Student number: 219098891

UNIVERSITY OF KWAZULU NATAL

Brain Computed Tomography (CT) Findings in Paediatric Patients Who Present with New Onset Unprovoked Afebrile Seizures to the Emergency Department.

BY DR NOLUYOLO MAHLATI

219098891

This manuscript is submitted as a dissertation component in fulfilment for Masters by research for the Department of Radiology, School of Clinical Medicine, Colleges of Health Sciences, University of KwaZulu Natal, South Africa.

Candidate's Signature: [redacted] **Date: 11/10/23**

Supervisor: [redacted] **Date: 15/10/23**

Student number: 219098891

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OVERVIEW

Seizures are a common clinical problem at all ages, including in children. In the USA, it is estimated that 10% of the population will experience at least one attack of seizures in their lifetime. The role of imaging in children presenting with seizures has evolved in the last two decades due to the increasing availability of Magnetic Resonance Imaging (MRI) and a recognition of the importance of reducing the use of CT in children due to radiation risks. CT is also known to have reduced sensitivity for many conditions responsible for childhood seizures such as mesial temporal sclerosis, cortical dysplasias and small neoplasms.

At our institution, CT is still used extensively in the emergency setting for children presenting with seizures. It is important to investigate this practice to ensure the benefits outweigh the risks. American Academy of Radiology guidelines recommend the use of emergent neuroimaging for any child at any age who exhibits a post-ictal deficit (Todd's paresis) that does not resolve quickly or who has not returned to baseline within several hours. A study done by Sadeq and Karim in Kuwait in 2015 demonstrated no usefulness in evaluating paediatric patients who present with first attack of unprovoked afebrile seizures therefore recommending that neuroimaging should not be performed for these patients.

LITERATURE REVIEW

INTRODUCTION

Seizures are an emergency in paediatrics. A seizure in children is a common presentation in the Emergency Department as it is quite distressing to the caregivers(1). The caregiver must get information about the cause, management, and prognosis of the seizure. Almost 10% of children in the United States of America will experience a seizure in their lifetime with about 1,5-5.0% experiencing an afebrile seizure. The primary goal of emergency care is to abort the seizure and to identify potentially life-threatening aetiology(2).

The brain consists of nerve cells that communicate with each other through electrical activity. A seizure is defined as an abnormal paroxysmal neuronal discharge that is clinically manifested by motor, sensory, autonomic or behavioural disturbances. Anything that interrupts the connections between nerve cells in the brain can cause a seizure(3).

Seizures are classified into two types, focal(partial) and primary generalised seizures. Focal seizures originate from a localised area in the cerebral hemisphere. Focal seizures are designated as simple or complex. Complex partial seizures are associated with loss of consciousness and simple focal seizures are not. Simple focal seizures are less disabling and are confined to the neocortical structures within the limbic system and brainstem(4).

Focal seizures can disseminate and develop into a secondarily generalised seizure. Primarily generalised seizures originate from both cerebral hemispheres. These occur at an early age and are mostly associated with a family history of seizure disorders but are less likely to be associated with focal cerebral lesions. Some seizures are considered unclassified because the underlying mechanism of their origin or propagation is unknown. Because focal seizures can be subtle and unrecognised and may develop into secondary generalised seizures, the most common presentation is a generalised seizure.

The International League Against Epilepsy (ILAE) further categorizes seizures according to the aetiology. Acute symptomatic seizures occur during an acute illness in which there is a known neurological insult or systemic metabolic dysfunction in a previously neurologically intact child. Remote symptomatic seizures occur without an identified insult but with a history of a pre-existing neurological abnormality more than

1 week before. Idiopathic(cryptogenic) seizures occur with no clear cause in otherwise normal people with normal neurological examination and are usually asymptomatic(3, 5).

Seizures can be categorised into convulsive and non-convulsive seizures. Convulsive seizures have a motor component such as tonic-clonic, clonic or tonic. Non-convulsive seizures have impaired consciousness without a motor component(5). A provoked seizure is characterized by a specific trigger such as fever, central nervous system infection, head injury or intoxication. Unprovoked seizures are a type of seizure with no obvious precipitating cause and may be related to epilepsy(3, 6). Febrile seizures occur within 24 hours of having developed a fever. Afebrile seizures are not associated with fever.

Status epilepticus is a single seizure lasting for more than five minutes or two or more seizures within five minutes without the person returning to normal between the seizures(2, 7, 8). Status epilepticus is a life-threatening medical emergency associated with high morbidity or mortality, particularly if treatment is delayed. The primary goal of emergency care is to abort the seizure and to identify potentially life-threatening or reversible aetiology. Epilepsy is a type of chronic seizure disorder characterized by two or more unprovoked seizures at least 24 hours apart.

Computed Tomography (CT) is a medical imaging procedure that uses X-rays to build cross-sectional images of the body. The cross-sections are reconstructed from the measurement of attenuation coefficients of X-ray beams in the volume of the subject studied. Magnetic Resonance Imaging (MRI)is another medical imaging modality that uses non-ionizing radiation to send and create useful diagnostic imaging. MRI uses a radio wave antenna to send signals to the body and then a radiofrequency receiver detects the emitted signal which is converted into images by the computer.

MRI is the best method to avoid radiation exposure while providing more detailed diagnostic information(4, 5, 9, 10). However, Computed Tomography has a shorter scanning time, is cheaper and is more readily available in emergency care. Computed tomography is superior in detecting large structural abnormalities, acute vascular lesions and oedema. MRI is superior in demonstrating elusive brain developmental abnormality.

The role of imaging is to detect an underlying cerebral lesion (s) that may be the underlying cause of the child's seizure and to provide appropriate medical or surgical care(8). The purpose of performing neuroimaging in a child with unprovoked new-onset seizures is to look for intracranial pathology that may require immediate intervention. The purpose of elective neuroimaging is to detect abnormalities that may affect prognosis and therefore have an impact on long-term treatment and management (5, 8).

However, which patients with unprovoked seizures require neuroimaging and when imaging should be obtained is often debated.

It remains controversial whether neuroimaging is required in children with unprovoked afebrile new-onset seizures. The American Academy of Neurology (AAN) guidelines published in 2000 recommend the use of emergency neuroimaging for any child at any age who exhibits post-ictal deficits (Todd's palsy) that do not resolve quickly or who has not returned to baseline within several hours. "Todd's palsy is focal weakness in a part or all of the body after a seizure and usually subsides after 48 hours".

The International League against Epilepsy published in 2009 recommends that new-onset seizures/epilepsy with a medical emergency such as status epilepticus always merit emergency neuroimaging. American College of Radiology (ACR) recommends that afebrile seizures in neurologically intact children below 2 years of age without prior medical illness or documented trauma should be considered for an emergency CT scan. This may be a presentation for non-accidental injury.

Different research studies have concluded different results to support the role of neuroimaging in unprovoked first-onset seizures. A study done in Cairo demonstrated that about 20.6% of children from 6-12 years were found to have prevalent abnormalities on neuroimaging which mostly were brain atrophic changes that did not require urgent intervention. This study then concluded that there is a yield in neuroimaging in that age group as it detects structural abnormalities(9).

Another study demonstrated that only 11% of children had clinically significant abnormal findings on neuroimaging thus, together with the majority of research, concluding that neuroimaging studies are not useful in evaluating paediatric patients who present with a first attack of unprovoked non-febrile seizure. Emergent or urgent abnormalities occurred in less than 1%, suggesting that neuroimaging should not be routinely performed in the Emergency Department unless there is evidence of focal neurological deficits which is by AAN guidelines(2, 3, 6, 10,11).

A study that was done by Mohhamdi et al demonstrated that 27.1% of patients had abnormal findings of whom 9.2% were in the brain MRI group and 14.3% were in the CT scan group. This study demonstrated a lot of lesions to be in the white matter and that the location of the lesions was related to the type of seizure. They recommend brain imaging in all patients with new-onset unprovoked seizures and apart from some exceptions, brain MRI is superior to a CT scan(4).

Another study done by Haysma et al study demonstrated a significant abnormality in afebrile new-onset seizures in children less than 2 years with intracranial haemorrhage and suspected non-incidental injuries who required emergent intervention either surgically or medically(12). Therefore they recommend emergency neuroimaging for all children under 24 months presenting in the emergency department, which concurs with ACR guidelines(10, 13).

A study on status epilepticus suggested that longer seizure duration and older age were associated with urgent or emergent intracranial pathology. They then concluded that a substantial minority of children with unprovoked afebrile first-onset seizures presenting with status epilepticus have intracranial pathology requiring urgent or emergent neuroimaging. Therefore, they recommend that clinicians should strongly consider emergent neuroimaging for these patients(7, 13, 14).

Most studies concur with the AAN guidelines and have shown that neuroimaging in paediatric patients with new-onset seizures and no abnormal neurological deficit, status epilepticus or Todd's palsy do not require neuroimaging. However, some studies have shown that neuroimaging in all paediatric patients presenting with a seizure may be beneficial.

The most common conditions encountered from the studies, that require urgent medical or surgical treatment include; subdural haematoma, Arterio-Venous malformation, ischaemic stroke, cerebral oedema, hydrocephalus and meningitis (14, 15). The most common conditions encountered from the studies, that do not require emergency management include; gliotic lesions, multiple demyelinating lesions, congenital abnormalities like corpus callosum dysgenesis and periventricular leukomalacia(15, 16, 17, 18).

Many international studies have evaluated the role of neuroimaging in the paediatric population with first-time non-febrile convulsions, however, there has been little research conducted in South Africa. This gap in research is concerning as international guidelines from developed countries do not always apply to the patient population and disease profile of developing countries. The potential for this gap is to develop guidelines which would be suitable for a resource-limited country such as South Africa.

In conclusion; The role of imaging in unprovoked new-onset seizures remains debated. MRI is superior to a CT scan in detecting structural brain abnormalities. However, a CT scan is more readily available after hours and is easier for most clinicians to read. Obtaining adequate history in this patient group can be challenging, thus adequate clinical exam remains paramount in the decision to perform neuroimaging.

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SUBMISSION READY MANUSCRIPT

Title: Brain Computed Tomography (CT) Findings in Paediatric Patients Who Present with New Onset Unprovoked Afebrile Seizures to the Emergency Department

Journal: South African Medical Journal

Authors:

Dr Noluyolo Mahlati, radiology registrar, Greys Hospital Radiology Department, Private Bag X9001, Pietermaritzburg 3200, email: noluyolom91@gmail.com, Telephone: 0785035791

Dr Matthew Goodier, radiology consultant, Greys Hospital Radiology Department, Private Bag X9001, Pietermaritzburg 3200, email: goodiermatt@gmail.com Telephone: 0338973108

Affiliated Institutions:

Greys Hospital, Pietermaritzburg, KwaZulu-Natal Department of Health.

Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban.

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Title: Brain Computed Tomography (CT) Findings in Paediatric Patients Who Present with New Onset Unprovoked Afebrile Seizures to the Emergency Department.

Abstract

Background: Seizures are a common clinical presentation in the paediatric emergency setting. Neuroimaging is crucial to the initial workup. CT scan is more widely available than Magnetic Resonance Imaging. Many international studies have evaluated the role of neuroimaging in the paediatric population with first-time non-febrile convulsions, however, there has been little research conducted in South Africa.

Objectives: The study evaluated the yield of computed tomography (CT) brain in non-febrile paediatric patients presenting with new-onset seizures in a resource-limited setting.

Methods: A retrospective audit of paediatric patients who presented with new-onset afebrile seizures and underwent a CT brain scan carried out at Grey's Hospital, a tertiary hospital in Kwa-Zulu Natal.

Result:153 children with new onset afebrile seizures were included in the study. A total of 39/153(26 %) had recorded neurological abnormalities of whom 24/39 (61%) had abnormal CT scans. Among the patients with recorded neurological findings 15/153(17%) had normal CT scan findings and 24(36%) had abnormal CT scan findings. The majority of patients had normal CT scan findings 86/153(56%) with abnormal CT findings demonstrated in 67/153 (44%) cases. Among the abnormal CT findings, 42/67(28%) potentially required medical or surgical intervention.

Conclusion: Neuroimaging plays an important role in the investigation of children with first-onset afebrile convulsions in our setting since more than a quarter (42/153, 27%) of our cohort demonstrated CT abnormalities requiring some form of intervention

Keywords: paediatric; seizure; new-onset; afebrile seizures; CT scan findings; neuroimaging; resource limited setting;

INTRODUCTION

Seizures are a common clinical problem at all ages with a broad range of underlying pathologies. Seizures in children are often a benign symptom of febrile illness however, they may be a sign of a serious intracranial abnormality such as infection, haemorrhage or neoplasia. Seizures are a medical emergency, especially in the paediatric population and account for one of the most common presentations to the Emergency Department (ED)(1). The primary goal of emergency care is to abort the seizure and to identify a potentially life-threatening aetiology(4). Almost 10% of children in the United States of America will experience a seizure in their lifetime with about 1.5-5.0% experiencing afebrile seizures(5). A seizure is defined as abnormal paroxysmal neuronal discharge which is clinically manifested by motor, sensory, autonomic or behavioural disturbances(6). Any pathology that interrupts the connections between nerve cells in the brain can result in a seizure (3). Seizures are briefly classified into focal(partial) and primary generalised seizures where focal seizures originate from a localized area in the cerebral hemisphere and primarily generalised seizures originate from both cerebral hemispheres. Focal seizures can become secondarily generalized(7).

Neuroimaging plays an integral role in the evaluation, management and treatment of patients presenting with seizures and its role in children has evolved in the last two decades due to the increasing availability of Magnetic Resonance Imaging (MRI), which is considered the imaging modality of choice, and a recognition of the importance of reducing the use of Computed Tomography (CT) in children due to the radiation risk. However, CT scan is more widely available than MRI due to its affordability, especially in a developing middle-income country such as South Africa. The International League Against Epilepsy (ILAE) published imaging guidelines for new-onset epilepsy in 2009, affording a five-point scale classification (described in the results) on neuroimaging findings which are not specific to new-onset seizures but is relevant in assessing the outcome of emergent imaging(8,9). Additionally, the American Academy of Neurology (AAN), the Child Neurology Society (CNS), American Academy of Paediatrics (AAP) and the American Epilepsy Society (AES) published guidelines regarding neuroimaging for the assessment of a child with new-onset afebrile seizures which advise emergent neuroimaging for children with persistent post-ictal neurological deficit and children who fail to return to baseline after within a few hours (8). Thus, there seems to be a consensus that a child is allowed at least one simple seizure in their

lifetime without any further investigation provided the child was well prior, there are no recurrent seizures, no associated abnormal neurology and no status epilepticus.

However, the precise role of neuroimaging in paediatric patients who present with new-onset seizures in a country such as South Africa with limited resources, differing disease profiles such as a high burden of infectious diseases like Human Immunodeficiency Virus (HIV) and Tuberculosis (TB), delayed hospital presentation as well as delayed referral to a tertiary institution is still to be clarified. The study evaluated the yield of computed tomography (CT) brain in non-febrile paediatric patients presenting with new-onset seizures, identified the most common emergency radiological findings as well as the radiological findings that will alter the acute medical and surgical management and determined the factors associated with positive radiological findings in patients presenting with this type of seizure in a resource-limited setting.

METHODS

Study design and participants

This was a retrospective study carried out at Grey's Hospital using data from 01st January 2011 to 31 December 2020. Patients from 29 days to 12 years of age with a history of new-onset afebrile seizures for which the patients had not been medically evaluated were included in the study.

Children younger than 29 days were excluded because they have neonatal seizures which is considered a different clinical entity with different aetiology from seizures in older children. Patients with provoked seizures including documented febrile seizure in the previous 24 hours with a temperature ≥ 38.0 °C were excluded as these patients have a presumed non-structural case for seizures. Those whose radiology report had not been reviewed by a specialist radiologist were excluded as the radiology report findings were more likely to be invalid. Those with a recent history of trauma and blocked ventriculoperitoneal (VP) shunt, a history of previous neuroimaging or medical/surgical treatment for a seizure were excluded from the study as the cause for seizures in these patients was known or presumed.

Setting

Grey's Hospital is a referral tertiary academic Hospital located in Pietermaritzburg, South Africa, which falls in the Umgungundlovu health district. It offers tertiary services to the Western half of KwaZulu-Natal which includes 5 health districts with a total population of 4,5 million.

Data Collection

Although the setting was Grey's Hospital, a tertiary institution in Kwa-Zulu Nata, data from Ladysmith Provincial Hospital was included. Ladysmith Provincial Hospital is a 458-bed regional and district Hospital situated at Ladysmith in the Uthukela health district, South Africa. At the time this research was conducted, images were faxed to Grey's Hospital for reporting.

A folder with all paediatric patients (0-12 years) who had undergone computed tomography (CT) of the brain during the study period was created on the Picture Archiving System (PACS) by the IT specialist. Patients who were eligible for this study were identified by searching electronic records of all paediatric CT reports and images on the PACS. This was correlated with the history provided on the Radiology Information System (RIS) for the history of "convulsions", "seizures" or "epilepsy". All CT scan reports were reviewed by several specialist radiologists with differing levels of experience, most of whom had been specialist radiologists for at least 2 years.

Computed Tomographic Scanning Methodology

The scans were performed using a Siemens Somatom Sensation Cardiac 64 slice scanner (Siemens Medical Solutions SW, Erlangen) with 0.5s gantry rotation speed and tube voltage of 120KV. The tube current was determined using an automated current modulator. Scans were performed using a slice thickness of 5mm, pitch of 1.15 and image reconstruction of 1 mm.

For contrast-enhanced scans, 1mg/kg Omnipaque 300 contrast was manually injected intravenously. The predominant scanning technique included only post-IV contrast scans to mitigate the risk of radiation exposure, a few patients had both pre-IV and post-IV contrast scans and a small number of patients had only a pre-IV contrast scan performed. Our paediatric department follows the aforementioned guidelines

when assessing the need for neuroimaging in these patients, requesting imaging for patients with localizing signs and patients presenting with status epilepticus.

Statistical analysis

Descriptive statistics (frequencies and percentages) were used to summarise the data by neurological and CT findings. Risk factors associated with abnormal neurological findings and CT abnormalities were determined using the Chi-Square test. Stata V17 statistical software was used for the analysis. A p-value lower than 0.05 was considered statistically significant.

Ethical Consideration

Ethics approval for this study was granted by the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal (00002514.2021). There was no physical contact with the patients during the study. Privacy and anonymity were maintained by allocating a patient a study number and thus the patient's name was concealed and only identifiable to the primary researcher.

RESULTS

A total of 153 children with new-onset afebrile seizures were included in the study. Of these patients, 58/153(37.9%) were under 2 years and 92/153(60%) were males with a male-to-female ratio of 1.5:1. The median age of presentation was 6 years. A summary of the CT findings about demographics is presented in Table 1.

A total of 39/153(26%) had recorded neurological abnormalities of whom 24/39(62%) had abnormal CT findings. Using a Chi-square test a statistically significant association between the presence of abnormal neurological findings and an abnormal CT scan was found (p=0.01) as presented in Table 2.

The majority (n=86; 56%) had normal CT scans, while 67/153(44%) had abnormal findings, of whom almost two-thirds s 42/67 (63%) had CT features potentially requiring medical or surgical intervention.

No statistically significant difference between males and females was found as presented in Table 3. The findings were classified into emergent(acute process requiring immediate, urgent intervention), focal (focal lesions responsible for seizure but not requiring immediate intervention) subacute or chronic (process responsible for seizure that does not require immediate intervention but has important therapeutic or prognostic implications), static-remote(non-progressive lesions of the central nervous system that occurred remotely in time) and non-specific (lesions not requiring immediate intervention that may be responsible for a seizure) findings with emergent, focal and subacute were further grouped into major findings that require urgent or elective management and static remote and nonspecific findings grouped into minor findings which require no immediate management, or no treatment at all. A total of 49/153 (32%) patients had major findings including meningitis, cerebral oedema, stroke, pineoblastoma and hydrocephalus. The major white matter diseases were HIV encephalopathy and acute disseminated encephalopathy (ADEM). A total of 18/153 (12%) had minor findings including cerebral atrophy, old infarctions and gliosis. Table 3 shows the CT scan categories in children with new-onset afebrile seizures as well as the description of abnormal findings in children with new-onset afebrile seizures.

Cerebrovascular pathology was the most common emergent finding evident in 13/153(8.5%) cases 1 with intraventricular haemorrhage, 4 with Dural venous sinus thrombosis, 1 with subdural haemorrhage, 7 with ischemic infarction and 1 with acute peripheral haemorrhage in the temporal horn with no definite cause. **Figure 1** shows selected images of some of the cases of cerebrovascular accidents.

CT imaging features suggestive of meningitis were the second most common emergent finding noted in 11/153 (7.2%) cases of which 3 cases were associated with cerebral oedema and 4 were associated with hydrocephalus. **Figure 2** shows selected images of some of the cases thought to represent meningitis.

Features of hypoxic-ischemic injury were seen in 4/153 (2.6%) cases with selected images demonstrated in **Figure 3**.

Focal lesions were seen in 8/153 (5.2%) of cases with rim-enhancing lesions being the most common seen in 3 patients followed by arachnoid cysts and calcified granulomas seen in 2 patients each and a pineal mass was seen in 1 patient. **Figure 4** shows selected images of the cases with multifocal ring-enhancing mass lesions and a pineal mass.

DISCUSSION

More patients in the sample had normal CT scan findings (56%) compared to abnormal findings (44%). This concurs with most of the existing data such as the study by Joson-Sanglay et al (1). In our study, 49 cases had major CT abnormalities and 18 cases had minor CT abnormalities (examples explained below). In studies conducted in developing countries, there is a variable positivity rate of CT scan ranging from 21.0% to 41.7% in developing countries which has been suggested could be due to selection bias or the high prevalence of neurocysticercosis, especially in the Indian subcontinent (2).

Our study found more males 91(59.9%) had presented with new-onset afebrile seizures than females 61(40.1%). However, there is no relationship demonstrated between gender and the likelihood of abnormal CT scan findings (p=0.24) as noted in previous studies (1,3,4,5,6,7,8). A study done by Poudel et al in Nepal also found male patients accounting for 61.7% and a study done by Mabaso et al in the adult population in South Africa consisted of more male patients accounting for 53.7% (2,3).

HIV is known to increase vulnerability to CNS infections, especially in patients who have a low CD4 count in the general population. Seizures in this population may also be related to brain injury from HIV vasculopathy and encephalopathy due to the direct effect of chronic HIV infection. The prevalence of HIV infection in the pediatric population has reduced over the years due to the increased use of antiretroviral therapy in HIV-positive mothers. In our study, only 10 patients were documented to be HIV positive with 5 of them having major findings. This does appear high but unfortunately due to the small number of patients, the association did not reach statistical significance (p=0.55).

About the clinical findings, 53 (43%) patients had an unclassified seizure type with focal seizures occurring in 61 (40.1%) when the seizure type was documented, out of these patients 17 cases had major findings and 7 had minor findings. In contrast to the adult population, a study done by Smith et al(9) in South Africa demonstrated generalized seizures as more common than focal seizures accounting for 86.7%. This difference is attributed to the fact that most pediatric patients with just generalized seizures for the first time are not sent for imaging and also because there was a significant number of patients

whose type of seizure was not documented. A total of 24(39%) patients out of 61 (40.1%) patients with documented focal seizures had abnormal CT brain findings thus there was no statistically significant association between seizure type and the presence of abnormal findings. These findings contrast that of Besli et al which show that patients with focal seizures are more likely to have abnormal imaging findings(10). The difference to thought to be secondary to the small study population as well as missing data from clinical information. There was no relationship between the side of the seizure and abnormal findings. Previous studies have suggested that patients presenting with status epilepticus and those who have not yet returned to baseline require neuroimaging (11,12). In our study, 3 patients presented with status epilepticus and all of them had abnormal neurological finding on CT scan.

A total of 39(26%) cases had recorded abnormal neurological findings, 10 cases had Todd's paralysis (a brief period of temporary paralysis following any type of seizure) and 29 patients had other neurological findings including low Glasgow Coma Scale (GCS) (15 cases) as well as a few cases with poor balance and opisthotonos. Out of the 39 cases with abnormal findings, 16 of them were emergent findings requiring urgent medical/ surgical intervention. Our study demonstrated that patients with abnormal neurological findings were likely to have any abnormal CT findings($p=0.01$). This concurs with previous studies such as the one done by Joson-Sanglay et al(1,2,9,13). She emphasized that these results show the importance of CT Brain imaging for patients with abnormal neurological findings and emphasized the need for the clear communication of the neurological examination findings from clinician to radiologist. This was not consistently found in the referral letters we reviewed during this study.

Emergent pathology accounted for the most common major findings seen in 32(20.9%) cases including cerebrovascular accidents and meningitis. In our study, cerebrovascular accident was the most common emergent finding accounting for 13(8.5%) cases with the most common out of these being arterial cerebral infarction followed by dural venous thrombosis. This differs from the results of the studies done by Joson-Sanglay et al and Poudel et al which both found cerebral atrophy to be the most common abnormality and it contrasts the previous South African study done in adult patients by Mabaso et al who attributed age as the major risk factor to cerebrovascular accidents.

Focal lesions were present in 7(4.6%) cases with ring-enhancing lesions secondary to infection and mass lesions such as pineal mass being the most common findings. Focal pathology is globally thought to be common in patients who present with focal seizures as well as abnormal neurology.

Non-specific pathology contributed 11.1% to the abnormal CT findings with cerebral atrophy being the most common finding seen in 14 patients. Most data have shown cerebral atrophy to be the most common abnormal CT finding in the pediatric population (1,2) Joson-Sanglay et al suggested that this observation helps the clinician identify the cause of atrophy which is commonly syndromic thus helping in the diagnosis and prognostication of the patient. In our study population, the appearance of cerebral atrophy is commonly attributed to Benign Enlargement of Subarachnoid Spaces (BESS) in infants as well as the result of previous cerebral ischemia/hypoxia in the perinatal period. Static-remote pathology was seen in 1 (0.7%) patient who presented with a subdural hygroma.

LIMITATIONS

The retrospective nature of the study is in itself limiting. The methodology requires a pre-imaging diagnosis of a seizure which may systematically underrepresent patients with atypical or subtle seizure types. The study relied on medical records which were incomplete for most of the patients such as information regarding the type of the seizure, the HIV status and concise neurological examination findings. As a result, p-values were calculated on smaller sample sizes and likely underestimated the power of our findings and the ability to investigate predictors of abnormal CTB findings. Due to this, the study findings cannot confidently be generalised, however, they highlight the importance of emergent CT Brain neuroimaging in this study population. Future research using a similar methodology but with larger sample sizes would address some of these limitations. Inadequate assessment or documentation of the presence of fever could not be ruled out and may be a cause of selection bias.

CONCLUSION

Neuroimaging plays an important role in the investigation of children with first-onset afebrile convulsions in our setting since more than a quarter (42/153, 27%) of our cohort demonstrated CT abnormalities requiring some form of intervention. The results of our study recommend neuroimaging in paediatric patients presenting with new-onset afebrile seizures.

Acknowledgements

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Competing interests

We declare that no personal or financial relationship has influenced us to write this article.

Author's Contribution

N.M. was the principal investigating author and prepared the manuscript. M.G was responsible for research conception, editing of the manuscript and supervisory role.

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Data availability

The data that support the research findings is available from the author.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency to the authors.

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ACRONYMS

Acronyms

CT- Computed Tomography

MRI- Magnetic Resonance Imaging

ILAE- International League Against Epilepsy

AAN- American Academy of Neurology

CNS- Child Neurology Society

AAP- American Academy of Paediatrics

AES- American Epilepsy Society

PACS- Picture Archiving System

RIS- Radiology Information System

HIV- Human Immunodeficiency Virus

CNS- Central Nervous System

TB- Tuberculosis

CVA- Cerebrovascular Accident

GCS Glasgow Coma Scale

TABLES

TABLE 1: CT abnormalities about demographics.

	Number of cases		Normal findings (Percentage in subgroups)		Abnormal findings (Percentage in subgroups)	
	n	%	n	%	n	%
Age <2	58	37.9	31	53	28	48
Age>2	95	62.1	55	57.9	30	31.6
Generalized seizure	38	25	20	52.6	18	47.6
Focal seizure	61	40	37	60.6	25	40
Unclassified seizure type	54	35	29	57.7	25	46.3
Neurological findings	39	25.5	15	38.5	24	61.5
HIV positive	10	6.5	3	30	7	70

HIV; Human Immunodeficiency Virus

Table 2: Correlation between sex and neurological findings with abnormal CT scan findings

	Number of negative CT scan findings	**Number of abnormal CT scan findings**	**p-value**
Sex			
Female	39(63.9%)	22(36.1%)	0.23
Male	47(51.1%)	45(48.9%)	
Neurologic findings			
No abnormal neurologic findings	71(82,6%)	15(17.4%)	0.01
With abnormal neurologic findings	43(64.2%)	24(35.8%)	

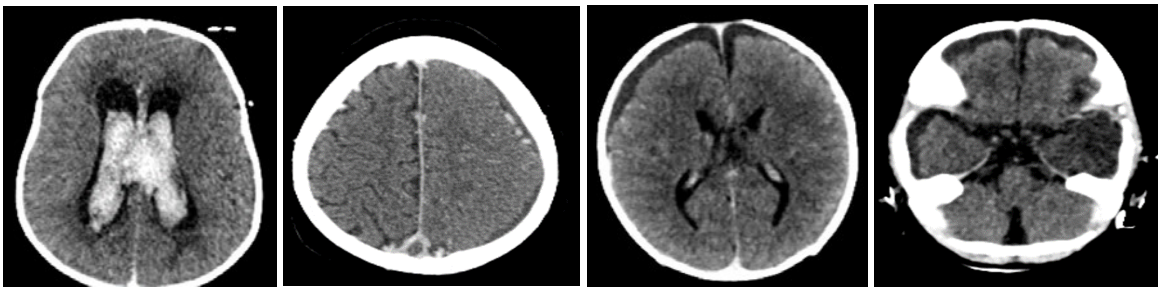
Chi-squared test

Table 3: Classification of abnormal neurological results and description of abnormal CT scan findings in children with new-onset afebrile seizures

	Number	**Percentage of total sample (n=153)**
Classification of abnormal neurological results		
Emergent	32	20.9
Focal	7	4.6
Subacute/chronic	10	6.5
Static-remote	1	0.7
Non-specific	17	11.1
Description of abnormal CT findings		
Atrophy	14	9.2
Non-specific calcifications	2	1.3
Meningitis	11	7.2
Hydrocephalus	5	3.3
CVA	13	8.5
Focal Lesion	8	5.2
Subdural effusion/hygroma	1	0.7
White matter disease	6	3.9
Hypoxia	4	2.6
Gliosis	3	2
Total	**67**	**43.8**

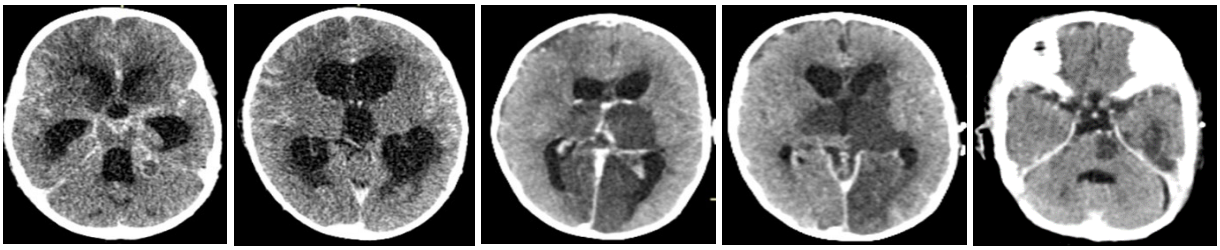
CVA; Cerebrovascular accident

FIGURES



a **b** **c** **d**

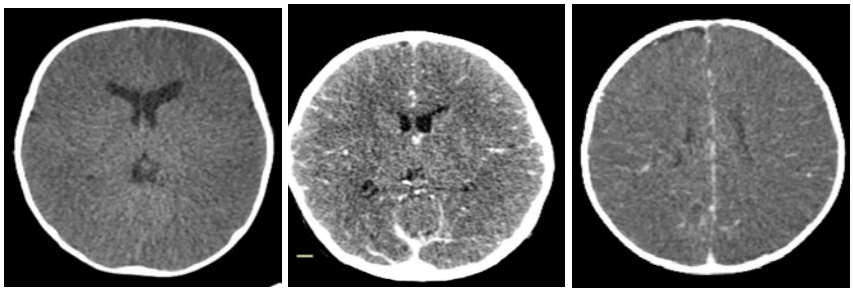
Figure 1: Cerebrovascular pathology as a cause of new-onset seizures in the paediatric population. (a) Intraventricular haemorrhage in a 2-month-old female. Axial nonenhanced CT brain: Hyperdense material is present in the septum pellucidum as well as in the body of the lateral ventricles bilaterally with associated hydrocephalus and periventricular hypodensities suggestive of subependymal oedema. (b) Subdural hematoma in an 11-year-old female. Axial enhanced CT brain: Hypodense biconcave isodense extra-axial collection in the left cerebral hemisphere involving the frontal, parietal and occipital regions consistent with chronic subdural hematoma. There is associated localized cerebral oedema. Additionally, there is a filling defect present in the posterior superior sagittal sinus in keeping with Dural venous sinus thrombosis. (c and d) Ischemia in a 1-year-old baby male. Axial enhanced CT brain: Image (c) demonstrates bifrontal-parietal subdural hygromas and image (d) demonstrates a non-enhancing wedge-shaped grey white matter hypodensity in the left temporal lobe extending into the internal capsule (image not included). The supra-clinoid left internal carotid artery demonstrates a narrow caliber when compared to the right suggestive of chronic middle cerebral artery territory infarction.
Source: Grey's Hospital PACS



a b c d e

Figure 2: Suspected meningitis as a cause of new-onset seizures in the paediatric population. (a and b) Axial enhanced CT brain of a 1-year-old male: Basal and leptomeningeal enhancement with a ring-enhancing lesion apparent in the left cerebellar peduncle complicated by cerebral oedema with raised intracranial pressure demonstrated by splaying of the sutures (image not included) as well as communicating hydrocephalus with subependymal oedema. Tuberculous meningitis (TBM) with a tuberculoma was thought to be the most likely diagnosis. There was opacification of the mastoid air cells and middle ear cavities bilaterally (image not included) consistent with otomastoiditis. (c, d and e) Axial enhanced CT brain images in a 2-month-old female: Basal enhancement with multiple hypodensities involving the occipital lobes, thalami and basal ganglia bilaterally, left temporal lobe and left pons with associated hydrocephalus with ependymal oedema. A diagnosis of suspected complicated TBM was given.

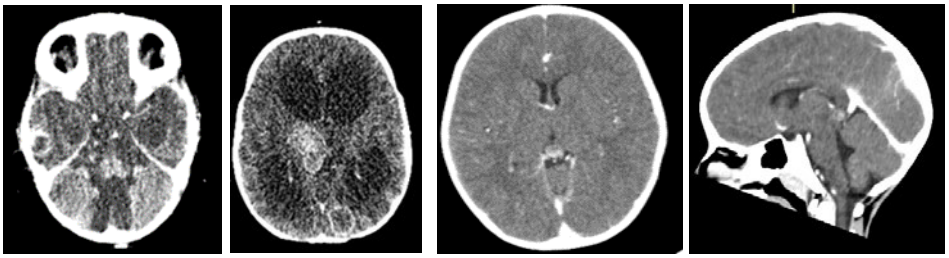
Source: Grey's Hospital PACS



a **b** **c**

Figure 3: Hypoxia as a cause of new-onset seizures in the paediatric population. (a) Axial enhanced CT brain of a 9-month-old male presenting with status epilepticus admitted with acute gastroenteritis and shock: Diffuse poor grey-white matter differentiation throughout both cerebral hemispheres. (b) Axial enhanced CT brain of a 4-year-old male with a depressed level of consciousness post seizures: Global hypodensity with poor grey-white matter differentiation present in both cerebral hemispheres. (c) Axial enhanced CT brain of a 9-month-old male presenting with status epilepticus post enema: Diffuse hypodense cerebral hemispheres with loss of grey white matter differentiation.

Source: Grey's Hospital PACS



a b c d

Figure 4: Focal lesions as a cause of new-onset seizures in a paediatric population. (a and b) Ring-enhancing lesions in a 5-month-old male presenting with low GCS and new-onset seizures. Axial enhanced CT brain: Diffuse hypodense bilateral cerebral hemispheres with rim-enhancing lesions in the right thalamus, left occipital lobes and right temporal lobe and communicating hydrocephalus with subependymal seepage**.** (c and d) Pinal mass lesion. Axial(c) and sagittal(d) enhanced CT brain Images: Well-defined round heterogenously enhancing mass lesion with no calcifications apparent, centred in the pineal gland thought to represent a pineoblastoma.

Source: Grey's Hospital PACS

APPENDICES

1. Research Protocol

University of KwaZulu-Natal
Mazisi Kunene Road, Glenwood, Durban, 4041
Tel: +27 31 260 8596
E-mail: enquiries@ukzn.ac.za

COLLEGE OF HEALTH SCIENCES

SCHOOL OF CLINICAL MEDICINE

PROTOCOL SUBMISSSION AND ADMINISTRATION

Student Name: NOLUYOLO MAHLATI Student Number: 219098891

Degree: MASTER OF MEDICINE Discipline: RADIOLOGY

Title: BRAIN COMPUTED TOMOGRAPHY (CT) FINDINGS IN PAEDIATRIC PATIENTS WHO PRESENT WITH NEW ONSET UNPROVOKED AFEBRILE SEIZURES TO THE EMERGENCY DEPARTMENT.

Declaration: This protocol has been reviewed by:

Supervisor Yes √ No ☐ Internal Discipline Review Yes √ No ☐

Supervisor:

Name: MATTHEW GOODIER

Signature: [redacted]

Date: 28/10/20

FOR OFFICE USE:

School Academic Leader of Research:

Name: Prof C Aldous

Signature:

Date:

Modified 29 May 2014

Keywords: Paediatric, CT Brain Imaging, Seizures, Unprovoked, Afebrile

Summary: This research investigates the use and value of CT brain imaging in paediatric patients presenting with unprovoked afebrile new onset seizures.

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1 INTRODUCTION

1.1 Background

Research into seizure disorder globally is an important clinical research topic. Unfortunately, guidelines based on international studies are not automatically valid in the South African context due to a difference in burden of disease. For example, it is possible that a higher incidence of infectious causes for seizures e.g. meningitis may necessitate unique approaches to neuroimaging in this country. Another consideration would be the reduced cost of CT compared to MRI which would influence the approach in a middle-income country such as South Africa with health resource constraints that might not present in high-income countries.

As yet, no studies have been performed in South Africa to support the use of international guidelines or the adoption of unique national guidelines.

1.2 Purpose

The purpose of this study is to evaluate the yield of neuroimaging using Computed Tomography (CT) scanning in new onset unprovoked seizures in paediatric patients presenting to the Emergency Department at Greys hospital from 2017 to 2019. Previous studies have been performed in the United States of America and some Asian countries yielding various results.

1.3 Objectives

The study seeks to achieve the following objectives:

a) Conduct an audit of CT brain imaging in a sample of paediatric patients presenting with unprovoked afebrile seizures for the first time.

b) Determine the yield of CT brain imaging in this group of patients.

c) Determine the conditions necessitating emergent medical or surgical interventions in unprovoked afebrile seizures in this population.

d) Determine the common structural brain abnormalities causing seizures in this population.

1.4 Defining the clinical problem

Seizures is common clinical problem at all ages, including children. In the USA, it is estimated that 10% of the population will experience at least one seizure in their lifetime. The role of neuroimaging in children presenting with seizures has evolved in the last two decades due to increasing availability of Magnetic Resonance Imaging (MRI) and a recognition of the importance of reducing the use of CT in children due to radiation risks. CT is also known to have reduced sensitivity for many conditions responsible for childhood seizures such as mesial temporal sclerosis, cortical dysplasias and small neoplasms.

At our institution CT is still used extensively in the emergency setting for children presenting with seizures. The use of CT in this setting is still an area of active investigation. American Academy of Radiology (AAR) guidelines recommend the use of emergent neuroimaging for any child at any age who presents with a post-ictal deficit (Todd's paresis) that does not resolve quickly or who has not returned to baseline within several hours. However, a study done by Sadeq and Karim in Kuwait in 2015 demonstrated no benefit in evaluating paediatric patients who present with first attack of unprovoked afebrile seizures therefore recommending that neuroimaging should not be performed for these patients.

1.5 Research Question/Hypothesis problem

Is brain Computed Tomography (CT) imaging of value in paediatric patients who present with new onset unprovoked afebrile seizures to the Emergency department?

1.6 Technical Reference Documentation

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2 ABBREVIATIONS AND ACRONYMS

This paragraph contains a glossary of abbreviations and acronyms.

AAN	:	American Academy of Neurology
ACR	:	American College of Radiology
AAR	:	American Academy of Radiology
BRECC	:	Biomedical Research Ethics Committee
CT	:	Computed Tomography
HIV	:	Human Immunodeficiency Virus
ILAE	:	International League Against Epilepsy
MRI	:	Magnetic Resonance Imaging
PACS	:	Picture Archiving System
RIS	:	Radiology Information System

3. LITERATURE REVIEW

Seizures are an emergency in paediatrics. Almost 10% of children will experience a seizure in their lifetime with about 1,5-5.0% experiencing an afebrile seizure(1). The primary goal of emergency care is to abort the seizure and to identify any potentially life-threatening aetiology (2). The brain consists of nerve cells that communicate with each other through electrical activity. A seizure is defined as abnormal paroxysmal neuronal discharge which is clinically manifested by motor, sensory, autonomic or behavioural disturbances. Anything that interrupts the connections between nerve cells in the brain can cause a seizure (3).

Seizures are classified into two types, focal(partial) and primary generalised seizures. Focal seizures originate from a localised area in the cerebral hemisphere. Focal seizures are designated as simple or complex. Complex partial seizures are associated with loss of consciousness and simple focal seizures do not. Simple focal seizures are less disabling and are confined to the neocortical structures with the limbic system and brainstem spares (4).

Focal seizures can disseminate and develop into a secondarily generalised seizure. Primary generalised seizures originate from both cerebral hemispheres. These occur at an early age and are most likely to be associated with a family history of a seizure disorder but are less likely to be associated with focal cerebral lesions. Some seizures are considered unclassified because the underlying mechanism of their origin or propagation is unknown. Because focal seizures can be subtle, unrecognised and may develop into secondary generalised seizures, the most common presentation is a generalised seizure.

The International League Against Epilepsy (ILAE) further categorizes seizures according to the aetiology. Acute symptomatic seizures occur during an acute illness in which there is a known neurological insult or systemic metabolic dysfunction in a previously neurologically intact child. Remote symptomatic seizures occur without an identified insult but with a history of a pre-existing neurological abnormality more than 1 week before. Idiopathic(cryptogenic) seizures occur with no clear cause in otherwise normal people with normal neurological examination (3, 5).

Seizures can be categorized into convulsive and non-convulsive seizures. Convulsive seizures have a motor component such as tonic-clonic, clonic or tonic. A non-convulsive seizure has impaired consciousness without a motor component

(5). A provoked seizure is characterized by a specific trigger such a fever, central nervous system infection, head injury or intoxication. Unprovoked seizures are a type of seizure with no obvious precipitating cause (3, 6). Febrile seizures occur within 24 hours of having developed a fever. Afebrile seizures are not associated with fever.

Status epilepticus is a single seizure lasting for more than five minutes or to or more seizures within a five minutes period without the person returning to normal between them (27, 8). Status epilepticus is a life-threatening medical emergency associated with high morbidity or mortality, particularly if treatment is delayed. The primary goal of emergency care is to abort the seizure and to identify potentially life-threatening or reversible aetiology. Epilepsy is a type of chronic seizure disorder characterized by two or more unprovoked seizures at least 24 hours apart.

Computed Tomography (CT) is a medical imaging procedure that uses x-rays to build cross- sectional images of the body. The cross-sections are reconstructed from measurement of attenuation coefficients of x-ray beams in the volume of the subject studied. Magnetic Resonance imaging (MRI) is another medical imaging modality that uses non-ionizing radiation to create diagnostic images.

MRI avoids radiation exposure while providing more detailed diagnostic information (4, 5, 9, 10). However, CT has shorter scanning time, is cheaper and more readily available in emergency care. CT is adequate for detecting large structural abnormalities, acute vascular lesions and oedema whereas MRI is superior in demonstrating more subtle brain abnormalities such as mesial temporal sclerosis or white matter disorders such as adrenoleukodystrophy.

The role of imaging is to detect an underlying cerebral lesion that may be the underlying cause of the child's seizure in order to provide appropriate medical or surgical care (8). The purpose of performing neuroimaging in a child with unprovoked first-time onset seizure is to look for intracranial pathology that may require immediate intervention. The purpose of elective neuroimaging is to detect abnormalities that may affect prognosis and therefor have an impact on long term treatment and management (5, 8). However, which patients with unprovoked seizures require neuroimaging and when imaging should be obtained is often debated.

The most common abnormalities causing seizures in this clinical setting may be divided into those that require urgent medical or surgical treatment which commonly include subdural haematoma, arteriovenous malformation, ischaemic stroke, cerebral oedema, hydrocephalus, and meningitis (15, 16) and those that do not require emergency management include such as gliotic lesions, multiple demyelinating lesions, congenital abnormalities like corpus callosum dysgenesis and periventricular leukomalacia (17-19).

Studies examining the role of neuroimaging in unprovoked first-onset seizures have yielded variable results. Mohamed et al demonstrated that 20,6% children from 6-12 years where found to have abnormalities on neuroimaging which mostly were consisted of atrophic brain changes that did not require urgent intervention. This study suggested that there is a rationale for neuroimaging in this age group as it detects significant structural abnormalities (9).

Dayan et al demonstrated that only 11% of children from age 29 days to 18 years had clinically significant abnormal findings on neuroimaging thus, together with majority of researchers, suggested that neuroimaging studies have no significant yield in evaluating paediatric patients who present with a first attack of unprovoked non-febrile seizure. Emergent or urgent abnormalities occurred in less than 1%, suggesting that neuroimaging should not be routinely performed in the Emergency Department unless there is evidence of focal neurological deficits. This approach is in accordance with AAN guidelines (2, 3, 6, 10-12).

A study by Mohhamdi et al demonstrated 27.1% of patients had abnormal findings of which 9,2% were in the brain MRI group and 14,3% were in the CT scan group. This study demonstrated that white matter lesions were a common seizure cause. They recommend brain imaging in all patients with after the first unprovoked seizures and that apart from some exceptions, MRI is superior to CT scan (4). Another study done by Haysma et al which was conducted in 377 children, demonstrated that 88 patients had abnormal findings (57 febrile and 31 afebrile seizures). Out of the 31 patients with afebrile seizures, 16(48%) had significant intracranial bleed and 11 (35,5%) were suspected non-accidental injury. Therefore, suggested that neuroimaging in afebrile first onset seizures in children less than 2 years should be performed (13). Both these studies concur with ACR guidelines (10, 14).

Todd et al suggested that children with unprovoked afebrile first onset seizures presenting with status epilepticus have intracranial pathology requiring urgent or emergent neuroimaging, therefore, recommend that clinicians should strongly consider emergent neuroimaging for these patients (7).

Thus, it remains controversial whether neuroimaging is required in children with unprovoked afebrile first onset seizures. The American Academy of Neurology (AAN) guidelines recommend the use of emergency neuroimaging for any child at any age who exhibits a post-ictal deficits(Todd's palsy) that does not resolve quickly or who has not returned to baseline within several hours (14). "The International League against Epilepsy recommends new- onset seizures/epilepsy with a medical emergency such as status epilepticus always merits emergency neuroimaging(3,5). The American Academy of Neurology has concluded that there is insufficient evidence to recommend the use of routine neuroimaging in the first unprovoked afebrile seizure.

The American College of Radiology (ACR) recommends that, afebrile seizures in neurologically intact children below 2 years of age without prior medical illness or documented trauma should be considered for emergency CT scan as it may be a presentation for non-accidental injury (10). Although recommendations of these organisations are commonly followed in South Africa, no studies have been performed in South Africa to support the use of international guidelines locally.

The burden of disease in South Africa differs substantially from that encountered in high-income Western countries with a far higher incidence of infectious diseases included complications of HIV/AIDS. The use of CT as a less-expensive investigative modality is also likely to be more appropriate in the South African setting. Because of these unique factors local research on this topic is vital. This study seeks to address this gap in the literature.

4 METHODS

A retrospective study of children with unprovoked afebrile seizures presenting to the Emergency Department at Greys hospital will be conducted. Patients eligible for this study will be identified by searching electronic records of all paediatric CT reports through

Picture Archiving System (PACS) and Radiology Information System (RIS) for history of "convulsions", "seizures" or "epilepsy".

4.1 Inclusion and Exclusion Criteria

4.1.1 Inclusion Criteria

i. First time onset or history of unprovoked seizure for which the patient had not been medically evaluated.

4.1.2 Exclusion Criteria

i. Neonates (<29 days of age)
ii. Febrile seizures in the previous 24 hours with a temperature ≥ 38.0 Celsius.
iii. Previous seizure neuroimaging or medical/surgical treatment.
iv. Recent toxin ingestion, high risk factors for seizures such as known metabolic disorder, bleeding disorders, known hydrocephalus or intracranial malignancy, recent head injury or operation, known neurological disorder, developmental delay and perinatal birth asphyxia

4.2 Sample Size

A sample size of 100 paediatric CT scans is required to estimate the proportion requiring emergency intervention to within ±14% with probability of 95% assuming a noninformative baseline of 50%. Stata V15 used in sample size calculation.

4.3 Data Collection Sheet

Data collection will be done in the form of a data collection sheet with variables and characteristics as depicted in **Error! Reference source not found.** below:

New onset unprovoked afebrile seizures in paediatric patients

Variable	Characteristics	Description
Patient Index		
Age		
Sex	Male Female	
HIV Status	Negative Positive Unspecified	
Duration of Seizure	< 5 minutes 5 - 30 minutes ≥30 minutes	
Seizure Characteristics	Focal Generalized Unclassified Other	
Neurological Findings	None Todd's paralysis Other	
Neuroimaging (CT scan) Findings	Non-specific Static-Remote Focal Sub-acute/Chronic Emergent	
Radiologist Reported the Scan	Registrar/Medical Officer Consultant	
Intervention	None Medical Surgical	

4.4 Confounding Factors

Focal seizures may be subtle with no loss of consciousness thus can be missed by the caregiver resulting in delayed presentation. A subset of patients with focal seizures may be missed as patients may only present when the seizures have become generalised.

Some patients in district hospitals may be classified and treated as epileptic with no neuroimaging performed. This study is only focused and limited to Greys hospital.

4.5 Database Design

Double data entry verification will be used to ensure validity by further reducing data errors. All the data will first be entered into a data file. Then the data is entered again and compared against the first data during the second data entry process to see if there are any discrepancies.

4.6 Statistical Analysis

Numeric variables will be compared using tests or Wilcoxon rank sum tests. Stata V15.1 will be used for statistical analysis. This will analyse the data from start to finish, clean the data, generate graphical and numerical summaries, and undertake statistical interference test. All analysis will then be presented in a comprehensive report that includes interpretations of the statistics and reports of the results.

5 METHODOLOGICAL CHALLENGES AND STUDY LIMITATIONS

5.1 Limitations

The methodology requires a pre-imaging diagnosis of seizures which may systematically underrepresent patients with atypical or subtle seizure types. The retrospective nature of the study can be limiting as, data collection and entering might contain errors. The study relies on medical records which might be incomplete for example regarding type of seizure and its duration, the HIV status and concise neurological examination findings. The study is limited to single institution over a limited time period hence cannot necessarily be generalised.

6 ETHICAL CONSIDERATIONS

Ethical approval has been applied for from the Biomedical Research Ethics Committee (BRECC). There will be no physical contact with the patients during this study period. The study poses no harm to the participants of the study. Validity of this study will be maintained by making sure that the conclusion correlates to the objectives and that an adequate sample size for the study's significance is obtained. Privacy and anonymity will be maintained by allocating a patient a study number and thus the patients name will not be revealed. All information collected will be stored in a Microsoft Excel spread sheet with accessibility only to the researcher. Acknowledgement of works of other authors used in any part of this dissertation with the use of Endnote application will be ensured.

7 FEASIBILITY

7.1 Timelines and Project Management

The estimated duration required for the research is stated in **Error! Reference source not found.** below:

Table 1: Estimated Research Duration.

Number of Weeks	Item
6	Ethics approval
16	Data collection and capturing
4	Data Analysis and Interpretation
2	Research Report Formulation

7.2 Participating Centres

The only participating centre for this research study will be the Greys Hospital in Pietermaritzburg, KwaZulu-Natal, South Africa.

7.3 Contributors and Authorship

The only participating contributors to this study are:

Table 2: Research Study Contributors.

Name	Post Designation	Role
Dr N Mahlati	Radiology Registrar	Author
Dr Matthew Goodier	Radiology Consultant	Supervisor

7.4 Study Funding and Progress

This study is currently self-funded with a starting budget of R1000.

8 STUDY SIGNIFICANCE

Unprovoked afebrile seizures remain a common presenting complaint in the paediatric population. Studies outside of South Africa have suggested that there is a low yield in performing neuroimaging in this group of patients. Unfortunately, guidelines based on international studies are not automatically valid in the South African context due to a difference in burden of disease.

As yet, no studies have been performed in South Africa support the use of international guidelines or the adoption of unique national guidelines.

2. BREC Approval

20 June 2023

Dr Noluyolo Mahlati (219098891)
School of Clinical Medicine
Medical School

Dear Dr Mahlati,

Protocol reference number: BREC/00002514/2021
Project title: BRAIN COMPUTED TOMOGRAPHY (CT) FINDINGS IN PAEDIATRIC PATIENTS WHO PRESENT WITH NEW ONSET UNPROVOKED AFEBRILE SEIZURES TO THE EMERGENCY DEPARTMENT.
Degree: MMed

RECERTIFICATION APPLICATION APPROVAL NOTICE

Approved:	**04 January 2023**
Expiration of Ethical Approval:	**03 January 2024**

I wish to advise you that your application for Recertification for the above protocol has been noted and approved by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

Note to PI:
Re : protocol deviation: PI and supervisor to apply via RIG for amendment and for condonation of changing the study active dates and enrolment numbers.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

The committee will be notified of the above approval at its next meeting to be held on 11 July 2023.

Yours sincerely

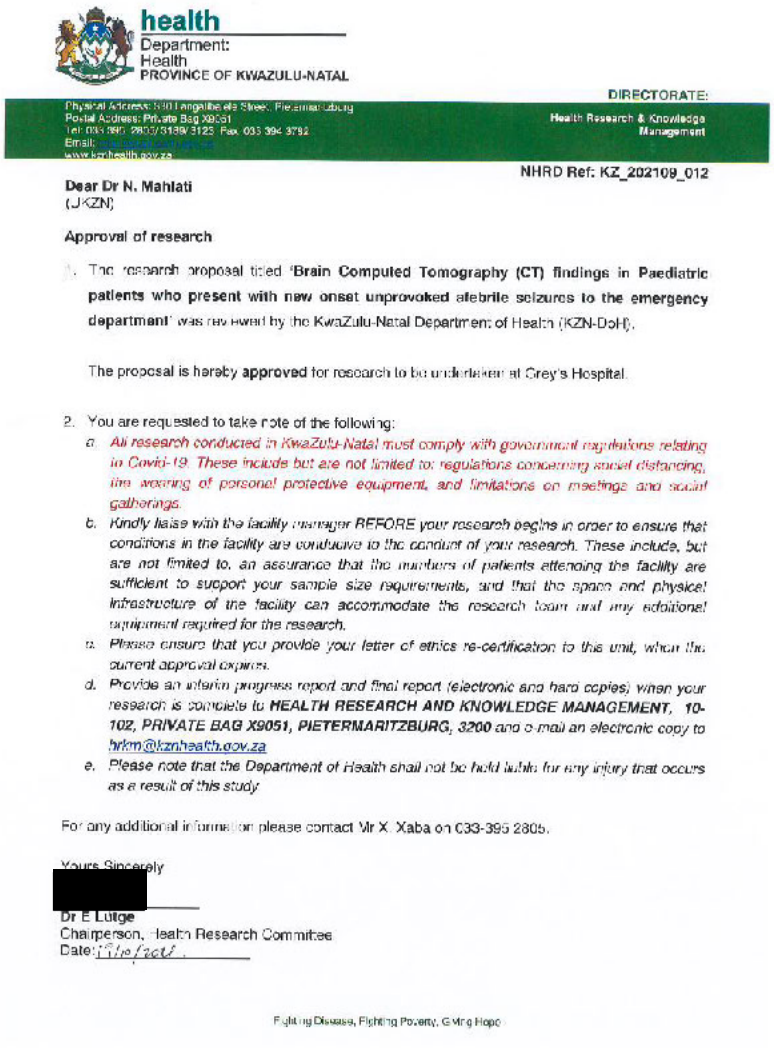
[redacted]

.....
Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee
Chair: Professor D R Wassenaar
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx
Founding Campuses: Edgewood Howard College Medical School Pietermaritzburg Westville

INSPIRING GREATNESS

3. Department of Health approval



health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE:
Health Research & Knowledge Management

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/3186/3125 Fax: 033 394 3782
Email:
www.kznhealth.gov.za

NHRD Ref: KZ_202109_012

Dear Dr N. Mahlati
(UKZN)

Approval of research

1. The research proposal titled **'Brain Computed Tomography (CT) findings in Paediatric patients who present with new onset unprovoked afebrile seizures to the emergency department'** was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby **approved** for research to be undertaken at Grey's Hospital.

2. You are requested to take note of the following:
   a. *All research conducted in KwaZulu-Natal must comply with government regulations relating to Covid-19. These include but are not limited to: regulations concerning social distancing, the wearing of personal protective equipment, and limitations on meetings and social gatherings.*
   b. *Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.*
   c. *Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.*
   d. *Provide an interim progress report and final report (electronic and hard copies) when your research is complete to* ***HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200*** *and e-mail an electronic copy to hrkm@kznhealth.gov.za*
   e. *Please note that the Department of Health shall not be held liable for any injury that occurs as a result of this study.*

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

[redacted]

Dr E Lutge
Chairperson, Health Research Committee
Date: 11/10/2021

Fighting Disease, Fighting Poverty, Giving Hope

4. Grey's Hospital Permission

KWAZULU-NATAL PROVINCE
HEALTH

Private Bag X 9001, Pietermaritzburg, 3200
261 Town Bush Road, Northern Park, Pietermaritzburg, 3201
Tel: 0338573321 Fax: 0338973398

GREY'S HOSPITAL
OFFICE OF THE CEO

To:	Dr. N. Mahlati Registrar – Dept. of Radiology
From:	Dr. K. B. Bilenge CEO - Greys Hospital
Date:	4 November 2020
Re:	Request for permission to conduct research at Grey's Hospital: *Brain Computed Tomography (CT) findings in Paediatric patients who present with new onset unprovoked afebrile seizures to the Emergency Department*

Dear Dr. Mahlati

Your request to conduct research at Grey's Hospital refers.
Permission to conduct the above study is hereby granted under the following conditions:

- Final ethics approval is a prerequisite for conducting your study at our hospital. Once obtained, please submit a copy of the full and final ethics approval;
- You are also required to obtain approval for your study from the Provincial Department of Health KZN Health Research Unit **prior to commencement**. You will find more information at: *http://www.kznhealth.gov.za/hrkm.htm*
- Confidentiality of hospital information, including staff and patient medical and/or contact information, must be kept at all times; **Patient/staff records are not to be removed from the hospital premises nor are you allowed to photocopy/ photograph them.**
- **You are to ensure that your data collection process will not interfere with the routine services at the hospital;**
- You are to ensure that hospital resources are not used to manage your data collection, e.g. hospital staff collecting and/or collating data; photocopying; telephone; facsimile, etc.;
- Informed consent is to be obtained from all participants in your study, if applicable;
- Policies, guidelines and protocols of the Department of Health and Grey's Hospital must be adhered to at all times;
- Professional attitude and behaviour whilst dealing with research participants must be exhibited;
- The Department of Health, hospital and its staff will not be held responsible for any negative incidents and/or consequences, including injuries and illnesses that may be contracted on site, litigation matters, etc. that may arise as a result of your study or your presence on site;
- You are required to submit to this office a summary of study findings upon completion of your research.
- You are requested to make contact with Dr D. T. Reitz – HoD – Dept. of Radiology at Grey's Hospital once you are ready to commence data collection.
- Please keep a copy of this approval on your person at all times whilst in the facility.

Recommended by:
[redacted]
Dr L. Naidoo
Senior Manager: Medical Services

Approved by:
[redacted]
Dr. K. B. Bilenge
Hospital CEO

GROWING KWAZULU-NATAL TOGETHER

SUPERVISOR'S REPORT

PLEASE NOTE; This must essentially be a descriptive and non-evaluative report

1. **Candidate: Noluyolo Mahlati** **Student no: 219098891**

2. **Registered title: Brain Computed Tomography (CT) Findings in Paediatric Patients Who Present with New-Onset Unprovoked Seizures to the Emergency Department.**

3. **Reference number: BREC/00002514/2021**

4. **Approved by Postgraduate Education Committee: Yes**

5. **Approved by Biomedical Research Ethics Committee: Yes**

6. **Supervision history:** I supervised the whole process Yes X No ___
   1. If no, I took over from another supervisor : (date)
   2. Describe the stage at which the student was at that time:

7. **Schedule of supervision (describe):**
   Commenced project in midyear 2020, Project submitted october 2023, corrections completed February 2024

8. **Adherence of the candidate to the schedule (describe):**
   As above.

9. **Level of guidance or assistance given (mark appropriate column)**

Step	No assistance	Minimal assistance	Average assistance	Massive assistance
Formulation of research topic		X		
Developing research proposal			X	
Literature search			X	
Defining theoretical basis			X	
Choosing research design			X	
Appropriate referencing			X	
Data collection instruments			X	
Conducting field work	X			
Developing the argument			X	
Solution of research problems			X	
Data analysis		X		
Expression, style and presentation			X	

10. **Describe the response of the candidate to suggestions or recommendations**

Excellent

11. Describe any resource constraints which influenced the candidate
nil

12. Any further information which is relevant
nil.

13. I saw/did not see the final version of the report that was handed in

14. I approve of/do not approve of the final version that was submitted

15. I am satisfied that, to the best of my knowledge, there is no plagiarism in the report.
Yes X No _____

Supervisor: Matthew Goodier

Signature: [redacted] Date: 20/2/2024

Co-supervisor: _____

Signature: _____ Date: _____