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TABLE OF CONTENTS

GENERAL INFORMATION	1C
INFORMATION FOR AUTHORS	1F
EDITORIAL NOTES	107
ORIGINAL ARTICLES	
A Five-Year Review of Laparoscopic Gynaecological Surgeries in a Private-Owned Teaching Hospital, in Nigeria	111
J. O. Imaralu, I. F. Ani, C. E. Onuoha, E. O. Grillo, F. A. Oguntade, C. C. Nwankpa	
Adolescent Obesity and its Association with Socio-Demographic Profile, Lifestyle Factors, Dietary and Physical Activity Patterns; Findings from Southwestern Nigeria	119
A. A. Adeomi, M. D. Olodu, R. O. Akande, S. Yaya, A. Adediti, R. Ajibade	
Association between Height and Blood Pressure in Middle Age and Older Adults in Southeast Nigeria	127
I. I. Chukwuonye, O. S. Ogah, U. U. Onyeonoro, E. N. Anyabolu, I. U. Ezeani, A. U. Ukegbu, U. Onwuchekwa, E. C. Obi, K. A. Ohagwu, O. O. Madukwe, I. G. Okpechi	
Central Nervous System Pathology in Children: A Single-Institution Experience in South-South Nigeria	134
M. O. Udoh	
Comparison of the Ivermectin and Lopinavir/Ritonavir Treatment Outcomes among COVID-19 Mild to Moderate Cases in Kaduna State.....	140
A. Oyefabi, S. Musa, H. Kambai, I. Usman, J. Gwamna, J. Sheyin, O. Ige, M. Abdullahi, J. Sunday, H. N. Kera, A. Atiku, H. Dauda, G. C. Umeh, T. Olasinde, A. Abdullahi	
Drugs of Abuse among In-Patients Receiving Treatment for Substance Use Disorders in a Tertiary Health Care Center in South-South Nigeria: An Exploratory Qualitative Study	147
C. J. Okafor, E. A. Essien, B. E. Edet, A. C. Okoro, O. Udofia	
Heavy Malaria Parasitaemia in Young Nigerian Infants: Prevalence, Determinants and Implication for the Health System	154
O. F. Folarin, B. P. Kuti, A. O. Oyelami	
Mortality Pattern in Surgical Wards in Northwestern Nigeria: A Single-Center Study.....	162
K. E. Amaefule, F. S. Ejagwulu, I. L. Dahiru, M. O. Ogirima, A. I. Aniko, J.O Njoku	
Preparedness and Perception on Virtual Learning during the COVID-19 Pandemic amongst Students of the Ekiti State University, Nigeria	170
A. O. Adeoti, A. Fadeyi, K. S. Oluwadiya	
Presentation and Management Outcomes of Goitres at a District Hospital in Abuja, North Central Nigeria: A 15-Year-Review	176
M. E. Aghahowa, H. C. Onyegbutulem, O. S. Basse, S. N. Esomonu, K. N. Ezike, R. M. Nwokorie, A. Ahmadu	
Prevalence, Pattern and Predictors of Elder Abuse in Benin City, Edo State, Nigeria: An Urban and Rural Comparison	183
O. H. Okojie, V. O. Omuemu, J. I. Uhunwangho	
The Efficacy of Local Infiltration Analgesia in the Control of Post-Operative Pain after Total Joint Replacement Surgeries	193
D. E. Ubiomo, U. E. Anyaehie, G. O. Eyichukwu, C. B. Eze	
The Prognostic Significance of the Size of Primary Malignant Breast Tumour in Ghanaian Women: A Retrospective Histopathological Review (2001–2014) in the Department of Pathology, Korle-Bu Teaching Hospital (KBTH)	198
E. M. Der	
CASE REPORTS	
High Intensity Focused Ultrasound Treatment for Uterine Fibroid in a Nigerian Hospital: A Case Report and Review of Literature	204
A. B. Ajayi, V. D. Ajayi, A. Njoku, O. Oyetunji, B. M. Afolabi	
Pulmonary Embolism: The Battle to Save Life in a Resource Poor Setting	208
G. C. Mbata, C. O. U. Eke, L. E. Okoli	
INDEX TO VOLUME 39, NO. 2, 2022	
Author Index	212
Subject Index	213



Central Nervous System Pathology in Children: A Single-Institution Experience in South-South Nigeria

*Pathologie du Système Nerveux Central chez l'Enfant :
L'expérience d'une Seule Institution dans le Sud-Sud du Nigeria*

M. O. Udoh

ABSTRACT

BACKGROUND: Neuropathology is fundamental to neurology, neurosurgery, and neuroscience practice in general. In parts of Nigeria and other sub-Saharan African countries, Neuropathology is just emerging, and more so Paediatric Neuropathology. Paediatric Neuropathology encompasses diseases of brain, spinal cord, nerves and muscle, affecting infants, children and adolescents, many of which are surgically managed or biopsied for diagnosis.

AIM: To determine the pattern of neurosurgical lesions in children diagnosed in Benin-City, Nigeria.

METHODS: a retrospective database study of biopsies from paediatric patients with neurosurgical lesions histologically evaluated at the Department of Pathology, University of Benin Teaching Hospital, Benin-City, Nigeria, between January 2007 and December 2020 was done. Demographic and clinical data were extracted from Departmental Records; histopathological diagnoses confirmed; and data analyzed using SPSS 20.0.

RESULTS: A total of 178 biopsies reviewed. Ages ranged between 2 days and 16 years. Male: female ratio was 1.02:1. There were 87 spinal; 53 intracranial; 32 skull; and 9 scalp lesions. Commonest were Neural tube defects – 56.7% (mostly myelomeningoceles); Intracranial neoplasms – 20.22% (mostly pilocytic astrocytoma and embryonal tumors); Intracranial suppurative lesions -5.06% and dermoid/epidermoid cysts – 5.06%.

CONCLUSION: Most Paediatric neuropathological conditions encountered in our environment can be managed with good outcomes if correctly and promptly diagnosed. There is a need to channel resources into prevention and prenatal diagnoses of NTDs; early diagnosis and management of brain tumors and other intracranial lesions; and better management of otorhinolaryngologic and intracranial infections in children. Neuropathology training and capacity development is also needed. **WAJM 2022; 39(2): 134–139.**

Keywords: Africa, Brain tumor, Nigeria, Neuropathology, Paediatric Pathology.

RÉSUMÉ

CONTEXTE: La neuropathologie est fondamentale pour la neurologie, neurochirurgie et de la pratique des neurosciences en général. Dans certaines régions du Nigeria et d'autres pays d'Afrique subsaharienne, la neuropathologie est tout juste émergente, et plus encore la neuropathologie pédiatrique. La neuropathologie pédiatrique englobe les maladies du cerveau, de la moelle épinière, des nerfs et des muscles. nerfs et des muscles, qui touchent les nourrissons, les enfants et les adolescents. sont traitées chirurgicalement ou biopsiées pour le diagnostic.

OBJECTIF: Déterminer le profil des lésions neurochirurgicales chez des enfants diagnostiqués dans la ville de Bénin, au Nigeria.

MÉTHODES: Une étude rétrospective de la base de données des biopsies de patients pédiatriques présentant des lésions neurochirurgicales évaluées histologiquement au département de pathologie de l'hôpital universitaire de l'Université du Bénin, Benin-City, Nigeria, entre janvier 2007 et décembre 2020. a été réalisée. Les données démographiques et cliniques ont été extraites des dossiers du département ; les diagnostics histopathologiques ont été confirmés ; et Les données ont été analysées à l'aide du logiciel SPSS 20.0.

RÉSULTATS: Un total de 178 biopsies ont été examinées. Les âges variaient entre 2 jours et 16 ans. Le rapport hommes/femmes était de 1,02:1. Il y avait 87 biopsies rachis, 53 intracrâniennes, 32 crâniennes et 9 lésions du cuir chevelu. Les plus fréquentes étaient. Anomalies du tube neural - 56,7 % (principalement des myéломéningocèles). intracrâniens - 20,22 % (principalement astrocytome pilocytique et tumeurs embryonnaires) tumeurs embryonnaires); lésions suppuratives intracrâniennes -5,06% et kystes dermoïdes/ kystes épidermoïdes -5,06 %.

CONCLUSION: La plupart des conditions neuropathologiques pédiatriques rencontrées dans notre environnement peuvent être gérées avec de bons résultats si elles sont correctement et rapidement diagnostiquées. Il est nécessaire de canaliser ressources dans la prévention et le diagnostic prénatal des ATN, le diagnostic et la prise en charge diagnostic et la gestion précoces des tumeurs cérébrales et autres lésions intracrâniennes intracrâniennes; et une meilleure gestion des infections otorhinolaryngologiques et intracrâniennes chez les enfants. intracrâniennes chez l'enfant. La formation en neuropathologie et le sont également nécessaires. **WAJM 2022; 39(2): 134–139.**

Mots-clés: Afrique, Tumeur cérébrale, Nigéria, Neuropathologie, Pédiatrie. Pathologie.

INTRODUCTION

While infectious diseases remain major contributors to childhood morbidity and mortality in Africa, there has been a progressive decline in the burden of disease and death in African children due to infections. This situation, attributable to widespread immunization against childhood killer diseases, has resulted in increased contribution to childhood morbidity and mortality by other conditions.¹ The need for Africa to give as much attention if not more, to paediatric subspecialties, as is given to adult medicine, is evident in the fact that worldwide, Africa is the only major region whose population of young people is projected to still greatly outnumber the elderly population by the year 2050.² There is evidence to suggest that some attention is already being given to aspects of paediatric practice but, there appears to be more focus on some areas than others.^{1,3-9}

Paediatric neuropathology practice is in its early stages in most parts of sub-Saharan Africa.⁹ Many African countries lack dedicated paediatric-oncology units and pathology services, and pathologists are non-existent in some places.⁹ In a survey involving 24 paediatric oncologists from 14 institutions in Nigeria, only two institutions were found to have a dedicated paediatric oncology ward. There was no population-based paediatric oncology tumor registry, no molecular diagnostic capability, nor efficient radiotherapy support service, and most centers struggle with inadequate blood and blood product support. It is evident that paediatric oncology services in Nigeria are still grappling with weak human capital, poorly developed infrastructure, weak regional and national referral systems, and poor support services.⁶ Many pathology laboratories in Nigeria are run by a single pathologist who may not have specialist training in the diagnosis of paediatric conditions. Although outstanding paediatric diagnostic centers with state-of-the-art facilities and highly qualified diagnosticians exist, they are in the minority and are mostly limited to larger centers.⁹

Paediatric neuropathology is even more handicapped than its 'parent

specialties', by lack of adequate infrastructure, material resources and personnel. A search of works done in the field of paediatric neuropathology in Nigeria revealed a number of publications on aspects of neuropathology, mostly paediatric neuro-oncology.^{1,3-9} A 2016 publication by Olasode and Onyia, addressed broadly paediatric neuropathology practice based on experience at a tertiary center in Ile-Ife, South-western Nigeria, giving an overview of neuropathology as seen in paediatric surgical lesions as well as the state of neuropathology service in the region. According to Olasode and Onyia, paediatric neuropathology in particular, has limited access to resources and few opportunities for professional advancement in Nigeria and Africa in general.⁹

This is a retrospective study of paediatric neurosurgical conditions seen and histologically analyzed at University of Benin Teaching Hospital, Edo state, Nigeria over a 14-year period. We describe patterns observed and highlight common paediatric neuropathologic lesions seen in the Nigerian south-south region. The significance of our findings in the light of previous work done in the Nigerian population and the state of neuropathology services in the country and patterns described elsewhere are discussed.

MATERIALS AND METHODS

A retrospective study of all paediatric neurosurgical conditions histologically evaluated and diagnosed at the histopathology department of the University of Benin teaching Hospital, Edo State, Nigeria over a 14-year period (January 2007 and December 2020). Demographic and clinical data on all lesions excised from neurosurgery patients between 1–16 years of age, were retrieved from departmental records. The data retrieved include age, gender, histological diagnosis. All diagnoses were made from haematoxylin and eosin stained, 3–5µm sections, of formalin fixed and paraffin embedded samples of tissue specimen. Additional special histochemical and immunohistochemical stains were employed where needed. All retrieved data was reviewed, and some cases reclassified where necessary.

Tumours were classified using the 2007 WHO Classification of Tumours of the Central Nervous System, and in later years the 2016 classification of CNS tumors; though extent was at times limited by the non-availability of some immunohistochemical stains. All data obtained was entered into the Statistical Programme for Social Sciences, version 20 (SPSS Inc, IL, USA) and analyzed and our observations compared with findings documented in the literature. Confidentiality of the identity of the patients and personal health information was maintained.

RESULTS

A total of 178 biopsies from paediatric neurosurgery patients were submitted for histologic examination during the period under review. The total number of surgical specimens received in the department within the same period was 40,470. Paediatric Neuropathology Surgical specimens therefore represent 0.45% of surgical specimen received. The 178 lesions evaluated were made up of 84 spinal/paraspinal lesions, 53 intracranial lesions, 32 skull lesions and 9 scalp lesions.

The average number of biopsies per year was 12.7. The lowest number of biopsies (2 cases) was seen in 2007, and highest (22 cases) in 2017. There were 90 males and 88 females giving an approximate male-female ratio of 1:1. The age range of patients was between 2 days and 16 years, and mean age was 3.85 ± 0.39 (5.20) years. Half of cases seen (50.56%) were in the first year of life (Figure 1) and majority of these (76.67%) were less than 6 months of age. These were mostly patients with Neural Tube Defects (NTDs).

Neural Tube Defects (NTDs) constitute 56.7% (101) of all lesions in this series. There were 50 males and 51 females, giving an approximate Male-female ratio of 1:1 for all NTDs. Spinal dysraphism were commoner in males, while encephaloceles were commoner in females with male-female ratios of 1.3:1 and 1:2.25 respectively. Greater than 80% of spinal dysraphism, and 77% of encephaloceles presented before their first birthday, majority of these before 6 months of age. The mean ages for spinal

dysraphism and encephalocele were 1year and 1year 7 months respectively.

Spinal dysraphism was the commonest lesion making up 42.13% of all lesions and 89.3% of spine lesions. Of these, myelomeningoceles made up 78.67%, followed by meningoceles (16%). Likewise, encephaloceles (26) made up 14.61% of all lesions and 81.25% of skull lesions, 69.23% of which were occipital encephaloceles (Table 1).

Intracranial lesions (53) made up 29.78% of all lesions seen. Of these, 67.9% (36) were neoplasms, making up 20.22% of all lesions seen. There were 16 males and 20 females. The ages of children with intracranial neoplasms ranged from 15months to 16 years. Mean age was 8.38 ± 5.5 years. Astrocytic tumors in general made up 41.67% of intracranial tumors. Pilocytic astrocytoma was the commonest tumor making up 25% of intracranial neoplasms seen. Next were embryonal tumors (mostly medulloblastoma) making up 16.67% (Table 2). At least 50% of tumors were located in the posterior fossa, 16.7% were sellar/suprasellar, 8.3% were parietal, and 5.6% frontal. In 19.4% of cases, location was uncertain. Low grade lesions (WHO grades I and II) constituted 63.9% of intracranial neoplasms in children while, 36.1% were high grade/malignant lesions.

In combination with spinal/paraspinal tumors, neoplasms constituted 22.47% of all lesions seen. Other intracranial non-neoplastic lesions are as displayed (Table 1). These were predominantly suppurative lesions (abscesses, subdural empyema), haematoma evacuations, and intracranial cysts. The single most common etiology for intracranial suppurative lesions in this review was chronic frontoethmoidal sinusitis. Intracranial cysts seen included two (2) epidermoid cysts and one (1) ependymal cyst, all in the posterior fossa.

Lesions besides NTDs and intracranial lesions, like fibro-osseous lesions of the skull; spinal/ paraspinal tumors; and scalp lesions, predominantly sub-galeal dermoid/epidermoid cysts, are as displayed (Table 1). Anterior fontanelle dermoid/ epidermoid cysts constituted 77.8% (7 of 9) of our scalp lesions. There were five (5) epidermoid and two (2) dermoid cysts seen in four (4) female and

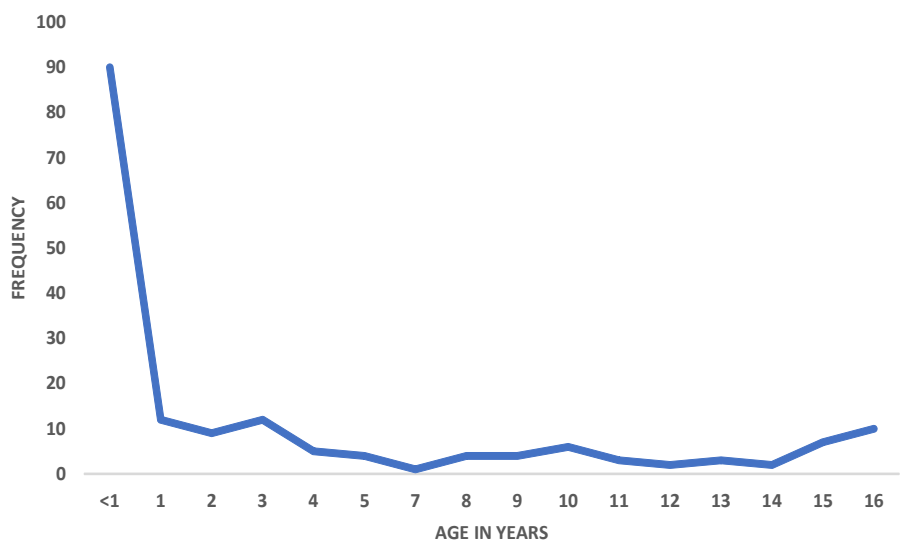


Fig. 1: Age Frequency Chart.

Table 1: Summary of all Histologically Evaluated Paediatric Neurosurgical Lesions

Site	Diagnoses	Frequency (%)
Intracranial lesions	Neoplasms	36 (20.22)
	Acute/chronic suppurative lesions	9 (5.06)
	Hematoma evacuations	4 (2.25)
	Cysts	3 (1.69)
	Post-meningitis meningeal fibrosis	1 (0.56)
Skull lesions	Encephaloceles	26 (14.61)
	• Occipital (18)	
	• Frontal (8)	
	Fibro-osseous lesions	4 (2.25)
	• Fibrous dysplasia (3)	
• Ossifying fibroma (1)		
Scalp	Osteomyelitis (mastoiditis)	2 (1.12)
	Benign neoplasms and epithelial cysts	
	• Lipoma (1)	
	• Seborrhic keratosis (1)	
	• Epidermoid cysts (5)	
Spinal lesions	• Dermoid cysts (2)	9 (5.06)
	Spinal dysraphism	
	• Myelomeningocele (59)	75 (42.13)
	• Meningocele (12)	
	• Lipo-myelomeningocele (1)	
	• Myelocele (3)	
	Laminotomy/Laminectomy specimens	5 (2.81)
Spinal/paraspinal tumors	4 (2.25)	
	• Neurofibroma (2)	
	• Teratoma (2)	
		178 (100)

three (3) male patients. Two (2) intracranial epidermoid cysts seen, were also in females, making a total of 9 dermoid/ epidermoid cysts in this series.

DISCUSSION

Congenital malformations of the central nervous system have been found to be second only to malformations of the gastrointestinal system.¹⁰ Neural

Table 2: Intracranial Neoplasms

Tumor Class	Diagnoses and Who Grades	Frequency (%)
Diffuse astrocytic and oligodendroglial tumors	Diffuse astrocytoma NOS WHO grade II (1)	4 (11.11)
	Glioblastoma NOS WHO grade IV (2)	
	Oligodendroglioma NOS WHO grade II (1)	
Other astrocytic tumors	Pilocytic astrocytoma WHO grade I (9)	11 (30.56)
	Pilomyxoid astrocytoma WHO grade II (1)	
	Anaplastic pleomorphic xanthoastrocytoma WHO grade III (1)	
Ependymal tumors	Ependymoma WHO grade II (2)	4 (11.11)
	Anaplastic ependymoma WHO grade III (2)	
Embryonal tumors	Medulloblastoma WHO grade IV (4)	6 (16.67)
	Primitive neuroectodermal tumor (WHO 2007) grade IV (1)	
Tumors of cranial and paraspinal nerves	Schwannoma	1 (2.78)
Meningiomas	Meningioma WHO grades I	4 (11.11)
Germ cell tumors	Teratoma	2 (5.56)
Tumors of the sellar region	Craniopharyngioma WHO grade I	3 (8.33)
Metastatic tumors	Extradural extension of Intra-orbital embryonal rhabdomyosarcoma	1 (2.78)
		36 (100)

Tube Defects (NTDs) constitute 56.7% of all lesions in this series. Spinal dysraphism were the most common (42.13%) especially myelomeningoceles and meningoceles, followed by encephaloceles (14.61%). In their review of Paediatric Neuropathology cases in Ile-Ife, Olasode and Onyia found NTDs to be very common, myelomeningoceles being the most common.⁹ In Lagos, Bankole, *et al* found that meningo-myelocele accounted for 96% of the cases in their review of one hundred and eight (108) patients with congenital midline swellings of the back, and spina bifida was the commonest indication for neurosurgical clinic referral apart from trauma.¹¹

Anyawu, *et al* in their study of 1456 neonates recorded a birth prevalence of NTDs of 2.75/1000 live births in Northwestern Nigeria.¹² Nnadi, *et al* also found a prevalence of 2.2/1000 live births.¹³ A systematic review and meta-analysis of forty-three studies on NTDs in Africa, by Oumer, *et al*, with a total of 6,086,384 participants found the pooled birth prevalence of NTDs in Africa to be 21.42 per 10,000 births. This is rather high. Nigeria was found to have an even higher pooled birth prevalence of 32.77 per 10,000 births.¹⁴

Amongst patients with NTDs male-female ratio was 1:1, similar to the finding of some authors,¹² although other authors document female preponderance amongst NTDs.¹³ In this study spinal dysraphism was slightly more common in males with male-female ratio of 1.3:1, while encephaloceles were more common in females and with a female-male ratio of 2.25:1.

NTDs include anencephaly which have been found to have varying birth prevalence in different studies.^{12,13,15} No case of anencephaly formed part of this study. Anencephalic babies and those with craniorachischisis tend to die during the perinatal period, whereas less severe NTDs get referred to the neurosurgical team for management.^{13,16} Greater than 80% of spinal dysraphism, and 77% of encephaloceles presented before their first birthday, majority of these before 6 months of age. This is similar to reports by other authors that half of patients present within the first two weeks of life even when not prenatally diagnosed.¹¹

Encephaloceles made up 14.61% of all lesions and 81.25% of skull lesions. Majority (69.23%) of encephaloceles were occipital, the rest frontal. Olasode *et al* also found a greater proportion of

occipital encephaloceles in their study.⁹ Frontal encephaloceles are rare and generally known to have a higher incidence in Asian countries (1/5000 live births) than western countries (1/35,000 to 1/40,000 live births).¹⁷ In Africans, evidence suggest that frontal encephaloceles are more common in East, then West Africa.¹⁸

Children with severe birth defects have a 15-fold increased risk of death during the first year of life, with 9–10% of such children dying during this period.^{12,16} Data from Northwestern Nigeria shows that perinatal mortality for NTDs could be as high as 81.3% despite established prenatal diagnosis in up to 50% of patients.¹³ NTDs like anencephaly and craniorachischisis are invariably lethal perinatally, whereas open spina bifida is compatible with postnatal survival but frequently results in serious handicap.¹⁶ Children with encephaloceles have been successfully managed with acceptable outcomes even in resource-constrained settings.⁹ In a Ugandan study of 110 patients with encephaloceles, surgery-related mortality was 3% and one-year and 5-year survival rates were 87% and 61% respectively.¹⁸

Intracranial lesions made up 29.78% of cases. Of these 67.9% were neoplastic lesions, making up 20.22% of all lesions. In combination with spinal/paraspinal tumors, neoplasms constitute 22.47% of all lesions seen. Previously published data from our center has shown that intracranial tumours in children are less common than congenital anomalies of the neuraxis.³ Childhood brain tumors constitute 5% of all childhood tumors.^{19,20} Astrocytic tumors made up 41.67% of intracranial childhood tumors studied. Pilocytic astrocytoma was the commonest making up 25% of intracranial neoplasms seen. Embryonal tumors (mostly medulloblastoma), meningioma, and craniopharyngioma were the other common histologic types. At least 50% of our tumors were located in the posterior fossa. In a previous study, we found almost equal numbers of supra- and infratentorial tumours in children, majority (54%) being gliomas.³ Publications from other centers in Nigeria have documented findings similar to this. Uche, *et al*, in Ibadan found low-grade

astrocytoma -25 %; and medulloblastoma -25 % as the most common tumors.²¹ Ndubuisi, *et al*, in Enugu found 51.9% supratentorial tumours, and 48.1% infratentorial tumours, their commonest histological types also being glioma-37.0%, medulloblastoma-24.1%, craniopharyngioma-20.4%, and meningioma-3.7%.¹⁹ The most common supratentorial tumours were glioma and craniopharyngioma, and the most common infratentorial tumour was medulloblastoma.¹⁹

While 63.9% of intracranial neoplasms in this series were low grade lesions (WHO grades I and II) for which surgery is usually adequate treatment with low to moderate risk of recurrence, 36.1% of tumors were high grade/malignant lesions. Malignancies in Africa are usually first seen at advanced stages, and fewer than 20% of children have access to curative treatment.²² Globally, the survival rate of children with malignancies has increased dramatically in recent years, in part because of improved diagnostic accuracy.⁹ But in low-middle income countries, the survival rates is still approximately 20%, compared to survival rates greater than 80% for most cancers in the developed world.⁶ Problems with diagnostic testing, including long delays in pathology reporting, limited immunohistochemistry capabilities, and lack of expertise in the histologic diagnosis of paediatric malignancies, are contributing factors to the poor overall survival of children with cancer in Africa.²²

Intracranial abscesses are significant health-care concern, especially in low resource settings like ours. The mortality and morbidity of brain abscesses range from 10% to 25%.²³ Disease outcomes are however changing due to improvements in diagnosis and therapy, antibiotics use, the HIV/AIDS epidemic and other immune deficiencies.²³ The single most common etiology in this review was chronic frontoethmoidal sinusitis. Previous work from our center has shown that the most common predispositions for intracranial abscesses are otolaryngologic and traumatic factors.²⁴ They occur most commonly in the second decade of life,

but the most susceptible single year of life is infancy.²⁴

Though uncommon, intracranial abscesses remain life threatening in children especially in resource-poor settings.²⁵ The mortality and morbidity of brain abscesses range from 10% to 25%.²⁶ In the series by Olorunmoteni, *et al*, case fatality rate was as high as of 33.3%.²⁵ Early presentation and treatment of local infections will improve outcome.

Fibro-osseous lesions of the skull, though only 2.25% of lesions seen, formed a significant 12.5% of skull lesions. There was no fibro-osseous lesion of the skull reported in the study from Ile-Ife by Olosode and Onyia although a case of reparative fibroma of the spine was reported.⁹ Conversely a significantly larger percentage of osteomyelitis of the skull was reported by them (6 of 111) compared to the findings in this study (2 of 178).

Congenital inclusion cysts of the anterior fontanelle, also known as Adeloje-Odeku cysts constituted 77.8% (7 of 9) of our scalp lesions. When first described by two Nigeria Neurosurgeons, Adeloje and Odeku in 1971. It was considered a disease of African children.²⁷ They described 18 cases of a congenital cystic swelling located over the anterior fontanelle in Nigerian patients who were otherwise clinically normal; 17 of which turned out to be dermoid cysts, with female-male ratio of 2:1.²⁷ Other authors across the globe have subsequently reported similar lesions in various races.²⁸⁻³¹ Reports have also shown these cysts could be Dermoid or epidermoid cysts and may be seen in locations other than the anterior fontanelle.³² Calvaria involvement is well recognized; as well as intracranial and intraspinal ones.³³⁻³⁵ We report in this study 5 epidermoids and two dermoid cysts from 4 female and 3 male patients. Two intracranial posterior fossa epidermoid cysts in 2 females, were also encountered, making a total of 9 dermoid/epidermoid cysts in this series. Olosode documented a rather small fraction of 4 subgaleal cysts constituting 16% of scalp lesions amongst childhood cases seen in Ile-Ife.⁹ The prognosis for this condition is good, complete surgical resection usually being curative.^{29,36}

CONCLUSION

Paediatric neuropathological conditions can be managed with good outcomes if correctly and promptly diagnosed. Most of the world's children live in areas such as Africa, with few neuropathologists,⁹ yet many paediatric diseases are individually rare enough to pose a diagnostic challenge to the general pathologist. Paediatric pathology in general, and paediatric neuropathology more specifically, are faced with the challenges of limited access to resources and few opportunities for professional advancement in Africa. This relative non-availability of specialized training makes the provision of a high-quality service difficult.²⁴

There is a need to channel resources into prevention and prenatal diagnosis of NTDs, and early diagnosis and management of brain tumors and other intracranial lesions. Better management of otorhinolaryngologic and intracranial infections in children is advocated, and Neuropathology training and capacity development is crucially needed.

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