of 50 cases involved sinus violation. The statistical analysis showed a p-value of **0.03**, suggesting that sinus violation was significantly associated with postoperative PTBE in this cohort.

DISCUSSION

Post-operative PTBE was also reffered to as "postoperative haemorrhagic infarction," or "brain swelling" in various literature. Meningioma contributes significant proportion of intracranial tumors. Postoperative PTBE is significant factor in patient outcome and its management. There are various factors which contributes in its management. Our study showed certain factors which significantly contributes in postoperative PTBE.

Sex

The data shows a slight female predominance in both groups (No peritumoral brain edema: 17 females vs. 12 males; With peritumoral brain edema: 14 females vs. 7 males). The p-value of 0.563 suggests no significant difference in the occurrence of peritumoral brain edema post-meningioma resection between sexes.This aligns with studies like Li LM *et al.*1 & Ogasawara C *et al.* 2 which also found no significant sex-related difference in postoperative outcomes for meningioma patients.

Chief Complaints

A spectrum of symptoms were noted with the highest occurrence observed to be headache. However, no statistically significance was associated between type of chief complaints and the development of peritumoral brain edema. Fiani B *et al.* 3 reported that symptom type did not

predict postoperative complications in brain tumor resections, which corroborates the findings in our study.

Duration

The duration of symptoms ranges widely from 10 days to 6 years. The results did not demonstrate a significant correlation between the duration of symptoms and the presence of peritumoral brain edema (p = 0.330). San A*et al.* 4 similarly noted no significant impact of symptom duration on postoperative edema in their cohort of brain tumor patients.

Seizures

Our study suggests that the presence of preoperative seizures, regardless of the type (focal or general), does significantly influence the development of peritumoral brain edema **(p = 0.048)**, as a study by Shen H *et al.* 5found that preoperative seizures were a predictor of postoperative neurological complications, like peritumoral edema.

Tumor location and Origin

No significant difference in peritumoral brain edema based on tumor origin (p = 0.175). However, tentorial and parasaggital origins had a higher proportion of cases with edema.Research by Brandi G *et al.* 6 indicated that tumors located in proximity to ventricles or major blood vessels are more likely to result in peritumoral edemaBaumgarten P *et al.* 7observed that tentorial meningiomas tend to have a higher incidence of postoperative complications, aligning partially with your findings regarding edema.

Tumor Shape

It was observed that irregular tumor shapes may be associated with a lower incidence of postoperative peritumoral edema compared to regular shapes. A study by San A*et al.* 4 supports the notion that irregular tumor shapes are associated with different biological behaviours and could potentially influence surgical outcomes and edema formation.

Tumor MRI T2 Intensity

No statistically significant difference was found in the incidence of peritumoral brain edema based on the T2 intensity of the tumor on MRI (p = 0.108). Hyperintense tumors were more prevalent in both groups. Baumgarten P *et al.* 7 found a correlation between MRI signal intensity and tumor consistency, which could impact surgical outcomes and edema, although their findings are not directly corroborative due to differing methodologies.

Midline Shift

The data shows a diverse range of midline shifts in patients undergoing meningioma resection. The most notable finding is the higher prevalence of no midline shift (0 cm) among the group with peritumoral brain edema (71.4%) compared to the group without edema (44.8%). However, the statistical test resulted in a p-value of 0.140, indicating no significant association between the degree of midline shift and the presence of peritumoral brain edema.This result aligns with studies like those by Shen H *et al.* 5, which suggested that while midline shift is a crucial marker for brain shift and potential complications, its predictive value for specific postoperative outcomes like edema may not be straightforward.

Tumor Consistency

There was a significant difference in peritumoral brain edema development based on tumor consistency. Patients with firm tumors were more likely to develop edema compared to those with mixed soft and firm tumors (p = 0.004). This is consistent with findings from the study by Shin C *et al.* 6, which reported that firmer tumors could be associated with increased manipulation during surgery, potentially leading to greater disturbance of surrounding tissues and increased edema.

Histopath WHO Grade

The WHO grade of the tumor did not significantly correlate with the development of peritumoral brain edema (p = 0.279). Most cases, both with and without edema, were of lower grade (grade 1). According to research by Rajagopalan V *et al.* 7, lower-grade meningiomas often exhibit less aggressive behavior, which may explain the lack of significant findings related to edema across different grades.

Prominent Nucleoli

The presence of prominent nucleoli was significantly associated with occurrence of peritumoral brain edema perioperatively including postoperative PTBE**(p = 0.03)**. This could suggest that cellular features might have an influence on the tumor's interaction with surrounding brain tissue. This finding is somewhat novel as not many studies specifically correlate histological features like nucleoli prominence with postoperative

outcomes such as edema, suggesting an area for further research.

Preoperative Mannitol Use

The use of preoperative mannitol shows a statistically significant association with the presence of peritumoral brain edema, where those not receiving mannitol preoperatively were more likely to develop edema **(p = 0.001)**. This finding suggests that mannitol, used to reduce intracranial pressure, might also play a role in mitigating brain swelling post-surgery.Similar to the findings by Brandi G *et al.* 8, this table supports the practice of using mannitol as an effective measure to reduce postoperative complications, aligning with its known osmotic effects to decrease brain tissue water content.

Preoperative Steroid Use

There was a significant correlation between the non-use of steroids preoperatively and the increased occurrence of peritumoral brain edema **(p = 0.002).** The data indicates that 68.2% of patients who did not receive steroids preoperatively developed edema compared to only 22.2% in those who did.This is consistent with research by Baumgarten P *et al.* 9, which underscores the anti-inflammatory benefits of steroids in reducing the risk of postoperative brain swelling and improving surgical outcomes.

Anti-Epileptic Drug Use

All patients in the study were administered anti-epileptic drugs, hence no variability or statistical significance can be assessed regarding the influence of these drugs on peritumoral brain edema.

Surgical Simpson Grade

While the Simpson grade indicates the extent of tumor resection, the chi-square test did not show a significant association with peritumoral brain edema development (p = 0.175). However, there was a trend suggesting that less complete resections (grade 3 and 4) may be associated with higher rates of edema.Ahmeti H *et al.* 10 also found no clear correlation between Simpson grading and postoperative complications such as edema, though they suggested a potential trend towards complications in less extensive resections.

Sinus Violation

There was significant association found between sinus violation during surgery and the development of postoperative PTBE **(p = 0.03)**. This suggests that sinus involvement is a critical factor in the pathogenesis of edema in this context. Nassiri F *et al.* 11 study aligned with this finding, showing that sinus violation does significantly impact postoperative inflammatory responses or edema may be due to compromised venous return or blood loss which needs further study.

CONCLUSION

The study explores various factors to identify potential predictors of peritumoral brain edema following meningioma resection. Key findings indicate that while some factors such as sex, chief complaints, symptom duration, preoperative seizures, tumor location, and sinus violation do not significantly impact the occurrence of edema, other factors demonstrate noteworthy associations.

These findings integrate with and expand upon existing literature, suggesting that a multifactorial approach is crucial in predicting and managing postoperative outcomes like peritumoral brain edema. Implementing preoperative guidelines on interventions such as administration of mannitol and steroids, considering tumor physical characteristics during surgical planning, and possibly refining surgical techniques could enhance patient outcomes. Future research should focus on confirming these associations in larger, prospective studies and exploring the underlying mechanisms further, especially the intriguing link between histopathological features and postoperative edema.

LIMITATIONS

1. **Prospective Design:** The study's Prospective nature carries a risk of selection bias and limits the ability to establish causality.
2. **Sample Size:** The relatively small sample size of 50 patients may restrict the generalizability of the findings and reduce the statistical power to detect smaller effect sizes.
3. **Data Accuracy:** Reliance on the accuracy and completeness of medical records introduces the potential for information bias.
4. **Variability in Surgical Techniques:** Differences in surgical techniques and postoperative care protocols across different surgeons and institutions could influence the outcomes, making standardization challenging.
5. **Timing of PTBE Assessment:** Assessing PTBE on postoperative day 7 may not capture

the full extent of edema development or resolution over a longer postoperative period.

6. **Confounding Factors:** The study did not account for potential confounding factors such as genetic predispositions, underlying comorbidities, or detailed analyses of the effects of preoperative treatments, which could influence PTBE outcomes.
7. **Need for Larger, Prospective Cohorts:** Future studies with larger, prospective cohorts and standardized protocols are necessary to validate these findings and address these limitations.

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