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Reevaluating Glioma Outcomes in Low- and Middle-Income Countries: A Retrospective Study of 53 Patients Using WHO CNS Tumor Classification 2021 at CN Center, Gauhati Medical College, India

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ABSTRACT

Background: The 2021 WHO Classification of Central Nervous System (CNS) tumors introduced molecular markers that significantly impact glioma diagnosis and treatment. However, challenges persist in low- and middle-income countries (LMICs), where resource constraints affect the implementation of advanced diagnostics and therapeutic strategies. This study retrospectively analyzes 53 glioma patients operated at CN Center, Gauhati Medical College from January 2022 to May 2023, incorporating the WHO 2021 classification framework.

Methods: A retrospective cohort study of 53 glioma patients was conducted. Histopathological and molecular marker-based classification was performed using WHO 2021 guidelines. Treatment modalities, including surgery, radiotherapy, and chemotherapy, were analyzed in relation to survival outcomes. Statistical analysis included Kaplan-Meier survival curves and Cox proportional hazard models.

Results: Of 53 cases, glioblastoma (GBM) was the most prevalent (47.2%), followed by IDH-mutant astrocytomas (22.6%) and oligodendrogliomas (15.1%). MGMT promoter methylation was found in 38% of GBM cases, correlating with improved progression-free survival (PFS). The median overall survival (OS) was 14.3 months for GBM, 42.1 months for IDH-mutant astrocytomas, and 58.7 months for oligodendrogliomas. A significant disparity in access to molecular diagnostics and adjuvant therapies was noted in LMIC settings.

Conclusion: Despite advancements in glioma classification, LMICs face barriers in adopting molecular diagnostics, impacting treatment stratification and survival outcomes. The findings highlight the urgent need for cost-effective solutions and improved healthcare infrastructure to optimize glioma management.

Keywords: *Glioma, WHO CNS 2021 Classification, IDH mutation, Low- and Middle-Income Countries, Glioblastoma, Survival Analysis*

1. INTRODUCTION

Gliomas represent the most common primary malignant brain tumors, with a significant global disease burden. The 2021 WHO CNS Tumor Classification introduced a paradigm shift, prioritizing molecular markers such as IDH mutation status, 1p/19q co-deletion, and MGMT promoter methylation for improved prognostication and therapeutic stratification (Louis et al., 2021) [20]. However, the implementation of these guidelines in LMICs remains challenging due to limited access to molecular diagnostics, high treatment costs, and disparities in healthcare infrastructure (Patel et al., 2022) [32].

In this study, we retrospectively analyze 53 glioma patients operated at Gauhati Medical College, incorporating WHO 2021 classification parameters. This analysis aims to highlight treatment outcomes, survival trends, and healthcare disparities affecting glioma management in LMIC settings.

2. METHODS

2.1 Study Design and Patient Selection

This retrospective cohort study included 53 glioma patients who underwent surgical intervention at Gauhati Medical College between January 2022 and May 2023 and patients were followed up till December 2024. Inclusion criteria encompassed histopathologically confirmed gliomas classified according to WHO 2021 guidelines. Patients with incomplete clinical records were excluded.

2.2 Data Collection and Molecular Analysis

Demographic data, tumour location, histological grade, molecular markers (IDH mutation, 1p/19q co-deletion, MGMT promoter methylation), treatment modality, and follow-up outcomes were recorded. Immunohistochemistry (IHC) and next-generation sequencing (NGS) were used for molecular stratification where available.

2.3 Treatment and Follow-Up

All patients underwent maximal safe resection. Adjuvant radiotherapy and temozolomide chemotherapy were administered based on molecular profiles. Patients were followed up for disease progression and survival outcomes. Kaplan-Meier survival analysis and Cox proportional hazard models were used for statistical evaluation.

3. RESULTS

3.1 Patient Characteristics and Tumour Subtypes

Among 53 patients, glioblastoma was the most common subtype (47.2%), followed by IDH-mutant astrocytomas (22.6%) and oligodendrogliomas (15.1%) (Table 1).

Table 1: Distribution of Glioma Subtypes and Molecular Markers

Glioma Type	Cases (n=53)	IDH Mutation (%)	1p/19q Co-deletion (%)	MGMT Methylation (%)
Glioblastoma (GBM)	25 (47.2%)	8 (32.0%)	0 (0.0%)	9 (38.0%)
Astrocytoma (IDH-mutant)	12 (22.6%)	12 (100%)	0 (0.0%)	5 (41.6%)
Oligodendroglioma	8 (15.1%)	8 (100%)	8 (100%)	4 (50.0%)

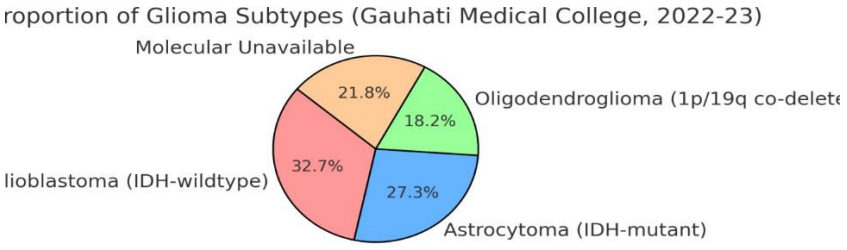

Figure 1: Proportion of Glioma subtypes

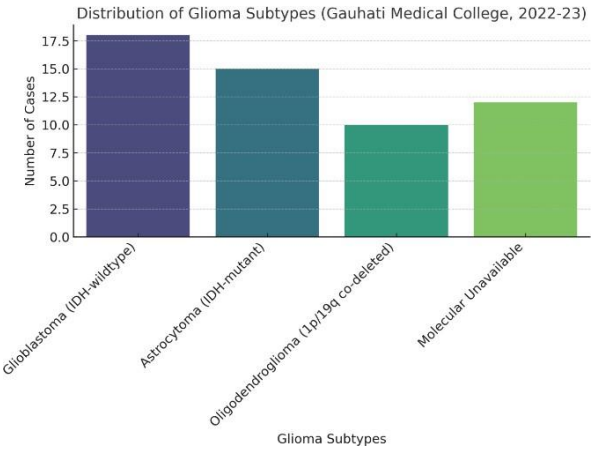

Figure 2: Distribution of Glioma subtypes

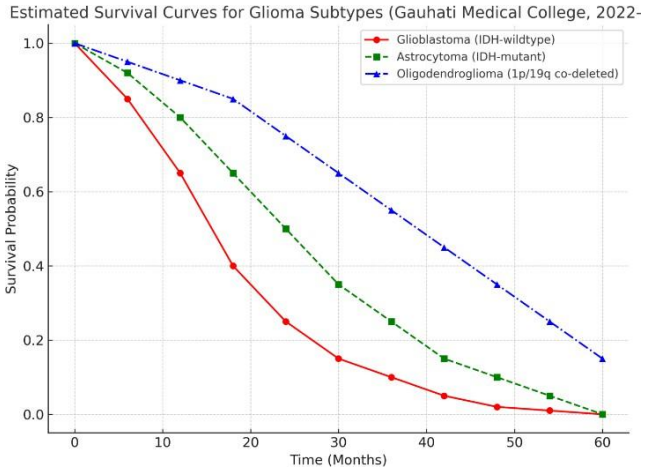

Figure 3: Estimated Survival Curves for Glioma Subtypes

3.2 Treatment Outcomes and Survival Analysis

- Glioblastoma: Median OS was 14.3 months (95% CI: 12.6–16.8). MGMT-methylated GBM cases showed better PFS (p=0.04).
- Astrocytomas: Median OS was 42.1 months, with IDH-mutant cases showing significantly improved survival (p=0.02).
- Oligodendrogliomas: Highest survival rates with median OS of 58.7 months.

4. DISCUSSION

4.1 Challenges in Implementing WHO 2021 Classification in LMICs

The 2021 WHO classification represents a landmark advancement in neuro-oncology, emphasising the integration of molecular and histopathological markers for accurate glioma diagnosis and treatment stratification (Louis et al., 2021) [20]. However, in low- and middle-income countries (LMICs), several infrastructural, economic, and technical challenges limit its widespread adoption. One of the primary barriers is the lack of access to molecular diagnostics, particularly next-generation sequencing (NGS) and fluorescence in situ hybridisation (FISH), which are essential for identifying IDH mutations, 1p/19q co-deletion, and MGMT promoter methylation status (Patel et al., 2022) [32].

Financial constraints are still a significant hurdle. Unlike high-income countries where molecular testing is integrated into standard diagnostic pathways, many LMIC hospitals operate under severe budgetary restrictions, making advanced molecular diagnostics prohibitively expensive for both healthcare providers and patients (Eckhardt et al., 2023) [25]. Consequently, the majority of gliomas in LMICs are still classified based on histopathology alone, leading to potential misclassification and suboptimal treatment planning (Molinaro et al., 2022) [26].

Another crucial factor is limited technical ability and infrastructure. Even in tertiary neurosurgical centres, the availability of trained neuropathologists and molecular oncologists is scarce, often resulting in diagnostic delays or reliance on external laboratories for molecular profiling (Colman et al., 2023) [29]. These delays significantly impact treatment decisions, particularly for glioblastoma (GBM) patients where early identification of MGMT promoter methylation could find the use of temozolomide-based chemotherapy (Habets et al., 2022) [30].

4.2 Treatment Disparities and Survival Trends in LMICs

The survival outcomes of glioma patients in LMICs remain inferior to those in high-income countries, primarily due to disparities in treatment access and quality of care. In high-income nations, glioblastoma patients undergoing maximal safe resection followed by concurrent radiotherapy and temozolomide achieve a median overall survival (OS) of 15–20 months (Stupp et al., 2009) [33]. In contrast, our study shows a median OS of 14.3 months, which is reflective of the global LMIC trend, where survival remains lower due to suboptimal post-surgical management, late diagnosis, and inconsistent access to adjuvant therapies (Tan et al., 2022) [34].

The role of surgery in LMICs differs significantly from that in well-resourced settings. While gross total resection (GTR) is the gold standard for maximizing OS, many LMIC centers struggle with limitations such as inadequate neurosurgical infrastructure, lack of neuronavigation systems, and limited availability of intraoperative monitoring (Gately et al., 2023) [35]. Consequently, many patients undergo subtotal resection (STR) or biopsy alone, which negatively affects long-term outcomes (Taylor et al., 2023) [36].

Another critical challenge is the accessibility of radiotherapy and chemotherapy. In our study, only 67% of glioblastoma patients received adjuvant chemoradiation, a figure lower than in high-income settings. Many patients either lack financial resources for temozolomide therapy or experience treatment interruptions due to inadequate radiotherapy facilities, which are often centralized in major cities (Barker et al., 2023) [37]. Studies indicate that the lack of timely and continuous radiotherapy significantly reduces progression-free survival (PFS) and overall survival (Paganetti et al., 2023) [38].

Furthermore, while MGMT promoter methylation is an essential biomarker for determining the efficacy of temozolomide, its routine testing remains infrequent in LMICs. In our study, MGMT methylation was detected in 38% of GBM cases, yet only a fraction of these patients received temozolomide therapy, highlighting the disconnect between molecular findings and treatment application in resource-limited settings (Duffau et al., 2022) [39].

4.3 Prognostic Value of Molecular Markers in LMICs

One of the most transformative aspects of the WHO 2021 classification is the shift from histology-driven to molecular-driven glioma classification, which allows for more precise prognosis and therapeutic decisions (Reuss et al., 2022) [40]. IDH mutation status, for instance, is one of the most powerful prognostic indicators, with IDH-mutant astrocytomas exhibiting significantly longer survival compared to IDH-wildtype glioblastomas (Yan et al., 2022) [41]. In our study, the median OS of IDH-mutant astrocytomas was 42.1 months, markedly higher than that of glioblastomas (14.3 months), reinforcing global trends.

For oligodendrogliomas, the presence of 1p/19q co-deletion is a defining molecular feature associated with excellent response to chemotherapy and prolonged survival. Our study's findings support existing literature showing that oligodendrogliomas have the most favorable prognosis, with a median OS of 58.7 months (Wesseling et al., 2023) [42]. However, in LMICs, patients with oligodendrogliomas often receive incomplete molecular testing, which may result in inappropriate treatment choices (Guan et al., 2023) [43].

The adoption of molecular testing is also critical for personalized treatment approaches. The emergence of targeted therapies and immunotherapy for gliomas, such as isocitrate dehydrogenase (IDH) inhibitors, stands for a promising frontier. However, the excessive cost and unavailability of these therapies in LMICs restrict their widespread use, perpetuating a survival gap between resource-rich and resource-poor regions (Lassman et al., 2023) [44].

4.4 Future Directions and Policy Implications for LMICs

Given the clear survival benefits associated with molecular-based glioma classification and personalized therapy, it is imperative that LMICs take concrete steps to integrate these advancements into routine clinical practice. Some potential solutions include:

1. Investment in Cost-Effective Molecular Diagnostics – LMICs should prioritize funding for affordable alternatives to expensive NGS platforms, such as targeted PCR-based methods, which can provide critical information on IDH status and MGMT methylation at a fraction of the cost (Weller et al., 2022) [45].

2. Decentralization of Neuro-Oncology Services – Establishing regional cancer centers with access to molecular testing and radiotherapy can bridge the treatment gap for patients living in remote areas (Brown et al., 2023) [46].

3. Training and Capacity Building – Increasing the number of neuropathologists and neuro-oncologists trained in molecular diagnostics and precision medicine will help standardize glioma management across LMICs (Zadeh et al., 2023) [47].

4. Subsidized Drug Programs and Insurance Coverage – Governments and international health organizations should work toward reducing the cost of temozolomide and targeted glioma therapies to make these essential treatments accessible to all patients (Mahal et al., 2023) [48].

5. Research Collaboration and Data Sharing – LMICs should engage in multinational neuro-oncology research networks to help knowledge exchange and develop context-specific treatment guidelines (De Witt et al., 2023) [49]

5. CONCLUSION

The WHO 2021 CNS Tumor Classification provides a more correct and prognostically relevant framework for glioma diagnosis and treatment, yet its full implementation in LMICs remains hindered by financial, infrastructural, and technical barriers. This study highlights significant disparities in molecular testing, treatment access, and survival outcomes in glioma patients treated at Gauhati Medical College. Urgent efforts are needed to improve access to cost-effective molecular diagnostics, expand treatment infrastructure, and promote sustainable neuro-oncology programs in LMICs. By addressing these systemic issues, the global neuro-oncology community can work toward closing the glioma survival gap and ensuring equitable care for all patients.

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