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Observational Study of Intracranial Low-Grade Gliomas: Clinical Features, Histopathology, and Treatment Outcomes

Tusharkanta Rath[1], Rabinarayan Panda[2]*, Rakesh Rout[1], Debendra Biswal[1], Sanjib Mishra[3], MK Dhir[3], AK Gouda[4]

[1]Post Graduate Student, Department of Neurosurgery, SCB Medical College & Hospital, Cuttack, Odisha, India
[2]Associate Professor, Department of Neurosurgery, SCB Medical College & Hospital, Cuttack, Odisha, India
[3]Professor, Department of Neurosurgery, SCB Medical College & Hospital, Cuttack, Odisha, India
[4]Assistant Professor, Department of Neurosurgery, SCB Medical College & Hospital, Cuttack, Odisha, India

***Address for Correspondence:** Dr. Rabinarayan Panda, Associate Professor, Department of Neurosurgery, SCB Medical College & Hospital, Cuttack, Odisha, India
E-mail: rabinarayanpanda80@gmail.com

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ABSTRACT

Background: Low-Grade Gliomas (LGGs) are primary brain tumors commonly diagnosed in young adults. These tumors are typically slow-growing but can undergo malignant transformation. This study aimed to evaluate the clinical, radiological, histopathological, and treatment outcomes in 48 patients diagnosed with LGGs at SCB Medical College & Hospital, Cuttack.

Methods: A hospital-based observational study was conducted on 48 patients with LGGs treated between May 2022 and August 2024. Demographic data, clinical presentations, radiological findings, histopathology, immunohistochemistry (IHC) markers, surgical management, adjuvant therapy, and outcomes were analyzed. Radiological evaluations included preoperative CT and MRI scans, with postoperative CT performed within 48 hours to assess resection extent. Histopathological examination confirmed diagnoses, and IHC was performed to evaluate IDH1 mutation and 1p19q co-deletion.

Results: The study included 70.8% male patients with a mean age of 36.2 years. The most common symptom was headache (83.3%), followed by seizures (75%). Most tumors were in the frontal lobe (33.3%), and 58.33% underwent gross total resection. Histologically, 54.2% were Diffuse Astrocytoma Grade-2 and 33.3% were Oligodendroglioma. Immunohistochemistry showed 85.4% IDH1 positivity, with 1p19q co-deletion in 35.4% of Oligodendrogliomas. Adjuvant temozolomide and radiotherapy improved survival and progression-free survival, with most patients becoming seizure-free.

Conclusion: The study aligns with previous research, showing that early diagnosis, aggressive surgery, and adjuvant therapy improve outcomes in LGG patients. Molecular markers like IDH1 and 1p19q co-deletion help predict treatment response and survival. Larger, long-term studies are needed to confirm these findings and optimize treatment strategies.

Key-words: Low-Grade Gliomas, Seizures, Radiotherapy, Temozolomide, IDH1 Mutation

INTRODUCTION

Central nervous system (CNS) tumors are classified based on their cell of origin and histopathological characteristics, which provide valuable insights into their behavior. LGGs are a group of primary brain tumors characterized by benign histology, including low proliferation rates and minimal neoangiogenesis [1].

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However, despite their seemingly benign nature, these tumors exhibit aggressive behavior due to their tendency to invade the normal brain parenchyma slowly. According to the World Health Organization (WHO) classification of brain tumors, LGGs are classified as grade II (out of IV), encompassing entities such as grade II astrocytomas (further subdivided into fibrillary and protoplasmic), grade II oligoastrocytomas, and grade II oligodendrogliomas. Pilocytic astrocytomas, often referred to as grade I astrocytomas, are occasionally considered low-grade gliomas due to their peculiar behavior, but they warrant separate consideration [2].

In young adults (aged 20–34 years), gliomas account for 32% of all primary CNS tumors, with 17% of these being

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astrocytic tumors and 28% classified as glioblastomas. LGGs are typically slow-growing and predominantly affect younger individuals (median age 35) and have a higher incidence in males (male/female ratio 1.5) [3]. The most common clinical presentation includes seizures, particularly partial seizures, but other symptoms such as headaches, personality changes, and focal neurological deficits are also frequently observed. These deficits can manifest as motor or sensory issues, dysphasia/aphasia, disinhibition, apathy, and visuospatial disturbances, depending on the tumor's location and size. Interestingly, LGGs often occur in or near eloquent areas of the brain, further complicating treatment and management [4].

The only established risk factor for the development of secondary brain tumors is CNS exposure to therapeutic or high-dose radiation. Radiologically, LGGs are distinguishable from higher-grade gliomas (grades III and IV), which exhibit greater tumor heterogeneity, contrast enhancement, restricted diffusion on diffusion-weighted MR sequences, and increased cerebral blood volume on perfusion-weighted MRI [5].

Genetic alterations, such as the loss of the 1p36 and 19q13.3 chromosomal regions, are common in LGGs, particularly in oligodendrogliomas. Additionally, mutations in the IDH1 gene, especially at amino acid position 132, are observed in the majority of WHO grade II and III astrocytomas and oligodendrogliomas, as well as in secondary glioblastomas originating from these lesions. In contrast, mutations in the IDH2 gene are rare in LGGs [6].

The median survival for patients with LGGs is approximately 10 years. Still, several negative prognostic factors, including older age (>40 years), larger tumor size (>5 cm), involvement of eloquent brain areas, and reduced Karnofsky performance status, have been identified [7].

The optimal treatment for LGGs remains a subject of debate. Treatment options include watchful observation, needle biopsy, open biopsy, and surgical resection. However, no class I or II evidence currently exists to determine the ideal management approach. While some advocate for an observational or "wait-and-see" policy due to the typically indolent nature of these tumors, others emphasize the importance of obtaining a tissue diagnosis through biopsy before deciding on further treatment [8]. Surgical resection, though controversial, has gained increasing support in recent studies. Surgery offers several benefits, including reliable histological diagnosis, symptom relief (particularly seizure control), and a potential reduction in recurrence and malignant transformation rates. However, the procedure is not without risks, as it can lead to permanent changes in the patient's quality of life [9].

Given the long natural history of LGGs, preserving neurological function during surgical resection is a primary goal. To achieve optimal outcomes, a combination of neuropsychological, neurophysiological, neuro-radiological, and intra-operative monitoring techniques must be employed [10]. This study aims to explore the epidemiology, clinical characteristics, radiological findings, surgical outcomes, and pathological features of intracranial low-grade gliomas, with a particular focus on the follow-up and management strategies for these tumors.

MATERIALS AND METHODS

Study Design and Setting- This study was a hospital-based observational study of 48 cases of Low-Grade Gliomas (LGGs) treated in the Department of Neurosurgery at SCB Medical College & Hospital, Cuttack, Odisha. Written informed consent was obtained from all patients before enrollment in the study, and the study protocol was approved by the hospital's local ethics committee. A well-defined scheme was followed to select cases for the study, ensuring consistency and reliability in data collection.

Study Period and Population- The study was conducted over 2 years and 4 months, from May 2022 to August 2024. The study population included patients presenting to the Department of Neurosurgery at SCB Medical College & Hospital, Cuttack, who were diagnosed and treated for Low-Grade Glioma.

Inclusion criteria

- Patients diagnosed and treated for Low-Grade Glioma as confirmed by histology between May 2022 and August 2024.

Exclusion criteria

- Patients who underwent any surgical intervention at other institutions.
- Patients who did not provide consent for participation in the study.

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- ❖ Patients who died before any intervention could be performed.

Evaluation- The study collected detailed information on the patients' demographic profile, clinical presentation, Karnofsky Performance Scale (KPS) score, course of illness, radiological evaluation, treatment, histological and molecular grouping, complications, and outcomes.

Radiological Investigations- All patients underwent preoperative evaluation with CT and MRI scans of the brain. Postoperative radiological evaluation, including contrast-enhanced CT brain, was performed within 48 hours of surgery to assess the extent of resection and any residual lesions. In cases with enhancing tumors, if no enhancement was seen, the tumor was considered totally resected. Areas showing contrast enhancement were considered residual tumor.

Surgery- The goal of surgery was to achieve maximal safe resection, ideally aiming for gross total or safe total resection.

Histology and Immunohistochemistry- The presumptive diagnosis of Low-Grade Glioma was confirmed through histopathological examination post-surgery. Standard histological preparations (hematoxylin and eosin staining) were used to assess general architectural and cytological features and to identify Low-Grade Glioma subtypes. Immunohistochemistry (IHC) was performed using primary antibodies against IDH1, 1p19q co-deletion, and Ki-67 to characterize the tumors' molecular features further.

Adjuvant Therapy- Patients were referred to a tertiary oncology center for adjuvant therapy, where they were assessed by an oncologist and treated with chemotherapy and/or radiotherapy. All patients received external beam radiotherapy (RT) with a total dose of 60 Gy, delivered in 30 fractions of 2 Gy each. Most patients received intensity-modulated radiotherapy (IMRT). Concurrent chemotherapy with temozolomide (TMZ) was administered at a dose of 75 mg/m²/day during the entire course of radiation. Following chemoradiotherapy (CRT), adjuvant TMZ (150-200 mg/m²) was administered 5 days per week for 6-12 cycles every 28 days.

Complications- Patients were closely monitored for complications during treatment. Operative mortality was defined as any death occurring within 30 days after surgery, either in or out of the hospital, or after 30 days but during the same hospitalization.

Follow-Up- Patients were scheduled for regular follow-up visits at the outpatient department at 1, 3, 6, and 12 months, with subsequent half-yearly follow-ups. Detailed neurological examinations were performed during each visit.

Outcome- Outcomes were analyzed based on recurrence, treatment completion, and mortality. Disease remission was defined as patients who completed their treatment and remained disease-free during subsequent follow-ups. "Lost to follow-up" referred to patients who completed treatment and achieved disease remission but failed to attend follow-up visits and could not be contacted. Recurrence was defined as the presence of new tumor growth or progression of the residual tumor as seen in follow-up imaging.

Progression-free survival (PFS) was calculated as the time from diagnosis (surgery date) to documented clinical or radiological progression or death. Overall survival (OS) was calculated from the date of diagnosis to death from any cause.

Statistical Analysis- The data collected were transcribed into Microsoft Excel sheets, and statistical analysis was performed using SPSS version 16.0. Associations between clinical features (e.g., sex, age at diagnosis, clinical risk group), radiological, histopathological, and molecular characteristics, and patient outcomes were investigated using the Chi-square test for multivariate analysis of discrete parameters.

RESULTS

In the present study, 48 patients with low-grade glioma were included. Among them, 34 patients (70.8%) were male and 14 patients (29.2%) were female, with a male predominance. The mean age of the patients was 36.2 years, with most patients belonging to the 20–40-year age group (Table 1).

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Table 1: Demographic Characteristics of Patients

Parameter	Category	Number (%)
Gender	Male	34 (70.8%)
	Female	14 (29.2%)
Age Group (years)	0–10	2 (4.2%)
	10–20	8 (16.7%)
	20–30	10 (20.8%)
	30–40	11 (22.9%)
	40–50	3 (6.3%)
	50–60	8 (16.7%)
	60–70	6 (12.5%)
Total		48 (100%)

Fig. 1 shows tumor locations in patients with low-grade glioma. In the present study, 33.3% of tumors were located in the frontal lobe, followed by the temporal lobe (12.5%), while 8.3% were found in the cerebellum.

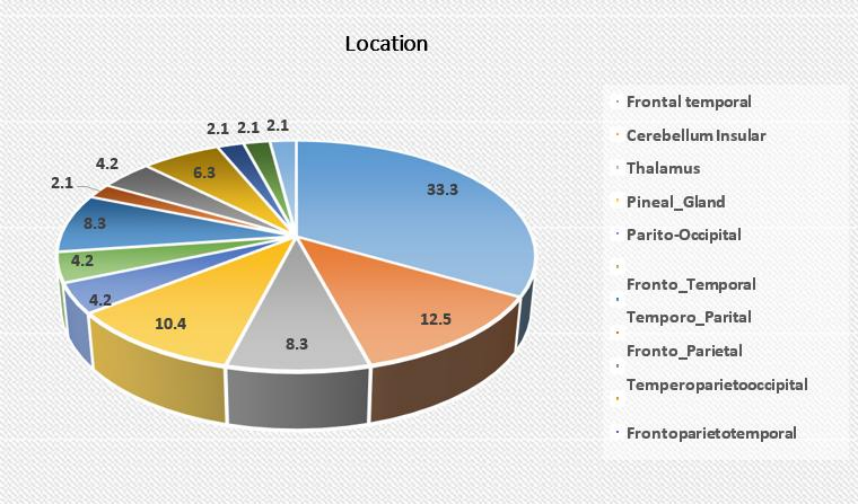

Fig. 1: Pie diagram demonstrating the locations of the LGG

Table 2 shows the clinical presentation of patients with low-grade glioma. Headache (83.3%) was the most common symptom, followed by seizures (75%), while other neurological symptoms were observed in fewer patients.

Table 2: Clinical parameters

Parameters	categories	Number	Percentage (%)
Headache	Yes	40	83.3
	No	08	16.7
Seizure	Yes	36	75.0
	No	12	25.0
Nausea & Vomiting	Yes	28	58.3
	No	20	41.7
weakness	Yes	25	52.1
	No	23	47.9
Altered sensorium	Yes	08	16.7
	No	40	83.3
Visual symptom	Yes	17	35.4

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	No	31	64.6
Language deficit	Yes	07	14.6
	No	41	85.4

Table 3 shows the distribution of tumors according to location. Frontal lobe involvement (33.3%) was the most common, followed by other lobes in smaller proportions.

Table 3: Location of Tumor

Location	Number	Percentage (%)
Frontal	16	33.3
Temporal	6	12.5
Cerebellum	4	8.3
Insular	5	10.4
Thalamus	2	4.2
Pineal gland	2	4.2
Parito-occipital	4	8.3
Fronto-temporal	1	2.1
Temporo-parital	2	4.2
Fronto-parietal	3	6.3
Parietal	1	2.1
Tempero-parietooccipital	1	2.1
Fronto-parietotemporal	1	2.1
Total	48	100

Fig. 2 shows the radiological findings observed in low-grade gliomas**.** Margin irregularity, signal heterogeneity, mass effect, and edema were common findings. Calcification was seen in grade-2 oligodendrogliomas**;** haemorrhage was present in 4.2% of cases, and choline/creatinine elevation was observed in 70.8% of cases.

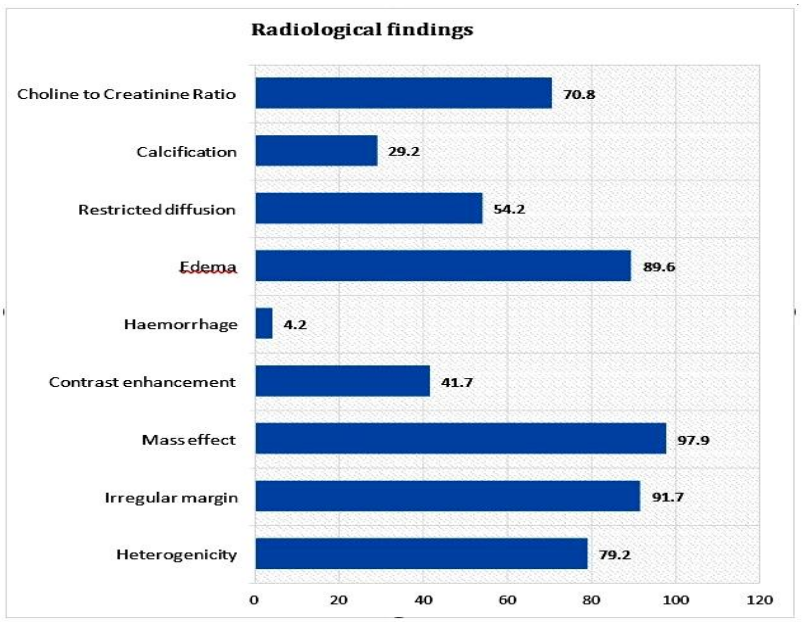

Fig. 2: Bar chart showing radiological findings observed in LGG

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In the present study, the clinical characteristics of 48 patients with low-grade glioma were analyzed. Single-lobar involvement was observed in 29 patients (60.4%), while 19 patients (39.6%) had multiple-lobar involvement. Tumors were more commonly located on the left side (50.0%) than on the right (45.8%), with 2 cases (4.2%) involving the pineal gland. Comorbidities were present in 7 patients (14.6%), whereas 41 patients (85.4%) had none. Most patients had a Karnofsky Performance Status (KPS) score greater than 70 (83.3%), while 16.7% had a KPS score below 70 (Table 4).

Table 4: Clinical Characteristics of Patients

Parameter	Category	Number	Percentage (%)
Lobes Involved	Single	29	60.4
	Multiple	19	39.6
Side of Tumor	Right	22	45.8
	Left	24	50.0
	Pineal gland	2	4.2
Comorbidity	Yes	7	14.6
	No	41	85.4
KPS Score	<70	8	16.7
	>70	40	83.3

In the present study, 28 patients (58.33%) underwent gross-total resection, and 20 patients (41.66%) underwent subtotal resection (Table 5).

Table 5: Extent of surgical resection

Extent of Resection	Frequency	Percentage (%)
GTR	28	58.33
STR	20	41.66
Total	48	100

Fig. 3 represents the treatment outcome after surgery. In this series, 35 patients (72.9%) completed treatment, while 13 (27.1%) did not.

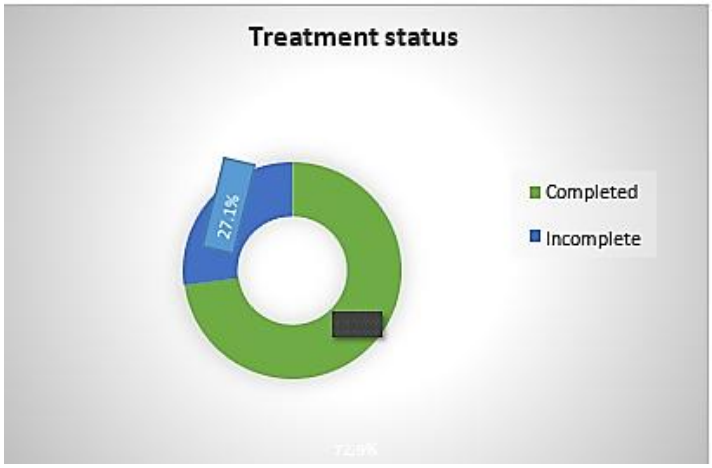

Fig. 3: Pie chart showing treatment outcome after surgery

In the present study, pathological markers and residual tumor status were analyzed among 48 patients with low-grade glioma. IDH1 mutation was positive in 41 patients (85.4%) and negative in 7 patients (14.6%). The 1p19q co-deletion was observed in 17 patients (35.4%), whereas 31 patients (64.6%) did not show it. Residual tumor was present in 18 patients (37.5%) after surgery, whereas complete tumor removal was achieved in 30 patients (62.5%) (Table 6).

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Table 6: Tumor Pathological Markers and Residual Tumor Status

Parameter	Category	Number	Percentage (%)
IDH1	Positive	41	85.4
	Negative	7	14.6
1p19q	Positive	17	35.4
	Negative	31	64.6
Residual Tumor	Yes	18	37.5
	No	30	62.5

In the present study, 35 patients (72.9%) completed treatment, while 13 patients (27.1%) had incomplete treatment. Post-treatment neurological symptoms showed significant improvement compared to preoperative status. Headache was present in 10 patients (20.83%), seizures in 8 patients (16.66%), nausea and vomiting in 4 patients (8.33%), and weakness in 15 patients (31.25%) following surgery and adjuvant therapy (Table 7).

Table 7: Treatment Outcome and Post-Treatment Neurological Symptoms

Parameter	Number	Percentage (%)
Treatment Outcome		
Completed	35	72.9
Incomplete	13	27.1
Post-treatment Symptoms		
Headache	10	20.83
Seizure	8	16.66
Nausea & Vomiting	4	8.33
Weakness	15	31.25

The number of lobes involved and residual tumor showed a statistically significant association with treatment status ($p<0.05$). However, side of tumor, KPS score, radiotherapy, chemotherapy, and IDH1 status did not show any significant association ($p>0.05$). In the present study, the association of various clinical and pathological factors with treatment status was analyzed. The side of the tumor, KPS score, radiotherapy, chemotherapy, and IDH1 status did not show any statistically significant association with treatment completion ($p > 0.05$). However, residual tumor volume showed a statistically significant association with treatment status ($p<0.05$), indicating that patients without residual tumor were more likely to complete treatment compared to those with residual tumor (Table 8).

Table 8: Association of Clinical and Pathological Factors with Treatment Status

Parameters	Category	Treatment		p-value
		Completed	Incomplete	
Lobes Involved	1	25	4	0.02
	2	10	5	
	3	0	2	
Side of Tumor	Right	16	6	0.73
	Left	19	5	
KPS Score	<70	5	3	0.60
	>70	30	10	
Radiotherapy	Yes	29	13	0.17

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	No	6	0	
Chemotherapy	Yes	29	13	0.17
	No	6	0	
IDH1 Status	Positive	31	10	0.37
	Negative	4	3	
Residual Tumor	Yes	7	11	0.001
	No	28	2	

DISCUSSION

This hospital-based observational study of 48 cases of Low-Grade Gliomas (LGGs) treated at SCB Medical College & Hospital, Cuttack, Odisha, aimed to evaluate the clinical, radiological, histopathological, and treatment outcomes in patients with LGGs. The findings were compared to those from four previous studies, shedding light on various trends and patterns in the management of LGGs.

Regarding gender distribution, our study found a male-to-female ratio of 2.42:1, with 70.8% of patients male. This aligns with Keshri *et al.* [11], who observed a similar male-to-female ratio of 2.33:1 in their study of 130 LGG patients. Shaw *et al.* [12] and Babu *et al.* [13] also reported a predominance of male patients, supporting the idea that LGGs are more common in males, although the underlying reasons remain unclear.

Regarding age distribution, the mean age at diagnosis in our study was 36.2 years, which is in line with the findings of Keshri *et al.* [11], who reported a similar average age of 39.4 years. Both studies suggest that LGGs predominantly affect younger individuals, typically in their 30s to 40s, confirming that age is an important factor in LGG development.

Clinical presentation in our study showed that 75% of patients presented with seizures and 83.3% with headaches. This is consistent with Pallud *et al.* [14], who found that seizures are the most common presenting symptom in LGG patients, occurring in 72%–89% of cases. The presence of seizures in LGGs has been associated with better postoperative outcomes, as patients who present with seizures tend to have a more favorable prognosis, especially when tumor resection is achieved.

Regarding tumor location, our study found that 33.3% of LGGs were in the frontal lobe, like the findings of Keshri *et al.* [11], who also reported the frontal lobe as the most common site for LGG. In contrast, Schomas *et al.* [15] observed more tumours in the temporal lobe. This suggests that although the frontal lobe is the most common location, there may be regional variations in LGG distribution.

Regarding surgical outcomes, 58.33% of patients in our study underwent gross total resection (GTR), while 41.66% underwent subtotal resection (STR). These results are similar to those of Keshri *et al.* [11], who reported a GTR rate of 72%. Gross total resection has been shown to improve seizure control and reduce the risk of malignant transformation, as demonstrated by Majchrzak *et al.* [16].

Finally, adjuvant therapy in our study, including temozolomide (TMZ) and radiotherapy (RT), showed favorable outcomes with improved survival and progression-free survival (PFS), consistent with the findings of Hoang-Xuan *et al.* [17] and Ricard *et al.* [18]. These studies emphasized the importance of early adjuvant therapy in improving long-term outcomes for LGG patients. This single-center, observational study with a small sample size limits generalizability. Short follow-up and selective molecular profiling restrict long-term outcome analysis and interpretation of prognostic factors.

CONCLUSIONS

In conclusion, low-grade gliomas were most common in young adult males, with headache and seizures being the predominant clinical presentations. The frontal lobe was the most frequently involved site, and diffuse astrocytoma grade-2 was the most common histological type. IDH1 positivity was high, and 1p19q co-deletion was observed in a subset of oligodendrogliomas. Surgical resection followed by adjuvant radiotherapy and chemotherapy improved survival, progression-free survival, and seizure control. Early diagnosis, maximal safe resection, and appropriate adjuvant therapy are crucial for favorable outcomes in LGG patients.

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CONTRIBUTION OF AUTHORS

Research concept- Tusharkanta Rath, Rakesh Rout
Research design- Rakesh Rout, Debendra Biswal
Supervision- Rabinarayan Panda, Sanjib Mishra
Materials- Debendra Biswal, MK Dhir
Data collection- MK Dhir, AK Gouda
Data analysis and interpretation- Rabinarayan Panda, Sanjib Mishra
Literature search- Tusharkanta Rath, Debendra Biswal
Writing article- Rakesh Rout, MK Dhir, AK Gouda
Critical review- Rabinarayan Panda, Sanjib Mishra
Article editing- Debendra Biswal, Tusharkanta Rath
Final approval- Rabinarayan Panda, Sanjib Mishra

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