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Epidemiological and Histopathological Aspects of Gliomas in two Pathology Laboratories in Antananarivo

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ABSTRACT

Introduction: *Gliomas are primary tumors of the central nervous system that mainly arise from glial cells. Their diagnosis is primarily based on histopathological examination, although recent World Health Organization classifications increasingly incorporate molecular criteria. This study aimed to describe the epidemiological, clinical, paraclinical and histopathological features of gliomas diagnosed in the Pathology laboratories of the Hospital Center of Soavinandriana and the University Hospital Center Joseph Ravoahangy Andrianavalona in Antananarivo.*

Materials and Method: *This was a bicentric, retrospective, descriptive and analytical study conducted in two Pathology laboratories in Antananarivo over a ten-year period, from January 2013 to December 2022. All histologically confirmed cerebral gliomas were included. Data were collected from examination request forms, available medical records and pathology reports. The variables included age, sex, clinical information, imaging findings, type of specimen, macroscopic features, histological type and histoprognostic grade.*

Results: *A total of 68 glioma cases were collected, representing 26.9% of primary brain tumors. The mean age of patients was 33.67 ± 19.18 years, ranging from 1 to 70 years. Male predominance was observed, with a sex ratio of 1.4. Intracranial hypertension was the most frequent clinical finding, reported in 64.7% of cases. Brain CT scan was the most commonly performed imaging examination, used in 97.1% of cases. The frontal lobe was the most frequent tumor location. Histologically, oligodendroglioma (grade II) was the most common type, accounting for 29.4% of cases, while glioblastoma multiforme (grade IV) was the most frequent high-grade glioma. Low-grade gliomas represented 61.7% of cases. Statistically significant associations were found between age and histological type ($p = 0.0005$), sex and histological type ($p = 0.012$), as well as age and histoprognostic grade ($p = 0.0007$).*

Conclusion: *This study highlights the epidemiological and histopathological particularities of gliomas diagnosed in two Pathology laboratories in Antananarivo. The findings show a predominance of low-grade gliomas, a relatively young affected population and male predominance, particularly in glioblastoma cases. They also underline the limitations related to restricted access to MRI, immunohistochemistry and molecular biology. Strengthening the technical platform is necessary to improve integrated diagnosis, glioma classification and patient management in Madagascar.*

Keywords
Brain, Epidemiology, Gliomas, Histology, Madagascar, Pathology.

Introduction
Gliomas constitute a heterogeneous group of primary tumors of the central nervous system developed from glial cells or their precursors. Their clinical presentation, radiological appearance, and evolutionary behavior vary according to the histological type and tumor grade. While brain imaging guides the diagnosis and specifies the location of the lesion, confirmation relies on pathological examination, essential for identifying the glial nature of the tumor, assessing malignancy criteria, and establishing the histoprognostic grade [1-3].

The epidemiology of gliomas shows a variable incidence depending on regions and data collection methods, with a slight male predominance and a distribution differing according to age: low-grade gliomas are more often observed in young subjects, while high-grade forms, particularly glioblastoma, predominate in older adults [4-7]. Their classification has evolved significantly, moving from an essentially morphological approach in the 2007 WHO classification to an integrated diagnosis combining histology and molecular data, notably IDH status and 1p/19q codeletion, in the 2016 and 2021 WHO classifications [8-15]. This study therefore aimed to describe the epidemiological, clinical, paraclinical, and histopathological aspects of gliomas diagnosed in two Pathology laboratories in Antananarivo over a ten-year period.

Materials and Method
It was a bicentric, retrospective, descriptive, and analytical study conducted in two Pathology laboratories in Antananarivo: the Pathology laboratory at the Hospital Center of Soavinandriana and the Pathology laboratory at the University Hospital Center Joseph Ravoahangy Andrianavalona. The study period extended from January 2013 to December 2022, a total of 10 years. The study population included individuals with brain lesions referred for anatomopathological examination in the two laboratories during the considered period. All cases of histologically confirmed cerebral gliomas were included. Duplicates corresponding to the same diagnosis in the same patient, and incomplete records were excluded. Due to the unavailability of immunohistochemistry and molecular biology at the study sites, the diagnosis and histoprognostic classification were established mainly based on the morphological criteria of the 2007 WHO.

The data were collected from examination request forms, available records, and anatomopathological reports. The variables analyzed concerned age, gender, clinical information, imaging data, tumor location, type of sample, macroscopic aspects, histological type, and histoprognostic grade. Quantitative variables were expressed as mean ± standard deviation; associations between variables were interpreted with a significance threshold set at $p < 0.05$.

Results
During the study period, 253 primary brain tumors were recorded in the two laboratories. Among them, 68 were gliomas, representing a proportion of 26.9%. Primary brain tumors other than gliomas accounted for 73.1% of cases. The age of the patients ranged from 1 to 70 years, with an average of 33.67 ± 19.18 years. The age group from 1 to under 20 years was the most represented, with 22 cases, or 32.4%. This was followed by the age group from 20 to under 40 years, which had 20 cases, then the age group from 40 to under 60 years, with 18 cases. Patients aged 60 years or older accounted for 8 cases. The male gender predominated with 40 cases, or 58.8%, compared to 28 cases in females, or 41.2%. The sex ratio was 1.4. Clinical information was dominated by intracranial hypertension syndrome, observed in 44 cases, or 64.7%. Other presentations included comitial crises, deficit syndromes, and associations of signs. The preferred tumor location was frontal, with 12 cases, or 17.6%.

The brain scan was the most frequently performed radiological examination, involving 66 patients, or 97.1% of cases. MRI was much less frequently requested, with 2 cases, or 2.9%. From an anatomopathological perspective, biopsy was the most common type of sampling, with 33 cases, or 48.5%. On macroscopic examination, firm consistency predominated, observed in 48 cases, or 70.6%. The whitish color was the most frequently noted aspect, with 19 cases, or 27.9%. These macroscopic elements, however, were variable and needed to be interpreted alongside microscopic criteria.

The histological study showed a predominance of oligodendrogliome (grade II) with 20 cases, or 29.4% of all gliomas, followed by polymorphic glioblastoma (grade IV) with 18 cases, or 26.5%, and it constituted the most frequent high-grade glioma. Astrocytomas accounted for 26 cases, or 38.2% of gliomas. Among astrocytomas, pilocytic astrocytoma (grade I) and diffuse astrocytoma (grade II) (Figure 1) each represented 10 cases, or 38.5% of astrocytomas, followed by Anaplastic Astrocytoma (grade III), 6 cases, or 23%. Oligoastrocytoma accounted for 4 cases, or 5.9% of gliomas, equally divided between oligoastrocytoma (grade II) and Anaplastic Astrocytoma oligoastrocytoma (grade III). All glioblastomas were polymorphic glioblastomas (grade IV) (Figure 2).

Regarding the histoprognostic grade, low-grade gliomas, corresponding to grades I and II, accounted for 42 cases, or 61.7%. High-grade gliomas, corresponding to grades III and IV, represented 26 cases, or 38.3%. The number of cases per grade was 10 for grade I, 32 for grade II, 8 for grade III, and 18 for grade IV (Table 1).

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Table 1: Distribution of gliomas according to histoprognostic grade.

WHO Grade	Number (n=68)	Percentage (%)
I	**10**	**14.7**
II	**32**	**47.0**
III	**8**	**11.8**
IV	**18**	**26.5**

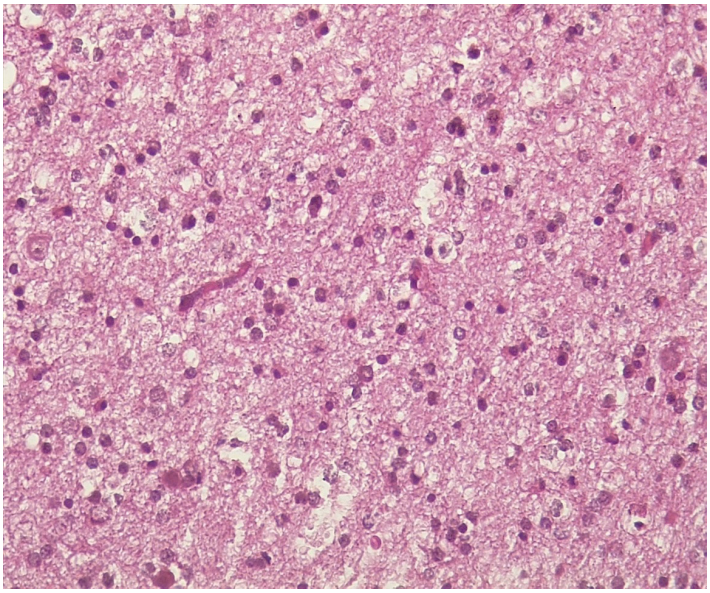

Figure 1: Brain Tumor-resection : Diffuse astrocytoma.
Hematein – Eosin Stain. Magnification X 400
Source : Department of Pathology and Cytology, Hospital Center of Soavinandriana, Antananarivo Madagascar.

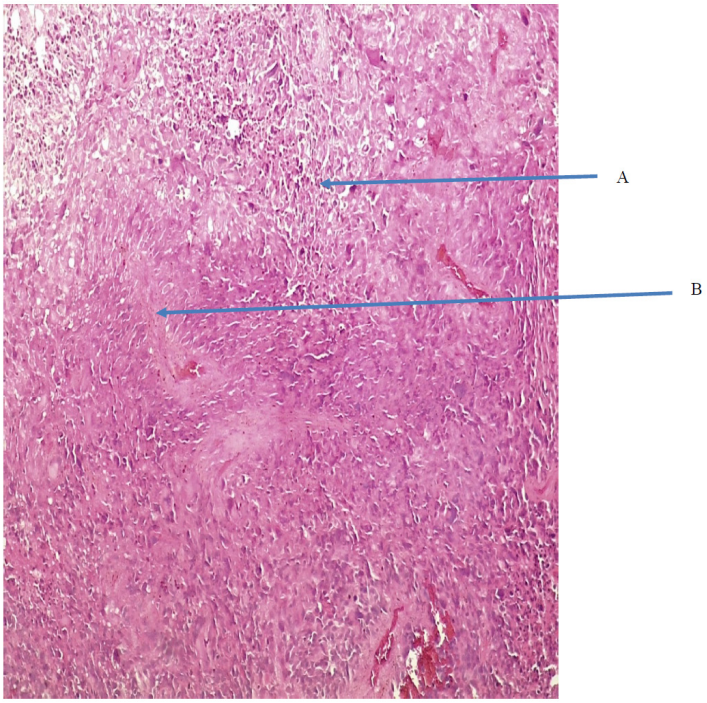

Figure 2 : Brain tumor-Resection : Glioblastoma with tumor proliferation (A) and necrosis (B).

Hematein – Eosine Stain ; Magnification X 100.
Source : Department of Pathology and Cytology, Hospital Center of Soavinandriana, Antananarivo Madagascar.

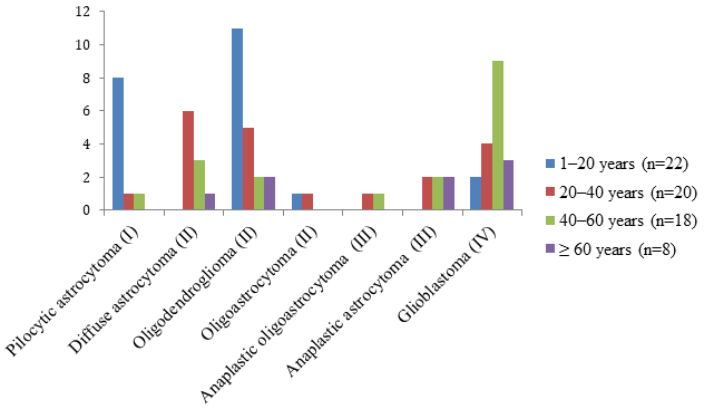

Figure 3: Association between age and histological type.

Discussion

The frequency of gliomas observed in this series, 26.9% of primary brain tumors, is lower than some proportions reported in industrialized countries. In the United States, data from the CBTRUS "(Central Brain Tumor Registry of the United States)" registries and other series indicate that gliomas hold a significant place among central nervous system tumors [6,15]: in the CBTRUS 2011–2015 report, gliomas represented about 26% of all primary brain and central nervous system tumors, and glioblastomas about 14.7% of all primary tumors and 56.6% of all gliomas. In France, studies have reported higher proportions among primary tumors of the central nervous system with 43,929 histologically confirmed cases, of which 42.4% were gliomas [16], compared to 26.9% in the present series. In contrast, the results of the present study are close to some Malagasy data, notably the series by Tongavelona and Bemmo, which reported comparable or lower proportions [14,15]; in Tongavelona's series covering 117 cases, the explicitly reported glial tumors represented about 22.2% of the cases. These discrepancies can be explained by the type of source used. Population registries capture a larger number of cases, whereas hospital or anatomopathological series depend on access to neurosurgery, the performance of a sample, and its transmission to the laboratory.

The average age of 33.67 years appears relatively young compared to European, North American, or North African series, where the average age is often higher. In the French census published by Zouaoui et al. in 2012, the reported average age was 52.3 years and the median age was 56 years, representing a difference of approximately 18.6 years compared to our average [16]. In the Moroccan series by Hamza in Agadir, the average age was 47.6 years, with 47% of patients over 60 years old, whereas subjects aged 60 or over accounted for only 8 cases out of 68 or 11.8%, in this study [17,18]. This particularity could be related to the demographic structure of Madagascar, characterized by a generally young population. However, this result aligns with

certain local or African series in which gliomas frequently affect children, adolescents, and young adults [15,19]; In the Moroccan pediatric series by Hazmiri, the average age was 8.28 years and astrocytomas accounted for 29.41% of childhood brain tumors.

Male predominance, with a sex ratio of 1.4 is consistent with data in the literature, which generally report a higher frequency of glioma in men. This trend has been found in several studies conducted in Morocco, Algeria, China, and France, with sex ratios often ranging around 1.5 to 1.8 depending on the series; for comparison, the Moroccan series by Hamza in Agadir reported 64% men and 36% women, which corresponds to a sex ratio close to 1.8 [4,17,20-24]. Multiple explanations have been proposed. Hormonal factors could be involved, particularly through the potential influence of sex hormones on certain mechanisms of tumor proliferation or progression. Genetic, epigenetic, and immunological differences between men and women have also been suggested [25-28]. In the present study, the male predominance is particularly marked for glioblastoma, with a sex ratio of 3.5, which reinforces the hypothesis of a gender effect on the most aggressive forms.

Intracranial hypertension was the most frequent clinical finding, observed in nearly two-thirds of cases, that is, 44 patients out of 68, or 64.7%. This result is important because it suggests that many patients are diagnosed at a symptomatic stage, when the tumor volume or peritumoral edema causes an increased intracranial pressure. This proportion is close to that reported in the Moroccan series from Agadir, where the signs of intracranial hypertension affected 68% of patients, and to some earlier Malagasy data where headaches and vomiting were found in 69.05% of cases according to Bemmo A. [15,17]. It is, however, higher than the bicentric series by Tongavelona in Antananarivo, in which ICH represented 18.8% of the revealing signs [14]. In countries where access to imaging is earlier, epileptic seizures or neurocognitive disorders may be more frequently reported as the initial presentation, particularly for low-grade gliomas [29,30]. In resource-limited settings, diagnostic delay, self-medication, geographical distance, the cost of examinations, and the lack of specialized pathways may contribute to the predominance of more advanced signs such as increased intracranial pressure.

The frontal location was the most frequent in this series, with 12 cases out of 68, or 17.6%. This predominance is reported in several studies, including some Malagasy and North American data [14,31,32]. In the Malagasy series by Tongavelona, the supratentorial region represented 23.93% of the locations, including 11 frontal cases, or 9.40% of all central nervous system tumors [14]. In this study, the frontal location is almost twice as high as that observed in this Malagasy series, which could be explained by the fact that this study concerned only gliomas. The frontal lobe represents a large brain region, which can mechanically increase the likelihood of observing tumors there. Clinically, frontal lesions can lead to varied, sometimes insidious manifestations, such as changes in behavior, cognitive disorders, or motor deficits. Their recognition may be delayed, especially when the initial signs are subtle. The diversity of locations observed in the study, however, reminds us that glioma can affect different regions of the brain, with prognostic and therapeutic implications depending on the proximity to functional areas.

The frequent use of brain CT scans as an imaging examination, performed in 97.1% of cases, that is, with 66 patients out of 68, reflects an important reality of the Malagasy context. MRI was requested in only 2 cases, or 2.9%, which contrasts with the modality usually recommended for the optimal evaluation of gliomas. In industrialized countries, MRI is generally considered the reference examination for the assessment of gliomas, as it allows better characterization of tumor volume, infiltration, edema, necrosis, anatomical relationships, and surgical planning [33,34]. However, the CT scan remains more available, faster, and often less expensive. Its predominant use in this study should therefore be interpreted not as an ideal diagnostic choice, but as a marker of accessibility constraints. This situation can, however, have an effect on preoperative accuracy, the assessment of tumor extent, and the neurosurgical strategy.

The biopsy represented the most frequent type of sampling, with 33 cases out of 68, or 48.5%. Partial and total resections combined therefore accounted for 35 cases, or 51.5%. This result could be explained by several factors: deep or functionally critical tumor location, clinical condition of the patient, minimal diagnostic objective, limitations of the neurosurgical facility, or difficulty in performing a complete resection without major neurological risk. In other series, particularly in centers with wider access to functional surgery, neuronavigation, or intraoperative MRI, total or subtotal resection can be more frequent [31,35]. In a French series, resections accounted for 78% of cases, versus 22% for biopsies [16], which contrasts with our biopsy proportion of 48.5%. A biopsy remains essential, however, when a wide excision is not indicated or feasible, as it allows obtaining the histological diagnosis necessary for therapeutic guidance.

Histologically, oligodendroglioma was the most frequent type in this series, with 20 cases out of 68, or 29.4%. This result differs from many international studies in which glioblastoma is often the dominant histological type, particularly in adults [6,36]. In the CBTRUS 2011–2015 report, glioblastoma accounted for about 14.7% of all primary brain and central nervous system tumors and 56.6% of all gliomas [6], whereas it accounted for 18 cases out of 68, or 26.5%, in this series. Several explanations can be discussed. The first is related to the relatively young age of the studied population, low-grade glioma being more often observed in young subjects. The second relates to the retrospective and anatomopathological nature of the study, which includes only cases that underwent sampling and histological diagnosis. The third concerns the absence of molecular biology: some tumors morphologically classified as oligodendroglioma could be reclassified differently according to the 2016 or 2021 WHO criteria if the IDH status and the search for 1p/19q codeletion were available [9-11].

Glioblastoma accounted for 26.5% of gliomas and was the most common high-grade glioma. In the literature, glioblastoma is often associated with rapid progression, strong parenchymal infiltration, significant angiogenesis, and necrosis, factors that explain its poor prognosis [10,37]. Comparatively, the 26.5% proportion observed in this series is lower than that reported in CBTRUS for the share of glioblastoma among gliomas, estimated at about 56.6%, but it is close to that observed in some African or Maghreb hospital series, such as Hamza's study in Agadir, where glioblastoma accounted for 27.5% of histological diagnoses [6,17].

The male predominance observed for this entity in the present series is also consistent with several recent studies on sex differences in glioblastoma [25,26]. However, it is particularly pronounced here, since 14 of the 18 glioblastomas, or 77.8%, involved men. The peak frequency between 40 and 60 years concerned 9 cases out of 18, or 50% of glioblastomas, and 3 other cases, or 16.7%, were observed after 60 years. This younger peak than that reported in Western registries could be explained by the local demographic structure and by the recruitment biases inherent to hospital series.

The overall predominance of low-grade glioma, observed in 61.7% of cases, or 42 cases out of 68, contrasts with certain European or Asian series where high-grade glioma is predominant [36,38,39]. However, it aligns with some African or hospital-based studies in which low grades are strongly represented [40,41].

In this study, low-grade glioma was mainly observed in subjects under 20 years old, while high-grade glioma predominated between 40 and 60 years of age. This association between age and grade was statistically significant. Biologically, it can be explained by the progressive accumulation of genetic alterations, changes in the tumor microenvironment, and age-related immune changes that favor the emergence of more aggressive tumors [42,43].

The statistical analysis showed three important associations. The first concerns the link between age and histological type, with a concentration of pilocytic astrocytomas and oligodendrogliomas (grade II) in young subjects, and an increase in glioblastoma in older subjects. The association was statistically significant with $p = 0.0005$, which means that the distribution of histological types varied markedly according to age groups. The second concerns gender and histological type, marked by the male predominance of glioblastoma; this association was also significant with $p = 0.012$. The third concerns age and grade, confirming the frequency of low grades in young individuals and high grades in older age groups, with a significant association at $p = 0.0007$. These associations support the relevance of an integrated interpretation of gliomas, taking into account both demographic parameters, morphology, and, ideally, molecular markers.

One of the major limitations of this series is the absence of immunohistochemistry and molecular biology at both study sites. However, current classifications require an integrated reading of gliomas, notably through the analysis of IDH status, the presence of 1p/19q co-deletion, ATRX loss, p53 expression, MGMT promoter methylation in certain contexts, and other relevant alterations [9-11,13]. This limitation can lead to an approximate classification of certain entities, particularly diffuse gliomas. It can also explain the persistence of old categories such as oligoastrocytoma, an entity that has largely disappeared from current classifications in favor of molecular reclassification. The gradual implementation of a minimal immunohistochemical panel and, when possible, targeted molecular tests would constitute a major advance for neuropathological diagnosis in Madagascar.

Conclusion

This retrospective bicentric study conducted in two Pathology laboratories in Antananarivo described the epidemiological and histopathological aspects of 68 cases of gliomas diagnosed between 2013 and 2022. Gliomas accounted for 26.9% of primary brain tumors. The patients were relatively young, with an average age of 33.67 years, and a male predominance was observed. The most frequent clinical information was intracranial hypertension, probably reflecting a diagnosis often made at a symptomatic stage. Brain CT scan was the predominant imaging examination, reflecting the constraints of access to MRI.

Histologically, the series was marked by a high proportion of low-grade gliomas, notably oligodendrogliomas and low-grade astrocytomas. Nevertheless, the pleomorphic glioblastoma constituted the most frequent high-grade glioma, with a male predominance. The statistical associations observed between age and histological type, between gender and histological type, as well as between age and grade confirm the importance of demographic factors in the expression of gliomas.

The results highlight the need to improve neuropathological diagnosis in Madagascar. Strengthening the technical platform, particularly progressive access to immunohistochemistry and molecular biology, would allow diagnoses to be adapted to current WHO classifications and improve therapeutic management.

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