

# Histo-Epidemiological Aspects and Preliminary Immunohistochemical Profile of Gliomas Diagnosed in Burkina Faso between 2014 and 2023

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**How to cite this paper:** Ouattara, S., Ido, F.A.H.A., Savadogo, I., Lougué, M.B., Zabsonré, D.S., Zouré, A.A., Ouédraogo, A.S., Lamien/Sanou, A. and Lompo, O.M. (2026) Histo-Epidemiological Aspects and Preliminary Immunohistochemical Profile of Gliomas Diagnosed in Burkina Faso between 2014 and 2023. *Open Journal of Pathology*, 16, 177-192.

<https://doi.org/10.4236/ojpathology.2026.164019>

**Received:** June 10, 2026

**Accepted:** August 14, 2026

**Published:** August 17, 2026

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## Abstract

**Introduction:** Glial tumours are primary tumours of the central nervous system. They may be localised or diffuse. Diffuse gliomas are the most common primary tumours of the central nervous system encountered in neuro-oncological practice. The 5th edition (2021) of the WHO classification of tumours of the central nervous system requires that the morphological diagnosis be supplemented by the identification of molecular alterations using immunohistochemistry and molecular biology techniques. These techniques are still struggling to be implemented in resource-limited settings such as those in Burkina Faso. We initiated this study with the dual aim of establishing the histo-epidemiological profile of gliomas diagnosed in Burkina Faso between 2014 and 2023 according to the 2007 WHO classification, and of reporting the molecular alterations associated with diffuse gliomas using immunohistochemical techniques in line with modern criteria. **Methodology:** We conducted a cross-sectional, descriptive, and analytical study involving retrospective data collection, including all cases of histologically confirmed gliomas from all pathological anatomy laboratories in Burkina Faso between 1 January 2014 and 31 December 2023. For each case, we collated the available sociodemographic, clinical, ra-

diological, and pathological data. An immunohistochemical re-evaluation was then carried out on diffuse gliomas using formalin-fixed, paraffin-embedded (FFPE) tissue blocks. The panel of antibodies used included antibodies against: GFAP, IDH1-R132H, p53, ATRX, Olig2, INA, and Ki-67. **Results:** Over a ten-year period, we collected data on 463 CNS tumours, of which 154 were gliomas, representing 33.33%. The average annual incidence of gliomas was 15.4 new cases. The sex ratio was 1.75. The mean age of patients was 32.7 years, with a median of 30 years and a range of 1 to 80 years. Standard histological examination revealed 62.99% astrocytic tumours, 26.62% glioblastomas, and 9.09% oligodendrogliomas. Immunohistochemical analysis of 33 cases identified an IDH mutation in 78.8% of cases and yielded the following profiles: 1) Seven low-grade astrocytomas (grade 2) with IDH mutation. 2) Four anaplastic astrocytomas (grade 3) with an IDH mutation. 3) Five gliomas without an IDH mutation (IDH wild-type), requiring further investigation. 4) Five cases suggestive of oligodendroglioma (requiring confirmation by testing for 1p/19q co-deletion). 5) Most notably, 12 cases initially classified as “IDH-mutated glioblastomas” were reclassified as “grade 4 IDH-mutated astrocytomas” according to the 2021 WHO classification. **Conclusion:** This study, the first of its kind in Burkina Faso, confirms that gliomas affect a young population there, with a clear predominance of male patients. Above all, it highlights the very high prevalence of IDH-mutated gliomas (nearly three-quarters of the cases analysed). This molecular profile has direct implications for prognosis and treatment options. However, it should be interpreted with caution as it is based on a sample of only 33 cases and cannot be generalised at this stage of the study. Furthermore, twelve (12) gliomas were reclassified using the 2021 WHO criteria. This clearly illustrates the role of immunohistochemistry, even in a resource-limited setting, in refining the diagnosis and better guiding patient management.

## Keywords

Gliomas, Immunohistochemistry, IDH Mutation, WHO 2021 Classification, Epidemiology, Burkina Faso

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## 1. Introduction

Glial tumours are primary tumours of the central nervous system. They may be localised or diffuse [1]. Diffuse gliomas are the most common form of primary brain and spinal cord tumour, accounting for the vast majority—around 80 percent—of malignant brain tumours. Globally, GLOBOCAN 2022 estimates reported more than 320,000 new cases and nearly 250,000 deaths annually [2]. In sub-Saharan Africa, Al-Fikri *et al.*, in a systematic review, reported an estimated standardised incidence rate of CNS tumours in Africa of 3.2 - 3.9 per 100,000, which is six times lower than that in high-income countries [3]. In Burkina Faso in particular, understanding the precise epidemiology of gliomas is hampered by a critical lack of data, mainly due to the absence of population-based cancer registries. The Ouagadougou Cancer Registry, which has been in existence since 1996, has not

yet been firmly established within the institutional framework.

The 2000s marked a decisive turning point in gliomagenesis with the discovery of key molecular alterations: 1p19q co-deletion, TP53 mutations, IDH1/IDH2 mutations, loss of ATRX, and EGFR amplification [4]-[6]. These advances led to a revision of the World Health Organisation (WHO) classification in 2016, establishing the so-called “integrated diagnosis” (integrated histo-molecular diagnosis) [7] [8], followed by a new edition in 2021 (CNS5), which established the predominant molecular profile [9]. Indeed, specific genetic alterations, such as mutations in the IDH1/IDH2 genes or the co-deletion of chromosomes 1p and 19q, have become diagnostic criteria in their own right, enabling a more precise classification and a better-established prognosis [5] [10] [11]. In this context, IHC has established itself as an accessible first step on formalin-fixed, paraffin-embedded (FFPE) tumour tissue, using validated markers [5] [12] [13].

Despite these numerous advances, the diagnosis of CNS tumours in general, and gliomas in particular, is still based on histopathological examination in Burkina Faso. The few studies that have been carried out on central nervous system tumours remain hospital-based series. Indeed, in a retrospective descriptive study, Zabsoulié *et al.* [14] reported 76 brain tumours at the Yalgado Ouédraogo University Hospital between 2005 and 2010. Zongo *et al.* [15], in their study on the epidemiology of cancers in Burkina Faso, reported that gliomas accounted for 0.2 percent of cases. To date, no study in Burkina Faso has examined the histo-molecular aspects of all gliomas in accordance with the WHO CNS5 classification (2021). Our study aims to address this gap in two ways: to establish the histo-epidemiological profile of the full spectrum of glial tumours diagnosed in Burkina Faso between 2014 and 2023, as defined by the 2007 WHO classification [16], including circumscribed gliomas (pilocytic astrocytoma, SEGA, pleomorphic xanthoastrocytoma); and to propose, using manual immunohistochemistry (IHC), a histo-molecular classification specifically for diffuse gliomas, the main targets of molecular diagnosis according to the 2016 and 2021 WHO classifications [8] [9].

## 2. Materials and Methods

### 2.1. Study Design, Setting, and Period

We conducted a cross-sectional study involving retrospective data collection over a ten-year period, from 1 January 2014 to 31 December 2023. This study was conducted across all departments of anatomical and cytological pathology (ACP) in Burkina Faso. These included the ACP departments of the following university hospitals: Yalgado Ouédraogo (CHU-YO), Bogodogo (CHU-B), Tengandogo (CHU-T), Sourô Sanou (CHU-SS), as well as the PHS laboratories of semi-public and private institutions: Saint Camille Hospital in Ouagadougou (HOSCO), Schiphra Protestant Hospital, SANDOF Polyclinic, and Philadelphie Polyclinic. All these laboratories offer standard histology services. Immunohistochemistry was performed at the Morphology and Organogenesis Laboratory of Joseph Ki-Zerbo University.

## 2.2. Case Selection Criteria

For the histo-epidemiological investigation, we included in this study all cases of histologically confirmed glioma within the specified period for which pathological reports were available, usable, and complete. For the immunohistochemical study, we included all cases of histologically confirmed diffuse gliomas within the specified period for which at least one paraffin-embedded tissue block (FFPE block) of sufficient quality for further analysis was available. Duplicate samples and those inadequately preserved for IHC were systematically excluded. Of the 154 cases of gliomas, archived FFPE blocks have so far been retrieved for 59 cases. We excluded twenty-six (26) cases for various reasons. Seven (07) of these blocks were depleted. In eleven (11) cases, there was insufficient tissue for immunohistochemical staining. In eight (08) cases, the immunohistochemical staining was uninterpretable, most likely due to poor fixation and/or inadequate dehydration. Thirty-three (33) cases met the quality criteria required for IHC analysis.

## 2.3. Study Methodology

Our approach consisted of three main stages:

Step 1: Collection of histo-epidemiological data. We comprehensively collected sociodemographic, clinical, radiological, and pathological data on all cases of glioma diagnosed during the specified period using a digital questionnaire. The collection of these data enabled the identification of paraffin blocks for immunohistochemistry and molecular biology studies.

Step 2: Characterisation of gliomas by immunohistochemistry. On thin sections of tumour tissue, we conducted an immunohistochemical study using the manual streptavidin-biotin complex technique, systematically employing the following antibodies: anti-IDH1 R132H (clone H09) (1:100 dilution), P53 (dilution 1:75), ATRX (dilution 1:200) and Ki-67 (dilution 1:150); anti-GFAP antibodies (dilution 1:400) and/or Olig2 antibodies (dilution 1:200) in cases of uncertainty regarding glial morphology; and anti-INA antibodies (dilution 1:300) in tumours of oligodendroglial morphology. The sections were first deparaffinised with xylene and rehydrated in alcohols of decreasing concentration. Unmasking was carried out using buffer solutions appropriate to the pH of each antibody in a water bath preheated to 98 degrees Celsius. After sectioning, the technique involved, in chronological order: peroxide incubation, Super Block incubation, primary antibody incubation, washing with PBS, polyvalent antibody incubation, washing with PBS, DAB incubation (substrate + chromogen), washing with bleach, counterstaining with Harris's haematoxylin, mounting, and observation. The slides were read independently by two experienced pathologists.

Step 3: Molecular biology tests (ongoing). To refine the diagnosis, additional molecular tests will be carried out on a selection of cases based on the IHC results. These aim to identify, using sequencing or molecular biology techniques (FISH, MLPA), other significant alterations: other IDH mutations, 1p/19q co-deletion, methylation status of the MGMT promoter, or EGFR amplification. These results

will be the subject of a future publication.

## 2.4. Data Analysis

The data were analysed using R (version 4.x) and Epi-Info (version 7.2.5). Quantitative variables (such as age) are presented as the mean, standard deviation, median, and 95% confidence interval. Qualitative variables (such as sex or histological type) are expressed as absolute numbers and percentages. Given the size of certain subgroups, the analysis was limited to descriptive statistics.

## 2.5. Ethical Considerations

This initial data collection phase was approved by the ethics committees of the various hospitals serving as data collection sites. Authorisation for data collection was granted by the senior management of these institutions. Patient data confidentiality was strictly maintained through a process of anonymisation and coding. An application for approval from the Burkina Faso Health Research Ethics Committee (CERS-BF) has been submitted for the molecular biology analysis phase.

## 3. Results

### 3.1. General Data

Between 1 January 2014 and 31 December 2023, 463 central nervous system tumours were histologically diagnosed in the pathological anatomy laboratories of Burkina Faso. This cohort included 154 gliomas, representing 33.26% of the total. The average number of new cases of glioma diagnosed per year at the national level was 15.4.

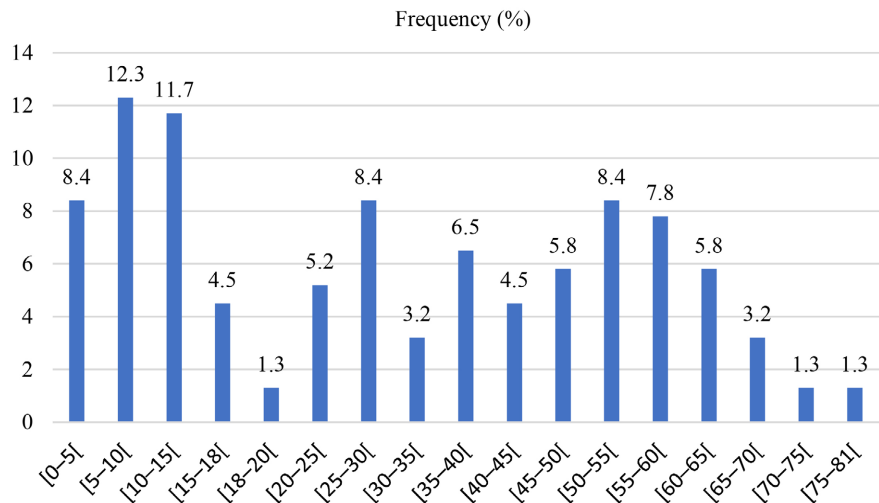
### 3.2. Sociodemographic Aspects

Our series comprised 98 men and 56 women, giving a sex ratio of 1.75.

The mean age at diagnosis was 32.7 years, with a median of 30 years and a range of 1 to 80 years. **Figure 1** shows the distribution of patients with gliomas by age group, and **Table 1** shows the distribution by age group and sex.

**Table 1.** Breakdown of patients with gliomas by gender and age group (n = 154).

| Age group    | Male             |                  | Feminine         |                  | Total<br>(n) | Sex-Ratio<br>M/F |
|--------------|------------------|------------------|------------------|------------------|--------------|------------------|
|              | Headcount<br>(n) | Frequency<br>(%) | Headcount<br>(n) | Frequency<br>(%) |              |                  |
| [0 - 18[     | 34               | 59.6             | 23               | 40.4             | 57           | 1.48             |
| [18 - 65[    | 56               | 63.6             | 32               | 36.4             | 88           | 1.75             |
| [65 - 81]    | 8                | 88.9             | 1                | 11.1             | 9            | 8.00             |
| <b>Total</b> | <b>98</b>        | <b>63.6</b>      | <b>56</b>        | <b>36.4</b>      | <b>154</b>   | <b>1.75</b>      |



**Figure 1.** Breakdown of patients with gliomas by age group (n = 154).

**3.3. Clinical and Medical Imaging Data**

The pathology request form included clinical information with a detailed description of clinical symptoms in 92 cases (61.7%). The form indicated that medical imaging had been performed in 102 patients (66.23%). These consisted of computed tomography (CT) scans (75.5%), magnetic resonance imaging (MRI) (18.6%), or both (5.9%). The location of the tumour was reported in 97 cases. The tumour was located in the supratentorial cerebral parenchyma (n = 53), the cerebellum (n = 37), the brainstem (n = 3), and the ventricles (n = 4).

**3.4. Histological Data**

Histological examination revealed astrocytic tumours, glioblastomas, oligodendrogliomas, and mixed tumours in proportions of 62.99%, 26.62%, 9.09% and 1.30%, respectively. **Table 2** details the numbers and frequencies of the different histological subtypes.

**Table 2.** Detailed breakdown by histological type and subtype according to the 2007 WHO classification (n = 154).

| Histological Type                        | Histological Subtype             | Staff Numbers (n) | Frequency (%) |
|------------------------------------------|----------------------------------|-------------------|---------------|
| ASTROCYTIC TUMOURS<br>n = 97<br>(62.99%) | Grade I pilocytic astrocytoma    | 44                | 28.9          |
|                                          | Grade II diffuse astrocytoma     | 30                | 19.7          |
|                                          | Grade III anaplastic astrocytoma | 16                | 10.5          |
|                                          | SEGA                             | 5                 | 3.3           |
|                                          | Pleomorphic xanthoastrocytoma    | 2                 | 1.3           |
| GLIOBLASTOMAS<br>n = 41 (26.62%)         | Grade IV glioblastoma            | 41                | 26.62         |



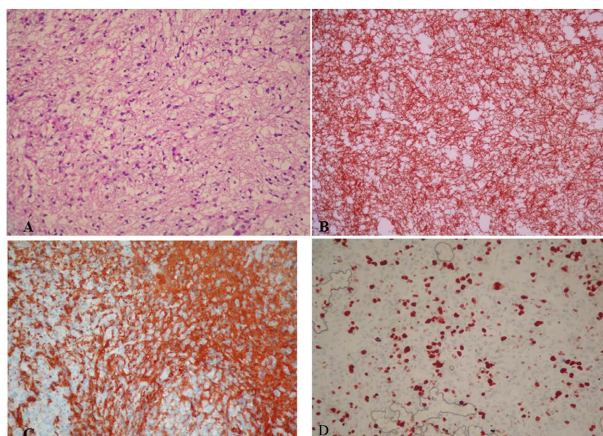
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|                                               |                             |     |     |
|-----------------------------------------------|-----------------------------|-----|-----|
| OLIGODENDROGLIAL<br>TUMOURS<br>n = 14 (9.09%) | Grade I oligodendroglioma   | 3   | 2.0 |
|                                               | Grade II oligodendroglioma  | 6   | 3.9 |
|                                               | Grade III oligodendroglioma | 5   | 3.3 |
| MIXED TUMOURS<br>n = 2 (1.30%)                | Grade II oligoastrocytoma   | 1   | 0.7 |
|                                               | Grade III oligoastrocytoma  | 1   | 0.7 |
| TOTAL                                         |                             | 154 | 100 |

**3.5. Immunohistochemical Study**

The IHC analysis in this preliminary phase has so far covered thirty-three (33) cases (a subset selected on the basis of quality criteria from the cohort). The IDH1-R132H mutation was detected in 26 cases (78.8%). This proportion should be interpreted with caution, as it reflects a selected subgroup and may overestimate the prevalence of the IDH mutation in the full series.

Of the thirty-three (33) cases analysed, twenty-three (23) received a confirmed WHO 2021 diagnosis based solely on IHC (Level 1): seven (07) Grade 2 IDH-mutant astrocytomas, four (04) Grade 3 IDH-mutant astrocytomas, and twelve (12) Grade 4 IDH-mutant astrocytomas (previously labeled as glioblastomas). The remaining 10 cases were given a provisional classification pending further molecular investigations (Level 2): three (03) probable IDH-mutated oligodendrogliomas requiring confirmation of 1p/19q co-deletion, two (02) oligodendrogliomas with an atypical profile requiring IDH2 sequencing and 1p/19q testing, and five (05) IDH1-R132H-negative cases requiring IDH sequencing to detect rare mutations. The first-level immunohistochemical profiles are shown in **Table 3(a)**, and those of the second level in **Table 3(b)**. Similarly, **Figure 2** shows microphotographs illustrating an IDH-mutated glioma as detected by immunohistochemical analysis.



**Figure 2.** Microphotographs A: Tissue sample stained with haematoxylin and eosin (HE) at 40× magnification: moderate proliferation of astrocytes. B: Anti-GFAP immunostaining: diffuse and intense mesh-like staining. C: Anti-IDH1 immunohistochemistry: intense cytoplasmic expression signal in tumour cells. D: Anti-Ki-67 immunohistochemistry: intense nuclear expression signal in tumour cells.

**Table 3.** (a) Level 1: Confirmed WHO 2021 diagnoses (n = 23), (b) Level 2: Provisional classifications pending molecular confirmation (n = 10).

| (a)                                                                                                                                                                                |           |                             |                           |                                                                                                           |                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------------------------|---------------------------|-----------------------------------------------------------------------------------------------------------|--------------------------------|
| Histological Type (WHO 2007)                                                                                                                                                       | n         | Profile IHC                 | IDH Status                | WHO Correspondence 2021 Confirmed                                                                         |                                |
| Grade II diffuse astrocytomas                                                                                                                                                      | 5         | IDH1+/P53+/<br>ATRX-/Olig2- | IDH R132H<br>mutation     | IDH-mutated<br>astrocytoma, grade 2                                                                       |                                |
| Grade II diffuse astrocytomas                                                                                                                                                      | 2         | IDH1+/P53+/<br>ATRX-/Olig2+ | IDH R132H<br>mutation     | IDH-mutated<br>astrocytoma, grade 2                                                                       |                                |
| Grade III anaplastic astrocytomas                                                                                                                                                  | 4         | IDH+/P53+/<br>ATRX+/Olig2-  | IDH R132H<br>mutation     | IDH-mutated<br>astrocytoma, grade 3                                                                       |                                |
| Grade IV Glioblastomas                                                                                                                                                             | 6         | IDH+/P53+/<br>Olig2-/ATRX-  | IDH R132H<br>mutation     | IDH-mutated<br>astrocytoma, grade 4                                                                       |                                |
| Grade IV Glioblastomas                                                                                                                                                             | 4         | IDH+/P53+/Olig2+            | IDH R132H<br>mutation     | IDH-mutated grade 4<br>astrocytoma                                                                        |                                |
| Grade IV Glioblastomas                                                                                                                                                             | 2         | IDH+/P53-(null)/<br>Olig2-  | IDH R132H<br>mutation     | IDH-mutated grade 4<br>astrocytoma                                                                        |                                |
| <b>Total Level 1</b>                                                                                                                                                               | <b>23</b> |                             |                           |                                                                                                           |                                |
| The 12 cases of glioblastomas (grade IV according to the 2007 WHO classification) are reclassified as “IDH-mutated astrocytoma, grade 4” according to the WHO 2021 classification. |           |                             |                           |                                                                                                           |                                |
| (b)                                                                                                                                                                                |           |                             |                           |                                                                                                           |                                |
| Histological Type (WHO 2007)                                                                                                                                                       | n         | Profile IHC                 | IDH Status                | WHO Provisional Classification 2021                                                                       | Investigation Required         |
| Grade III anaplastic astrocytomas                                                                                                                                                  | 3         | IDH1-/P53+/<br>ATRX-/Olig2+ | IDH<br>wild-type<br>(IHC) | High-grade diffuse glioma, IDH wild-type to be confirmed                                                  | IDH and EGFR/TERT sequencing   |
| Grade III anaplastic astrocytomas                                                                                                                                                  | 2         | IDH1-/P53-/<br>ATRX+/Olig2+ | IDH<br>wild-type<br>(IHC) | IDH wild-type glioma, unclassifiable entity                                                               | IDH sequencing and 1p/19q      |
| Anaplastic oligodendroglioma                                                                                                                                                       | 3         | IDH1+/P53-/<br>ATRX-/INA-   | IDH R132H<br>mutation     | PROBABLE Grade 3 IDH-mutated oligodendroglioma or Grade 3 IDH-mutated astrocytoma (if no co-localisation) | 1p/19q co-deletion (FISH/MLPA) |
| Anaplastic oligodendroglioma                                                                                                                                                       | 2         | IDH1-/INA+/<br>P53+/Olig2+  | IDH<br>wild-type<br>(IHC) | Atypical profile-Pending classification                                                                   | IDH2 sequencing and 1p/19q     |



**Continued****TOTAL LEVEL 1 10**

These 10 cases cannot be given a definitive 2021 WHO diagnosis without further molecular investigations. They are presented here on a provisional basis, pending the results of 1p/19q co-deletion testing (FISH or MLPA) and/or IDH sequencing (IDH1 non-R132H and IDH2).

**4. Discussion****4.1. General Data**

Over a ten-year period, we collected data on 463 CNS tumours, including 154 cases of gliomas (33.26%), making gliomas the second most common type after meningiomas. This proportion is consistent with data from the international literature, which estimates that gliomas account for approximately 30% of primary CNS tumours [17]-[19]. The annual incidence of gliomas was 15.4 cases. This is likely a significant underestimation of the actual incidence, linked to the absence of a national population-based cancer registry and constraints on access to neurosurgical care in Burkina Faso. Indeed, until 2020, Burkina Faso had only one neurosurgery department, located at the Yalgado Ouédraogo University Hospital in the capital. Whenever specialised neurosurgical care is required, patients are often forced to travel hundreds of kilometres. The neurosurgery departments at the Sourô SANON University Hospital in Bobo Dioulasso, the Ouahigouya Regional University Hospital, and the Tenkodogo Regional Hospital were opened in 2021, 2023, and 2024, respectively. Many patients die from CNS tumours in farming hamlets without ever receiving any diagnostic tests. Furthermore, interventional radiology and endoscopy are still in their infancy, and many CNS tumours strongly suspected of being gliomas remain undiagnosed with certainty. These cases, which lack histological confirmation and are not recorded in a pathological registry, are not included in this study, which focuses on histologically confirmed gliomas.

**4.2. Sociodemographic Data**

The mean age at diagnosis (32.7 years) is significantly lower than that observed in Western countries, where high-grade gliomas predominantly occur after the age of 50 [17] [20] [21]. This particularity could be explained by two factors: the very young age structure of the Burkinabe population and the high proportion (28.9%) of pilocytic astrocytomas, a common benign tumour in children and adolescents, in our series.

The male predominance (sex ratio 1.75) is consistent with data from the international literature [1] [22] and is particularly marked in the age group (sex ratio 8.0). This is consistent with the biology of gliomas: androgen receptors appear to promote glial tumour growth, and some studies suggest a protective role for estrogens.

### 4.3. Clinical and Medical Imaging Data

Clinical and paraclinical information, including a detailed description of clinical symptoms, the precise location of the tumour, and its radiological features, was reported to the pathologist in 61.7%, 62.98%, and 59.26% of cases, respectively. This represents under-reporting, reflecting clinicians' lack of familiarity with the diagnostic process in pathological anatomy. Clinical information is essential for histopathological analysis. In the anato-clinical process, it serves as a medical history.

Among the reported locations, cerebellar involvement ( $37/97 = 38.1\%$ , or  $40/97 = 41.2\%$  when including the brainstem) was predominant. This distribution is linked to the high proportion of pilocytic astrocytomas (28.9%), which develop predominantly in the cerebellum in children and adolescents [3] [23] [24]. This profile is consistent with the young median age in our series.

### 4.4. Distribution of Histological Types According to the 2007 WHO Classification

The 2007 WHO classification of tumours of the central nervous system, published by Louis *et al.*, served as the international standard for the histological characterisation of gliomas [16]. This fourth edition, based exclusively on histopathological and immunohistochemical criteria, defined diffuse gliomas into broad categories: diffuse astrocytoma (grade II), anaplastic astrocytoma (grade III), glioblastoma multiforme (grade IV), oligodendroglioma (grades II and III), and mixed oligo-astrocytoma (grades II and III). This classification was revised in 2016 [7], and a new edition was published in 2021 [9]. Until 2023, Burkina Faso had not incorporated molecular diagnosis of gliomas. All cases of gliomas diagnosed to date and included in our study between 2014 and 2023 were classified according to the criteria of the 2007 WHO classification. No molecular diagnosis was available.

In our series, astrocytic tumours accounted for 62.99% of all gliomas. This predominance of astrocytic tumours is also reported in the literature. Indeed, a systematic review of low-grade gliomas in Africa (Nigeria, Egypt, Morocco, Tunisia, Uganda, Cameroon, Ghana, and Kenya) found a predominance of astrocytic tumours, accounting for 81.1% of histologically diagnosed low-grade gliomas [3]. In Zimbabwe, a prospective study conducted from 2014 to 2016, using the 2007 WHO classification across the country, also found astrocytomas to be the most common type (57.1% of cases), with glioblastoma accounting for 12% of all gliomas [25]. In Ghana, in a series of 338 patients who underwent surgery for a CNS tumour, astrocytoma accounted for 60.4% of gliomas [26]. Similarly, the North American CBTRUS registries reported 76.4% astrocytic tumours in the United States between 2012 and 2016 [17]. In a series of 83,458 primary malignant brain tumours in Europe, EUROCare-5 reported 49% glioblastoma, 18% astrocytomas and 9% oligodendrogliomas/oligoastrocytomas [27]. This predominance of astrocytomas in our series is therefore consistent with regional and global trends.

#### Prevalence of glioblastoma among high-grade gliomas:

Among high-grade tumours, glioblastoma (grade IV) was the most common malignant histological type in our series (26.62%,  $n = 41$ ). This prevalence is also reported in the literature. According to CBTRUS (2012-2016), glioblastoma accounted for 57.3% of all gliomas in the United States, with an age-standardised incidence rate of 3.22 per 100,000 population [17]. In Algeria, Touati *et al.*, in a series of 333 gliomas diagnosed between 2008 and 2016 according to the 2007 WHO criteria, reported glioblastoma as the most common histological type, with a mean age of 48.07 years and a sex ratio of 1.87 [28]. In a hospital series of 1450 gliomas operated on in India, glioblastomas accounted for the majority of cases (41.4%), followed by diffuse astrocytoma (22.8%), pilocytic astrocytoma (6.3%), and oligodendroglioma (4.5%) [29]. It is important to note that according to the 2021 WHO classification, the term “glioblastoma” is now reserved solely for IDH wild-type gliomas [9]; IDH-mutated cases previously labeled “glioblastoma” must be reclassified as “IDH-mutated astrocytoma, grade 4”, with direct prognostic implications, as demonstrated by our immunohistochemical analysis.

#### **Prevalence of oligodendrogliomas and mixed oligoastrocytic tumours:**

Oligodendrogliomas (grades II and III) and mixed oligoastrocytic tumours accounted for 9.09% ( $n = 14$ ) and 1.30% ( $n = 2$ ) respectively in our series. This low proportion is also reported in the literature. Indeed, according to EURO CARE-5 data, oligodendrogliomas and oligoastrocytomas together accounted for 9% of brain tumours [30]. Some pathological series reported lower proportions of 3.5% for oligodendrogliomas of all grades and 1.9% for anaplastic oligodendrogliomas among CNS tumours. Under the 2007 WHO classification, the diagnosis of mixed oligoastrocytoma was based on purely morphological criteria, in the absence of any predictive markers of molecular abnormalities. This entity, for which inter-observer reproducibility was recognised as insufficient, has virtually disappeared with the introduction of IDH status and 1p/19q co-deletion in the 2016 revision of the WHO classification, and subsequently with the new CNS5 edition of 2021. The fact that our series includes cases of mixed oligoastrocytomas diagnosed prior to this molecular revolution is a direct consequence of the lack of molecular biology in Burkina Faso. None of the African studies included in the review by Nyalundja *et al.* provided molecular characterisation of the tumours, highlighting that our context is part of a shared continental reality [31].

#### **Distribution of low-grade and high-grade gliomas and African characteristics**

The distribution between low-grade gliomas (WHO grades I - II) and high-grade gliomas (WHO grades III - IV) in our series is worth noting. The high proportion of grade I pilocytic astrocytomas (28.9%, the most common single subtype) helps to distinguish our series from Western studies, where adult high-grade gliomas are largely predominant. This characteristic is consistent with the young demographic structure of our population and with African data. The review by Nyalundja *et al.* indeed reports that, in African series, the subtentorial location is predominant in pediatric series (71.6% of localisations), which corroborates the

high proportion of cerebellar pilocytic astrocytomas in children observed in our study [31]. In the Algerian series by Touati *et al.*, however, high-grade tumours with a supratentorial location predominate in adults and older people [28], as we noted in the 18 - 65 age group of our series.

#### 4.5. The Contribution of IHC and the 2021 WHO Reclassification

Our study is the first national series in Burkina Faso to include a systematic immunohistochemical assessment for the diagnosis of gliomas. It accurately reflects the state of diagnostic practices available in Burkina Faso over the period 2014-2023, in line with the reality across all sub-Saharan African countries, where no centre yet has the integrated molecular pathology required by the 2016 WHO and 2021 CNS5 classifications. In this context, our diagnoses of astrocytoma, oligodendroglioma, oligoastrocytoma, and glioblastoma according to the 2007 WHO classification remain valid histological diagnoses.

Immunohistochemical analysis of the 33 cases. Twenty-three (23) received a confirmed WHO 2021 diagnosis, requiring no further molecular investigation. The remaining 10 cases remain provisional classifications, with their definitive diagnosis contingent upon the detection of a 1p/19q co-deletion or IDH sequencing. This distinction is essential to avoid overestimating the significance of the results in a context where molecular biology is not yet routinely available in Burkina Faso. The profiles observed were grouped into four main categories:

Group A-Low-grade astrocytomas (n = 7): All cases exhibited an IDH1 mutation associated with a loss of ATRX expression and an accumulation of p53, a profile typical of IDH-mutated astrocytomas.

Group B-Anaplastic astrocytomas (grade III) (n = 9): Four (04) cases exhibited a typical IDH-mutated profile. Five (05) cases were negative for the IDH1 R132H mutation by IHC and require genetic sequencing for confirmation.

Group C-Anaplastic oligodendrogliomas (n = 5): Three cases showed a profile strongly suggestive of an IDH-mutated oligodendroglioma (IDH1+/P53-/ATRX-), for which a definitive diagnosis requires evidence of 1p/19q co-deletion. Two cases presented an atypical profile (IDH1-/INA+) requiring further molecular investigations.

Group D-Glioblastomas (n = 12): The most striking finding here is the reclassification. Eleven of the twelve cases expressed the IDH1 mutation. According to the 2021 WHO classification, these tumours are no longer referred to as “IDH-mutated glioblastomas” but as “grade 4 IDH-mutated astrocytomas”, an entity with a significantly more favourable prognosis.

The change in nomenclature introduced by the 2021 WHO classification is far from insignificant. Reclassifying twelve (12) tumours from “glioblastoma” to “grade 4 astrocytoma” has concrete implications. The latter entity is associated with a longer median survival (2 - 3 years versus 12 - 15 months) and a better response to standard chemotherapy (temozolomide). This information can be directly used by clinicians to discuss the prognosis with patients and tailor treatment.

#### 4.6. Limitations and Future Direction

This study has certain limitations, primarily the still small number of cases in which IHC was performed (33/154) and the lack, at this stage, of sequencing confirmation for all equivocal profiles and of survival data. These points are precisely the logical next step in our ongoing doctoral research, which plans to extend molecular analyses to the entire cohort.

#### 5. Conclusion

This update on the immunohistochemical profiles of gliomas in Burkina Faso confirms the predominance of IDH-mutated forms. However, it should be interpreted with caution as it is based on a sample of only 33 cases and cannot be generalised at this stage of the study. Its most significant contribution is the reclassification of several tumours as “grade 4 IDH-mutated astrocytomas”, a diagnosis with a more favourable prognosis that should guide better-informed treatment decisions. Certain complex or negative IHC profiles highlight the imperative need to pursue investigations using molecular biology techniques to reach a definitive diagnosis. Continuing this work, with a comprehensive molecular analysis of the cohort, will enable us to draw up an even more precise map of gliomas in our context.

#### Author Contributions

This study was carried out through close collaboration between the various authors, whose specific contributions are detailed below:

S. Ouattara was responsible for the overall design and coordination of the study, carried out the immunohistochemical (IHC) and statistical analyses, drafted the initial manuscript, and approved the final version.

F. A. H. A. Ido was responsible for data collection in the field, played an active role in the immunohistochemical analyses, and carried out a critical review of the manuscript.

I. Savadogo helped S. Ouattara to draft the first version.

B. M. Lougué was responsible for designing the data entry forms, coordinating data collection, and carrying out statistical analyses.

D. S. Zabsonré provided and validated all the neurosurgical clinical data and contributed to the review of the manuscript.

A. A. Zouré carried out the advanced statistical analyses using R software and contributed to the review.

A. S. Ouédraogo, A. M. Lamien/sanou, and O. M. Lompo all three carried out a thorough critical review of the manuscript and gave their approval for the final version submitted.

#### Conflicts of Interest

The authors of this study declare that there are no financial or personal conflicts of interest that could influence the results or interpretation of the work presented.

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