

Research Article

Brain tumours in the Western Cape Province of South Africa: A plea for a dedicated brain tumour registry in Africa

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ABSTRACT

Background: Epidemiological data on brain tumours provides valuable insight into risk factors, treatment modalities and prognoses of these tumours. Despite abundant epidemiological data from brain tumour registries in high-income countries, a critical data gap persists in low- and middle-income countries.

Aim: The aim of this study was to report on the epidemiology of brain tumours in South Africa's Western Cape province.

Methods: This retrospective study collected data from the National Health Laboratory Services database housed in the public healthcare sector in the Western Cape Province of South Africa. All pathology reports over 2 years (January 2018 to December 2019) that included the term "brain" or equivalent terms were analyzed to compile the epidemiological dataset.

Results: The dataset yielded 505 patients with brain tumours, with a mean age at diagnosis of 44 years (range: 0–82 years). A noteworthy subset (16%) of primary tumours occurred in individuals under 20 years of age. The top three primary tumour diagnoses in the study were gliomas, glioneuronal and neuronal tumours, meningiomas and pituitary tumours. Secondary brain tumours (18%) constituted a significant proportion of brain tumours, with lung and breast being the most common primary sites. Comparison with registries and audits from both high- and low-income countries revealed South Africa's unique landscape; ependymal tumours exhibited a substantial proportion, while nerve sheath tumours displayed a reduced proportion.

Conclusion: This study offers a unique perspective on brain tumour epidemiology in South Africa's Western Cape Province. It reports on unique trends and emphasizes the feasibility and necessity of establishing a dedicated brain tumour registry.

Key words: Brain tumours, Western Cape, brain tumour registry

INTRODUCTION

Worldwide, cancer statistics document that intracranial neoplasms encompass approximately 1.3% of all newly diagnosed cancers.⁽¹⁾ In many countries, brain or central nervous system (CNS) tumours are reported as part of a national cancer registry. This is also the case in South Africa, where the National Cancer Registry (NCR) is part of the National Health Laboratory Services (NHLS) conducting a pathology-based cancer surveillance. Since 2011, cancer is a reportable disease in South Africa. The most recent statistics of the NCR show that brain/CNS tumours make up 0.57 and 0.60% of all reported cancers for females and males respectively.⁽²⁾ Currently, the WHO recognizes more than 30 different neoplasms of the

CNS. As knowledge expands regarding risk factors, treatment modalities and prognosis, it becomes increasingly important to document the different types of intracranial neoplasms and their epidemiology in each region of the world.⁽³⁾ In 1992, the Central Brain Tumor Registry of the United States (CBTRUS) was established with the sole purpose of reporting on the epidemiology of primary brain tumours in the United States. It is currently the largest and most comprehensive brain tumour database worldwide and has had an enormous impact on understanding brain tumours.⁽⁴⁾ Countries like Canada followed suit, establishing their brain tumour registry in 2019.⁽⁵⁾ A recent publication underlined the importance of a brain tumour registry in Australia in 2022.⁽⁶⁾ Similarly, a plea

for establishing a central African registry of brain tumours was recently made.⁽⁷⁾ In South Africa, significant efforts have already been made to create a paediatric tumour database, and establishing a national brain tumour registry appears feasible.^(8,9) The current study was initiated to study the epidemiology of brain tumours in the Western Cape Province of South Africa but importantly to also motivate the creation of a national central brain registry in South Africa.

METHODS

This was a retrospective study that collected data from the NHLS database which is housed in the public hospital sector in the Western Cape Province of South Africa. We reviewed all pathology reports that included the term “brain” or equivalent terms such as cerebrum, cerebellum, brainstem, thalamus, striatum, insula, cortex, dura, arachnoid and meninges from 1 January 2018 to 31 December 2019. The lead author read all the reports and the data was captured onto an excel spreadsheet. All the pathology reports were categorized into neoplastic/ infective/ other. The demographic data included age and sex at diagnosis, as well as the HIV status and CD4 counts where available.

For metastatic brain disease, pathology reports of biopsies other than brain tissues were also included if they represented a primary tumour that had evidence of secondary spread to the brain. For instance, a biopsy of a primary lung cancer with brain lesions on Computed Tomography (CT) scan mentioned in the history was entered as a secondary brain lesion with lung primary. Those patients who had the same pathology biopsied more than once were only included as a single entry into the data set. Post-mortem samples were not included as none of the post-mortems during the study period represented patients with brain tumours.

Simple descriptive statistical formulas such as ratios, means and medians were used to describe the data. Occasionally inferential statistical formulas such as T-tests and Z-tests were used to compare means to determine whether a statistically significant difference existed between them.

The University of Cape Town Health Research Ethics Committee and the NHLS both approved the study.

RESULTS

The term ‘brain’ or equivalent terms were found in 589 pathology reports. Of these, 505 biopsy samples represented neoplasms, 30 of which had an infective aetiology and 54 were due to other conditions such as haematomas, vascular malformations, stroke, focal cortical dysplasia, cysts, or normal tissue.

Of the patients with neoplasms, the age at presentation ranged from neonates to 82 years with a mean of 44 years. 80 children and adolescent patients (0-19 years of age) with brain tumours were identified, representing 16% of

all patients with primary brain tumours. Overall, brain tumours were more common in females than in males; 54% (274) occurred in females and 46% (231) of neoplasms occurred in males. (Figure 1)

Gliomas, glioneuronal and neuronal tumours were the most common neoplasms (30%), followed by meningiomas (26%), metastases (18%) and sellar region tumours (12%). In the paediatric group, the most common neoplasms were gliomas, glioneuronal and neuronal tumours (51%), followed by choroid plexus (17%) and embryonal tumours (13%). (Figure 2.)

In the paediatric group, the largest proportion of tumours 43% (n = 35) occurred between the ages of 0 and 6 years, 35% (n = 28) were seen between 7 and 13 years and 21% (n = 17) between 14 and 19 years. The two most common World Health Organization (WHO) Grade IV tumours in the paediatric group were medulloblastoma (8%) and glioblastoma (8%). Medulloblastoma was more common in younger children (mean age of 8) while glioblastoma was more common in older children (mean age of 11.5) (Figure 3).

Of the glioblastomas, the majority (60%) were isocitrate dehydrogenase (IDH) wildtype with only 10% being IDH mutant. The remaining did not have IDH testing done (18%) or were variants such as gliosarcoma (6%), giant cell (3%) or epithelioid (3%) tumours.

Histologically proven primary CNS lymphoma occurred in three patients (0.81%); the mean age at diagnosis was 40 years and all were male and HIV positive (average CD4 count at diagnosis was 137 cells/ μ L with a range 50–256 cells/ μ L).

Overall, meningiomas were the second most common primary brain tumour, representing 32% of all primary brain tumours. The age range at diagnosis was 11 to 79 years of age, with a mean age of 49 years. Meningiomas were twice as common in females compared to males. Low grade (WHO I) meningiomas predominated, representing 84% of meningiomas, with WHO grade II and III representing 14% and 2% respectively. Notably, females were 5 times more likely than males to have WHO grade II meningiomas. Of the WHO grade I meningiomas, the meningothelial histological subtype was the most common (51%), followed by microcystic (10%) and transitional (8%) (Figure 4a & 4b).

Secondary brain tumours were found in 18% (94) of the study population and were more common in males than in females: 53 vs 41 respectively. Secondary neoplasms occurred exclusively in patients aged 30 years or older with the mean age at presentation of 57 years. Mean age of diagnosis of secondary brain neoplasms was comparable between males and females (t-test = 0.22, p = 0.83).

Of the secondary brain tumours, the most common primary sites were the lungs (57%), breasts (11%) and skin (5%). Other primary sites included liver, gastro-intestinal tract, multiple myeloma, prostate, salivary gland and contiguous spread of cholesteatomas, nasopharyngeal carcinomas,

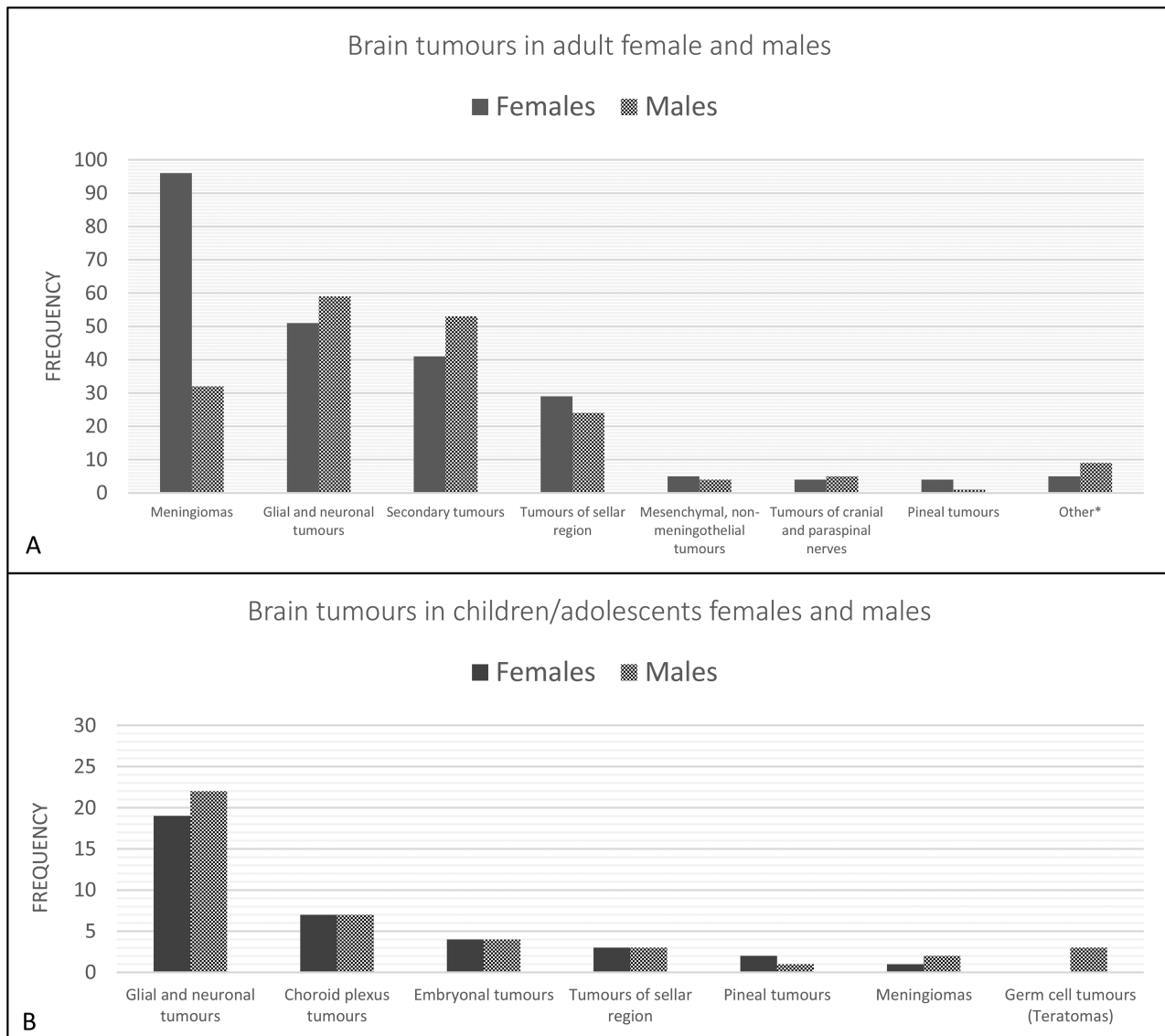


Figure 1: Comparison of tumour types females/males

A: Tumour types in adult females/males; B: Tumour types in children and adolescents, females/males

Other*in A: Represents rarer tumour subtypes such as choroid plexus tumours, embryonal tumours, germ cell tumours and haematolymphoid tumours.

and cancers of the oral cavity. There were also many lesions biopsied that were likely of secondary origin but with an unknown primary (11%) at the time of biopsy. (Figure 4c)

DISCUSSION

Brain tumours are relatively common; however, scant data describes the epidemiology of brain tumours in Sub-Saharan Africa.(10)

In numerous studies from high-income countries (HIC) such as Australia, Canada, United Kingdom (UK) and the United States (US), brain tumours are reported to occur predominantly in older individuals, with a mean age at

diagnosis of 59–61 years.(5,11–13) In the current study, the mean age at diagnosis was much younger at 44 years. This younger presentation has also been reported in other studies from low to middle-income countries (LMIC) such as Ghana, Zimbabwe and Nigeria, where the mean age at diagnosis varied from 32 to 50 years.(14–16) A single-centre prospective study performed in South Africa over a year mirrored the results of the current study, reporting intracranial neoplasms at a mean age of 43 years (range 2–73).(17) Different genetic, socioeconomic, and environmental factors have been cited as possible causes and similar factors may be responsible for the mean age disparity seen between HIC and LMIC.(18) In addition, LMIC tends to have younger

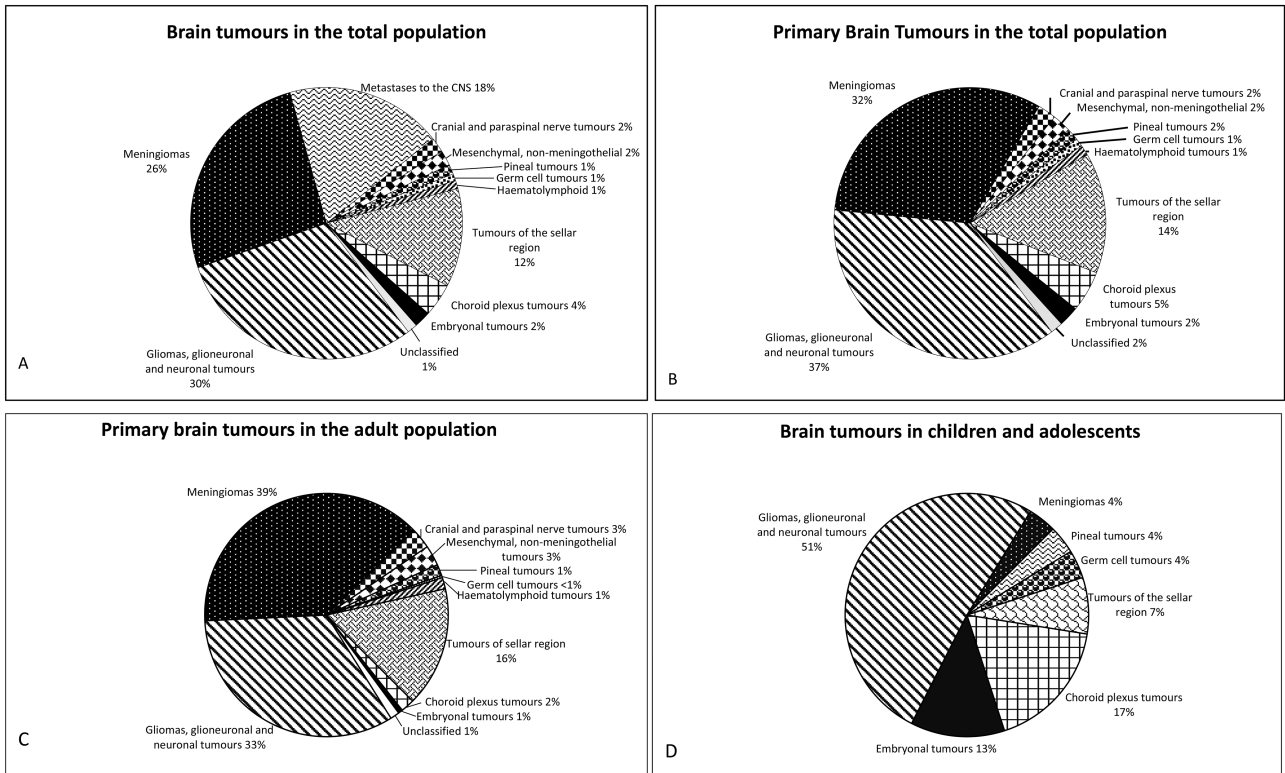


Figure 2: A: Tumour proportions in all patients; B: Primary brain tumours in all patients; C: Primary brain tumour proportions in all adults; D: Tumour proportions in children and adolescents

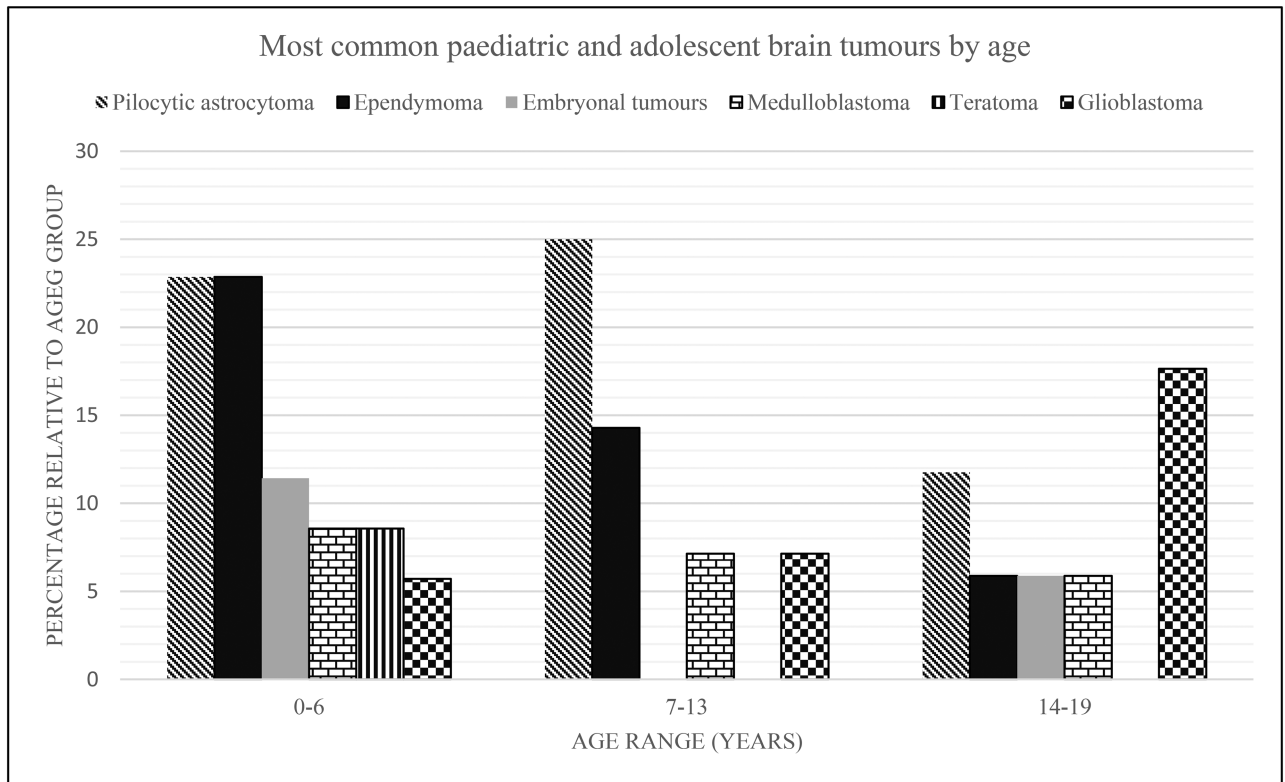


Figure 3: Tumour frequency (6 most common types) in the paediatric and adolescent group

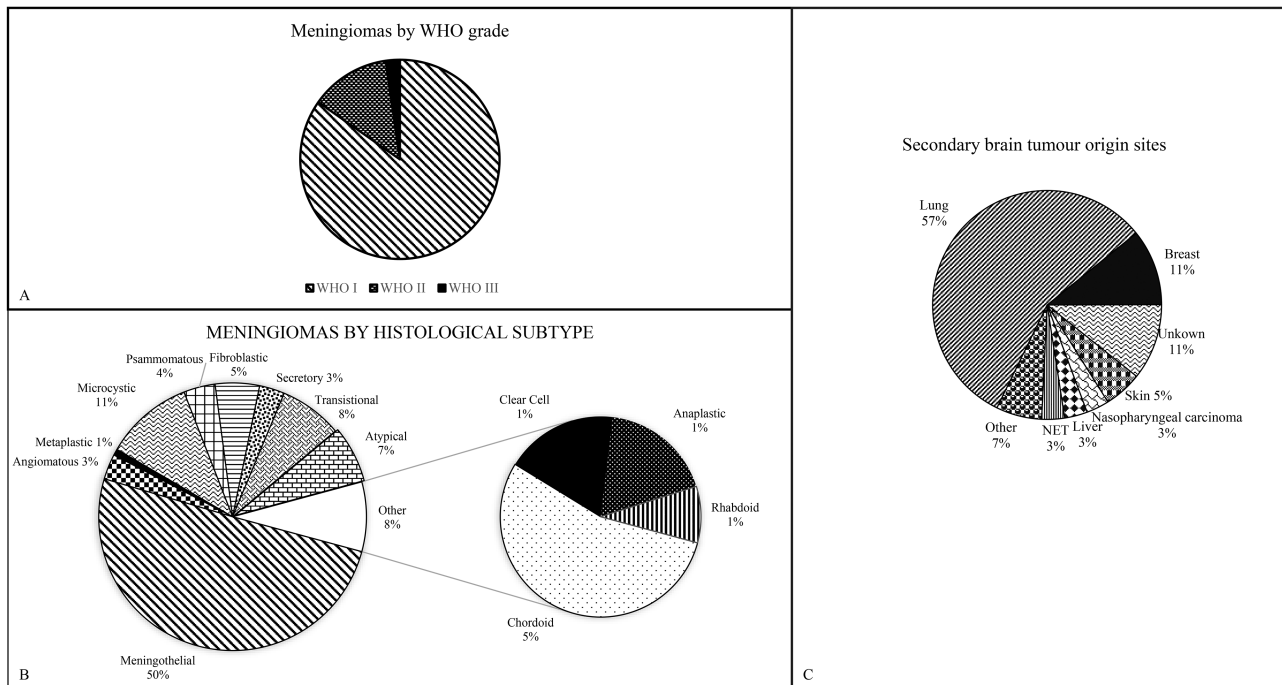


Figure 4: Meningiomas by WHO grading and histological subtype and secondary tumours by site of origin
Pie charts representing meningiomas by WHO grade (4a) and by histological subtype (4b); secondary tumours by site of origin (4c).

NET: Neuroendocrine tumour; *: Other includes cholesteatoma, multiple myeloma, cancers of the oral cavity, prostate cancer, gastro-intestinal malignancies, salivary gland tumours

populations with lower mean life expectancies, which may skew the average age towards the younger group.

Another difference between LMIC and HIC with regard to brain tumours, is the tumour proportions in different age groups. It has been shown that the proportion of brain tumours in children is larger in LMIC compared to HIC.(5,11,13) In the Western Cape, we found that 19.5% of primary brain tumours occurred in the paediatric/adolescent population, which we defined in accordance with CBTRUS as 0 – 19 years old. In contrast to this, the CBTRUS and the UK report only 5.7% and 5.3% respectively of all brain tumours to occur in their paediatric/adolescent populations.(11,13) In our study, 16% of brain tumours occurred in children between 0–14 years, which is comparable to other studies from Africa. A 2021 study from Cameroon found that 12% of tumours occurred in those aged 0–14 years old, while a study from Nigeria showed an even higher proportion (35.7%) of tumours to occur in children.(16,19) This discrepancy may be related to the relatively higher proportion of younger people in LMIC compared to HIC.

Similar to reports by the CBTRUS, the Brain Tumour Registry of Canada (BTRC) and Cancer Research UK, our study found that primary tumours occur more commonly (54%) in females.(5,11,13) However, a review by Mbi Feh

et al. on primary brain tumours in Africa from 1960 to 2017 reported a male predominance, with 54% of brain tumours occurring in male patients.(7)

Our study's most common primary tumours were gliomas, glioneuronal and neuronal tumours, meningiomas and tumours of the sellar region. This pattern is universal as reports from HIC (CBTRUS, BTRC and the Australians tumour registry) along with studies from LMIC (Ghana, Cameroon and South Africa) report the same top three primary brain tumour histological diagnoses.(5,11,12,14,17,19)

Some interesting differences were seen with the rarer tumour subtypes. Notably, choroid plexus tumours in the Western Cape (5% of primary tumours) made up a more significant proportion of the brain tumours as compared to data from HICs. The proportion of choroid plexus tumours in the US, Australia and Canada is 1.6%, 0.2% and 2.4% respectively, while ependymomas comprise 0.5%, 1% and 1.6% of primary brain tumours in Nigeria, Ghana and Cameroon respectively.(5,11–14,16,19) In contrast to this, nerve sheath tumours such as Schwannomas represent 8.3% and 11% of primary brain tumours in the US and Canada respectively – this is much higher than the proportions found in the current study and other studies from Africa. In our and Ibebuiké's study from South Africa, only 2%

of tumours were of nerve sheath origin.(20) The rates are even lower in other Sub-Saharan African countries with a Cameroon study reporting Schwannomas to make up only 1% of primary tumours, while none out of 178 patients in a neurosurgical centre in Nigeria reported a nerve sheath tumour.(16,19) The heterogeneous distribution of certain brain tumours by region warrants further study and the differences amongst various regions may provide valuable insight into the underlying determinants of disease.

The proportion of brain tumours attributed to primary CNS lymphoma is almost certainly higher than the 0.81% reported in the current study. Lv et al reports that approximately 4% of all brain tumours in the US are due to primary CNS lymphoma.(21) The proportion of CNS lymphoma is probably higher in Southern Africa due to the strong association of CNS lymphoma with HIV. In the current study, the low rate may be related to the fact that the diagnosis may have been made on imaging and CD4 counts alone. These patients are often not referred or are not candidates for biopsy and thus would be missed in a retrospective study design such as ours.

Secondary brain tumours prove difficult to study and their proportion is likely higher than the 18% found in our study. This study only included patients who had a biopsy of the secondary brain tumour or of the primary tumour combined with imaging evidence of brain metastasis mentioned in the report. Thus, patients whose diagnosis was based on clinical and/or imaging findings alone or whose physicians who had sent the biopsy of the primary tumour failed to mention the presence of brain lesions on imaging, were not included. Studies from other African countries (Ghana, Cameroon and Nigeria) report rates of metastases between 8% and 27%.(14,16,19) These studies did not include non-brain tissue biopsy samples of the primary cancer with our study being unique as it is the only study from Sub-Saharan Africa to include such samples.

In the international literature, an older Finnish study with a similar study design as ours, reported that brain metastases were found in approximately 18% of intracranial neoplasms, a result identical to our findings.(22) A review by Fox et al acknowledges the challenges of estimating the incidence of secondary brain tumours and proposes that secondary brain tumours are almost certainly more common than primary brain tumours.(23) Another recent study estimates that secondary brain tumours are approximately three times as common as primary brain tumours by extrapolation of the incidence of brain metastasis from the number of primary cancers and their risk of developing metastasis. (24) Internationally, lung cancer accounts for 30–60% of brain metastases, which correlates with the 57% found in this study. Similarly, breast cancer accounts for 5–30% of brain metastases in the literature, with our estimate of 11% falling within this range. The same correlation can be seen with most other cancers.(23)

As exemplified above, the utility of dedicated tumour registries is evident and explains why numerous HICs have

now established their own dedicated registries. Describing the epidemiology of a disease aids in targeting research and provides valuable information to policy makers when deciding how to dedicate funding. Having a dedicated registry to accurately describe the patterns, incidence, and prevalence of brain tumours in LMICs such as South Africa may shed more light on the cause of age disparities between different regions of the world. Although some may contend that low- and middle-income countries such as South Africa lack the means to establish such registries, this study conducted at a provincial level has demonstrated that baseline data is available and accessible. Notably, all pathological samples from South Africa's public healthcare sector are processed by the National Health Laboratory Service, with results being stored electronically in a comprehensive database containing most of the relevant biographical patient information along with their pathological diagnoses.

CONCLUSION

This study has underscored important distinctions between brain tumour profiles in South Africa and those in other low- to middle-income and high-income countries. This retrospective epidemiological investigation into brain tumours in the Western Cape of South Africa has also demonstrated the feasibility of creating a national registry of brain tumours in South Africa. As private pathological services also maintain electronic records and share epidemiological data with the public sector, a comprehensive brain tumour registry in South Africa is highly possible.

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