

**CLINICAL PROFILE AND OUTCOMES OF CHILDREN
WITH CEREBRAL VASCULAR DISEASE AT KENYATTA
NATIONAL HOSPITAL**

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**A DISSERTATION SUBMITTED IN PART FULFILLMENT FOR THE DEGREE OF
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UNIVERSITY OF NAIROBI

DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

This book is dedicated to:

- My family for their support during this study process.
- All children with cerebral vascular disease in Kenya. May their plight be known.

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ABBREVIATIONS

AIDS – Acquired Immune Deficiency Syndrome

AIS – Arterial Ischemic Stroke

AVM – Arterial Venous Malformation

CPISR – Canadian Paediatric Ischaemic Stroke Registry

CT scan – Computed Tomography Scan

CVD – Cerebral Vascular Disease

CVST – Cerebral Venous Sinus Thrombosis

HIV – Human Immunodeficiency Virus

ICD – International Classification of Diseases

KNH – Kenyatta National Hospital

MRA – Magnetic Resonance Angiography

MRI – Magnetic Resonance Imaging

MRV – Magnetic Resonance Venography

SAH – Subarachnoid Haemorrhage

SCD – Sickle Cell Disease

TOAST – Trial of ORG 10172 in Acute Stroke Treatment

WHO – World Health Organization

DEFINITION OF TERMS

Cerebral Venous Thrombosis: Acute onset of systemic or focal neurologic symptoms consistent with a blood clot in the venous sinuses of the brain and neuro-imaging evidence of thrombosis within cerebral veins or venous sinuses⁸

Childhood stroke: Stroke occurring in patients aged between thirty (30) days and eighteen (18) years⁹

Disability: Impairment of function to below the maximal level for the individual, either physically or mentally.

Haemorrhagic stroke: Acute focal neurologic deficit lasting more than 24 hours with neuro-imaging evidence of intracranial haemorrhage.⁸

Ischemic stroke: Acute focal neurologic deficit lasting more than 24 hours with neuro-imaging evidence of cerebral infarction.⁸

Outcome: Defined in this study as whether the impairments interfere with the child's daily activities. In good outcome there is no impairment whereas in poor outcome there will be impairment of the child's age appropriate activities of daily life.

Stroke: Rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.¹

Subarachnoid haemorrhage: Non-traumatic (or spontaneous) haemorrhage into the subarachnoid space, e.g. secondary to ruptured cerebral aneurysm or arteriovenous malformation.⁸

ABSTRACT

Background: Cerebral Vascular Diseases (CVDs) in childhood are an important cause of morbidity and mortality. They also have a significant financial impact on the families of the survivors. Most population based studies on childhood CVDs have been conducted in Europe and North America. However, little is known about cerebral vascular diseases in Sub-Saharan African children yet the risk factors, genetic predisposition and environmental context differs widely limiting replicability.

Objectives: The study aimed to describe the clinical profile of children aged 1 month to 18 years with cerebral vascular disease, their outcomes and to correlate the clinical outcomes with the major types of CVDs.

Methodology: This was a retrospective cohort study carried out at Kenyatta National Hospital (KNH) among children aged one month to eighteen years diagnosed with CVDs between October 2013 and April 2016. Data was collected from the health records department by reviewing patient files. This included the demographic data (age, sex), initial presentation, risk factors and outcome. Outcomes of interest included length of hospital stay, time from admission to diagnosis, presence of recurrent stroke, presence of residual impairment and mortality. Categorical data was summarized into percentages while continuous variables analysed and presented as means or medians where applicable. Type and cause of cerebral vascular disease was associated with clinical outcomes using Chi square test of associations for categorical outcomes and Student's t test for comparison of means for the continuous outcomes. Statistical tests were interpreted at 5% level of significance (p value less or equal to 0.05) and findings presented in form of tables, graphs and charts.

Results: A list of 145 files was identified. Eighty five (85) were included in the study. The median age was six (6) years (IQR 3.1-10.0) with a male: female ratio of 1.24:1. There were 47 (55.3%) males and 38 (44.7%) females. The most common clinical presentations included seizures (37; 43.5%), weakness (35; 41.2%), headaches (18; 21.2%) and altered consciousness (18; 21.2%). Sickle cell disease and intracranial infections were identified as the main risk factors at 22 (25.9%) and 20 (23.5%) respectively. Ischaemic stroke was the most commonly identified type of cerebral vascular disease (CVD) (57; 67%) followed by

haemorrhagic stroke (21; 25%). Subarachnoid haemorrhage and cerebral venous sinus thrombosis were the least common types of CVD; 6(7%) and 1 (1%) respectively.

The clinical outcomes of children with CVDs were as follows: mean length of hospital stay was 15 days and median duration from admission to diagnosis was 2 days (interquartile range 0-6.5).Fifteen (15) of the total 85 died (17.6%). Of those who were alive (70; 82.4%), 6 (8.6%) had recurrent stroke and 56 (80%) had residual impairment. Majority had weakness as a residual impairment (25; 44.6%).

Conclusion: Ischemic stroke was the most common type of cerebral vascular disease with Sickle Cell Disease and intracranial infections identified and the major risk factors. Many of the patients had multiple clinical presentations but seizures and weakness were the most common. In those with residual impairment, weakness was the most prevalent. There was 17.6% mortality.

1. INTRODUCTION

1.1 Introduction and Classification of Cerebral Vascular Diseases

Cerebral Vascular Diseases are defined as heterogeneous group of vascular disorders that result in brain injury. These result from disruption of cerebral blood flow either as a result of vessel luminal obstruction or vessel rupture.

Cerebral vascular diseases are classified as cerebral vascular accidents (stroke), subarachnoid haemorrhage and cerebral venous sinus thrombosis (CVST). Stroke is either ischemic or haemorrhagic. The World Health Organization (WHO) in 1977 defined stroke as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.¹ This definition included ischaemic and haemorrhagic stroke.

Ischemic stroke is further sub-classified into various subtypes as per the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification.² The TOAST classification denotes five sub types of ischemic stroke²:

1. Large-artery atherosclerosis (embolus / thrombosis)
2. Cardioembolism (high-risk / medium-risk)
3. Small-vessel occlusion (lacunae)
4. Stroke of other determined aetiology
5. Stroke of undetermined aetiology

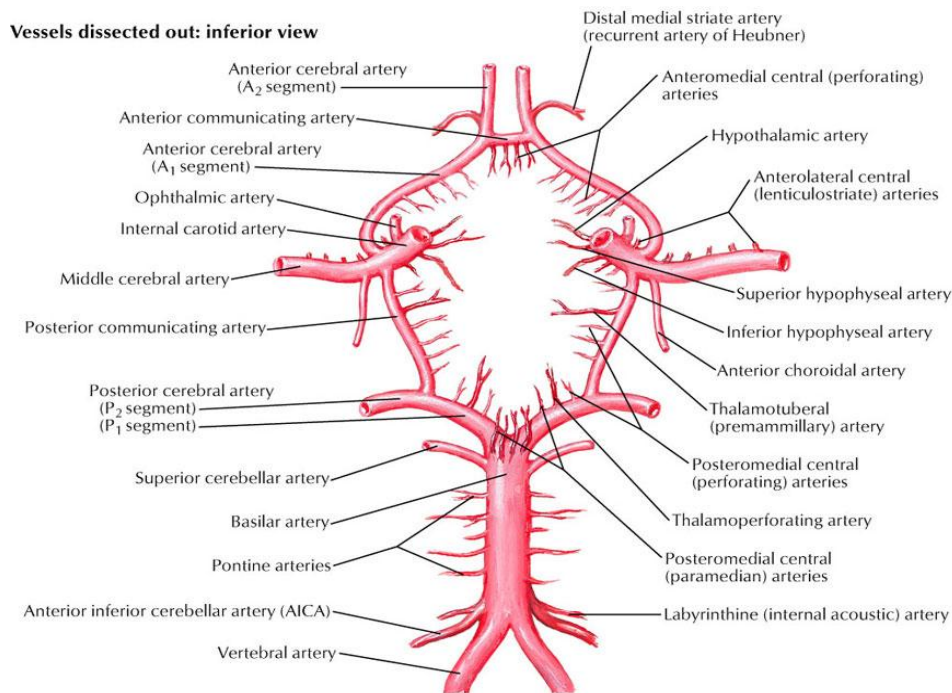
1.2 Vascular Anatomy of the Brain and Pathophysiology of CVDs

The brain is supplied by the carotid artery (mainly internal carotid) and the vertebral-basilar arteries. The internal carotid artery branches into anterior and middle cerebral arteries while the posterior cerebral artery emerges as a branch of the vertebral-basilar artery. The anterior, middle and posterior cerebral arteries are interconnected by the anterior and posterior communicating arteries to form the Circle of Willis.³

The anterior three-fifths of cerebrum is supplied by the internal carotid arteries, except for parts of the temporal and occipital lobes. The vertebral-basilar arteries supply the posterior two-fifths of the cerebrum, part of the cerebellum, and the brain stem.³

Figure 1 shows arterial blood supply to the brain.

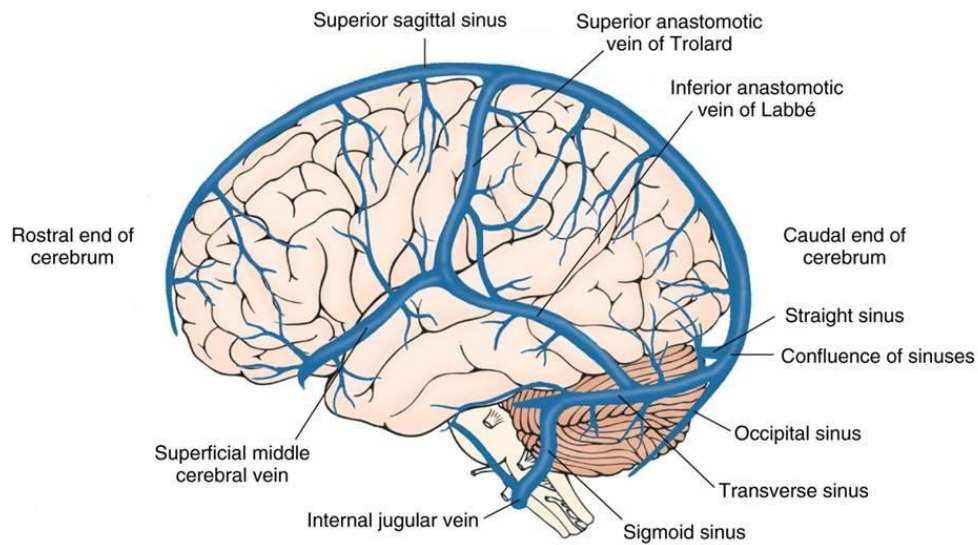
Figure 1: Cerebral arterial blood supply



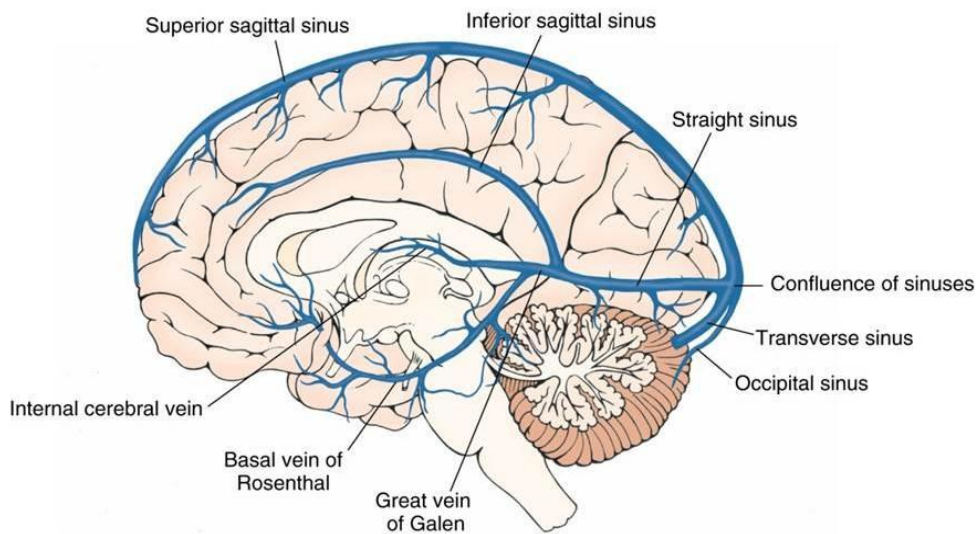
Cerebral venous drainage is divided into superficial and deep. In the superficial venous drainage, the cerebral hemispheres are drained by small venous structures in the pia mater. These form cerebral veins which traverse the subarachnoid space and drain into endothelial-lined sinuses within the dura mater. Most of these vessels eventually drain into the superior sagittal sinus, which joins the straight sinus and transverse sinus at the occiput to form the confluence of sinuses. From here, two transverse sinuses bifurcate and travel laterally and inferiorly and form the sigmoid sinuses which drain into the two jugular veins⁴.

The deep venous drainage is made up of deep cerebral veins found within the deep structures of the brain, which join to form the vein of Galen. This vein merges with the inferior sagittal sinus to form the straight sinus which then joins the superficial venous system at the confluence of sinuses.⁴ Figure 2 demonstrates venous drainage of the brain.

Figure 2: Cerebral venous drainage



A: Lateral aspect



B: Medial aspect

1.3 Pathophysiology of Stroke

1.3.1 Pathophysiology of ischaemic stroke

Ischaemic stroke occurs as a result of reduction or complete blockage of blood flow to a brain region. This may be either thrombotic or embolic. Normal cerebral blood flow is 50-60ml/100gm of brain tissue per minute. When cerebral blood flow falls to about 20-

25ml/100g of brain tissue per minute there is resultant ischaemia to the affected area. At this point, the tissue remains metabolically active but there is loss of electrical activity. Cerebral autoregulatory mechanisms compensate for the reduction in cerebral blood flow in response to ischaemia by local vasodilatation, opening of collaterals, and increasing the extraction of oxygen and glucose from the blood. This occurs to maintain normal tissue oxygen and glucose concentrations. If perfusion is not restored rapidly or if cerebral blood flow falls to less than 16ml/100g of brain tissue per minute permanent damage occurs (infarction). The area of infarction is known as umbra (core) whereas the tissue surrounding the infarcted area is referred to as the ischemic penumbra (border). Anaerobic respiration ensues with production of lactic acid which is toxic to cerebral cells. An ischaemic cascade follows with eventual tissue necrosis or apoptosis.³

1.3.2 Pathophysiology of haemorrhagic stroke

Haemorrhagic strokes usually occur due to vessel rupture with resultant compression of brain tissue from an expanding haematoma. This results in cerebral tissue injury. The pressure may also lead to reduced blood supply to affected tissue with resulting infarction.

Intracerebral haemorrhage results from small vessel rupture with bleeding into the brain parenchyma. This is commonly the result of blood vessel damage from chronic hypertension, vascular malformations, or the use medications associated with increased bleeding rates, such as anticoagulants, thrombolytics and anti-platelet agents.

Subarachnoid haemorrhage is the gradual collection of blood in the subarachnoid space of the brain dura. Non-traumatic subarachnoid haemorrhage typically results from rupture of cerebral aneurysms which may be congenital (absence of media of artery wall) or acquired (hypertensive).³

1.3.3 Pathophysiology of cerebral venous sinus thrombosis

Thrombus formation in the venous sinuses may occur following prothrombotic disorders, connective tissue disorders, dehydration, head and neck infections, haematologic disorders, procoagulant drugs and malignancies. This leads to obstruction of venous drainage. Continued enlargement of the thrombus can lead to increased venous pressure, increased intracranial pressure and cerebral oedema. If left untreated, intracranial pressure continues to rise and eventually compromises vascular supply leading to ischaemia and infarction.⁵

1.4 Incidence of Cerebral Vascular Diseases

Stroke is ranked among the top ten (10) causes of mortality in children in the United States⁶ and is an important cause of long term morbidity with a high financial implication⁷. Cerebral Vascular Diseases in children were initially considered very rare, possibly attributable to low index of suspicion by clinicians and subtle symptoms that may mimic other illnesses leading to missed or delayed diagnosis. However, the overall incidence of CVDs has been rising over the years with rates ranging from 1.2 to 13 cases per 100,000 of the population⁸⁻¹³. This rise has majorly been attributed to improved imaging¹⁴ and also increased survival of children with risk factors for CVDs such as those with congenital heart diseases and sickle cell anaemia.

Childhood CVDs have not been studied as extensively as in the adult population but the subject is gaining interest worldwide. Most population based studies have been done in Europe and North America. There are very few studies available on childhood CVDs in Sub Saharan Africa.

One study conducted by Ogeng'o et al at Kenya's National Referral Hospital (KNH) in 2008 revealed that paediatric stroke in the Kenyan population is not uncommon. This study was carried out between January 2004 and December 2008. Out of 712 cases of stroke admitted during the study period, they found that 32 were paediatric¹⁵. The estimated prevalence was 16/100,000 of the population which is slightly higher than the 1.2 to 13 cases per 100,000 quoted in the European and North American studies⁸⁻¹³.

2. LITERATURE REVIEW

2.1 Risk factors of Cerebral Vascular Diseases in the Paediatric Population

Risk factors of childhood cerebral vascular diseases are widespread and vary depending on geographical location. Cardiac disease is the commonest risk factor for arterial ischaemic stroke especially the cyanotic congenital heart diseases such as Tetralogy of Fallot. A Patent Foramen Ovale may allow for venous embolic events to pass from the right to left side of the heart with thrombo-emboli to the brain leading to ischaemic stroke. Coarctation of the aorta is sometimes associated with cerebral aneurysms which can predispose to haemorrhagic stroke. Cardiomyopathies (especially dilated cardiomyopathy), rheumatic heart disease, prosthetic valves, or valvular vegetation from endocarditis may lead to embolic clots with

resultant arterial ischaemic stroke. Treatment of cardiac diseases with cardiac catheterization may also result in arterial ischaemic stroke in children.¹⁶

Other risk factors include haematological disorders (like sickle cell anaemia, Protein C and S deficiency and Factor VII and VIII deficiency leading to intracerebral haemorrhage), infections (such as varicella, Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome (HIV/AIDS), bacterial meningitis, tuberculous meningitis, malaria etc.), Moyamoya disease (a chronic, non-inflammatory occlusive intracranial vasculopathy of unknown cause) vasculitis and malignancies e.g. acute leukaemia. Arteriovenous malformations are the commonest cause of haemorrhagic stroke. Cerebral Venous Sinus Thrombosis development is associated with head and neck infections, dehydration, perinatal complications, and coagulation disorders.^{8,9,16}

Bibi et al studied childhood CVDs over a 2 year period in Pakistan. Of the forty six (46) children, infectious causes were the most prevalent risk factor. Intracranial infections were diagnosed in 31(67.39%) children: 20 (43.4%) had meningo-encephalitis, 2 (4.34%) had bacterial meningitis, 3 (6.52%) had tuberculous meningitis, 3(6.52%) had pertussis encephalopathy, 2 (4.34%) had mumps encephalitis and 1 (2.17%) had cerebral malaria. Microcytic hypochromic anaemia was a risk factor in 28 (60.86%). Cardiac diseases were identified in 4 (8.69%), hypernatremic dehydration in 3 (6.52%) and congenital cerebrovascular anomalies in 2 (4.34%). Only 1 (2.17%) patient had stroke due to hypertensive encephalopathy secondary to acute glomerulonephritis and 4 (8.69%) patients had no identifiable risk factor.¹⁷

In Hong Kong, an 11 year study by Chung and Wong noted that complications related to congenital heart diseases (n=15, 30%) was the leading cause of cerebral vascular disease among the 50 patients included in the study. This was followed by hematologic diseases (n=14, 28%) and vascular diseases (n=13, 26%). Six (6) cases had no determined causes and 1 had a metabolic cause¹³

2.2 Clinical Presentation

Clinical presentation varies depending on the age of the child, type of cerebral vascular disease and affected vascular territory. In arterial ischaemic stroke, toddlers and older children typically present with acute focal neurologic deficit, e.g. hemiplegia. This may or may not be preceded by seizures. Children with CVST may present with lethargy, nausea,

vomiting, headache, seizures, altered level of consciousness or hemiparesis. On physical examination, dilated scalp veins, eyelid swelling or a large anterior fontanelle may be noted. An older child with haemorrhagic stroke will complain of headaches, vomiting or altered level of consciousness. Children less than one year are likely to have more non-specific symptoms such as lethargy, difficulty in feeding, irritability and apnoeic spells. Subarachnoid haemorrhage can also present as irritability and a bulging fontanelle in infants and the older children would complain of sudden acute onset headache, neck pain, meningismus or photophobia.^{16, 18}

The clinical presentation also varies depending on the affected vascular territory. Middle cerebral artery involvement would present as hemiplegia with upper limb predominance, hemianopia or dysphasia. Anterior cerebral artery involvement would present primarily with lower extremity weakness. Presence of vertigo, ataxia and nystagmus would suggest involvement of the posterior circulation. Bulbar dysfunction and dysarthria would suggest involvement of the lower brainstem whereas aphasia suggests involvement of the basal ganglia, thalamus or cerebral hemispheres.¹⁶

In Bibi et al's study among 46 children, 37 (80.43%) presented with weakness, 33 (71.73%) had hemiparesis or hemiplegia and 4 (8.69%) had monoplegia. Signs and symptoms of raised intracranial pressure was a noted clinical presentation in 31 (67.39%) children. Twenty eight (60.86%) presented with seizures, 26 (56.52%) presented with fever, 12 (26.08%) had cranial nerve involvement, 5 (10.86%) were aphasic and 10 (21.73%) presented in a comatose state.¹⁷

Chung and Wong in Hong Kong noted that the most common presentations were seizures (52%) and hemiplegia (34%) among the 50 subjects. Other presenting features included headaches (22%), decreased consciousness (30%), visual field defects (12%), dysphasia (10%) and lethargy (8%).¹³

2.3 Clinical Outcome after Childhood CVDs

Cerebral vascular diseases in childhood cause significant morbidity and mortality. Data from the Canadian Paediatric Ischaemic Stroke Registry of 2002 which included 402 children with AIS and 160 children with CVST showed that 27% of children were neurologically normal, 61% had neurological abnormalities, 21.6% had a stroke recurrence and 12% had died by the outcome evaluation period. The following factors were associated with poor outcome: neuro-

imaging abnormalities, seizures at presentation and infarct volumes greater than 10% of intracranial volume. There was a 20%-40% chance of stroke recurrence.⁹

A study conducted by Ganesan et al at Great Ormond Street Hospital, London between 1990 and 1996 aimed at describing the outcome of children with ischaemic stroke. The children were aged between 3 months and 15 years and the follow up period ranged between 3 months and 13 years. Out of the 128 children reviewed, information on outcome was only available for 105 (82%). Good outcome was reported in 37 children (40%) and poor outcome in 53 (60%). Poor outcome in this study was defined according to whether impairments interfered with daily life whereas good outcome was defined as having no impairments. Younger age at time of the stroke was related to a more adverse outcome. Four children (4%) were not able to walk at the time of follow-up and 38 children (42%) had speech and language difficulties. 59% of the children were reported by parents to need help relative to their peers in the school environment. There was no residual impairment in 13 children (14%)¹⁹.

A retrospective study was conducted by Tham et al in Singapore between October 1999 and May 2006 to highlight the factors predictive of outcome after childhood stroke. Twenty six (26) children were included in the study. Only 1 child was seen as an outpatient and the rest were admitted. Of the 25 inpatients, 16 (64.0%) had neurological deficits at discharge noted as hemiparesis in 12 children (48%), visual disturbances in 5 (20%), seizures in 4 (16%), speech difficulties in 4 (16%), ataxia in 3 (12%) and swallowing difficulties in 3 children (12%).

In terms of long-term outcome, majority were asymptomatic at follow-up. Two children (10%) had significant neurological impairment, while 6 (30%) had mild functional handicap. Two had severe neuropsychological problems (2/17, 11.8%) at follow-up and 2 children (2/17, 11.8%) had mild schooling difficulties.

On assessment for independence, 1 child (1/13, 7.7%) had moderately severe disability and required significant assistance with activities of daily living (grade 4 disability), while another child (1/13, 7.7%) required some assistance managing personal affairs (grade 3 disability). One child (3.8%), who had Moyamoya disease, had an ischaemic stroke recurrence 15 years after her initial one. There were no deaths directly resulting from strokes in this study population.²⁰

3. STUDY JUSTIFICATION AND UTILILTY

There is not much data on cerebral vascular diseases in children. Most population based studies have been carried out in Europe and North America with very little data from Africa. This is despite the fact that cerebral vascular diseases cause significant morbidity and mortality and prompt identification and timely management can significantly improve outcome.

The purpose of this study was to profile the children with cerebral vascular diseases in our set up and identify their characteristics and outcomes. This in essence would highlight the fact that cerebral vascular diseases do occur in children and therefore increase the index of suspicion among healthcare workers in a bid to improve diagnosis, timely intervention and outcome. This study will provide baseline information on cerebral vascular diseases in Kenyatta National Hospital and hopefully open doors to further research on cerebral vascular diseases in the Kenyan paediatric population.

4. RESEARCH QUESTION

What is the clinical profile and outcomes of children aged 30 days to 18 years presenting with cerebral vascular disease at Kenyatta National Hospital?

5. RESEARCH OBJECTIVES

5.1 Primary Objective

- To describe the profile of children age 30 days to 18 years presenting with and/or on follow up for cerebral vascular disease at Kenyatta National Hospital between 1st October 2013 and 30th April 2016

5.2 Secondary Objectives

- To describe the clinical outcome after cerebral vascular event
- To compare the clinical outcome with type of cerebral vascular disease

Clinical outcomes of interest to be studied included length of hospital stay, mortality, time from admission to diagnosis, history of stroke recurrence and presence of residual impairment.

The study period between October 2013 and April 2016 was chosen based on the following reasons:

- The computerised health record information systems crashed and data prior to October 2013 was unavailable.
- The process of getting files from the wards to the Health Records Department takes roughly two months and at the time of data collection, data was only available up to April 2016.

6. RESEARCH METHODOLOGY

6.1 Study Design

This was a Retrospective Cohort Study.

Given that cerebral vascular diseases are of relatively low incidence in our set up, a retrospective cohort design was considered the most suitable design for this study.

6.2 Study Site

The study was conducted at Kenyatta National Hospital mainly from the Health Records Department. Kenyatta National Hospital is located in Nairobi, Kenya. It is the county's national referral hospital. It serves as a teaching hospital for the University of Nairobi (UoN) College of Health Sciences. It has a total bed capacity of 1800 beds and approximately 40,000 annual paediatric admissions.

It is one of the three public hospitals in Nairobi (the other two being Mbagathi Hospital and Mama Lucy Kibaki Hospital). It was chosen given its vast catchment area, presence of specialists and its referral status.

The Health Records Department is located on the ground floor of Kenyatta National Hospital. Once a patient is discharged from the wards, the files are collected by the Records Clerk assigned to each ward and taken to the Health Records Department. Here, the files are then manually coded according to the ICD-10 codes based on the diagnosis indicated on the discharge/ death summary. Once the manual coding is complete, another clerk then inputs the codes into their computer systems. This process can take anywhere between one and two months. Anyone who needs to carry out research at this department can easily access the files as long as they have approval from the Ethics and Research Committee.

6.3 Study Population

Children aged thirty (30) days to eighteen (18) years with cerebral vascular diseases

6.4 Inclusion Criteria

- Children aged thirty (30) days to eighteen (18) years presenting with or diagnosed to have cerebral vascular disease at KNH between 1st October 2013 and 30th April 2016 (including those who were 30 days old to those who had not yet reached their 19th birthday)
- Relevant information was available in the records. This information included:

- Demographic data: age, sex, date of admission, date of discharge/ death
- Initial presentation
- Risk factors
- Diagnosis. Definitive diagnosis will be based on:
 - Clinical presentation (e.g. headaches, convulsions, lateralizing signs) with supporting evidence from neuro-imaging, either CT Scan brain, MRI/MRA or MRV of the brain (demonstration of an infarct, bleed or thrombus)
 - Post mortem findings where available (identification of an infarct, bleed or thrombus).
- Those with partially missing records but a definitive diagnosis could be made from the available information

6.5 Exclusion Criteria

- Children who do not fit the inclusion criterion for age.
- Patients who were identified as having a CVD but noted not to have CVD upon perusal of the patients file/ health records
- Patients who were identified as having CVD but the records were completely missing i.e. patients file not available for perusal to extract data
- Patients who were identified as having CVD but available information from the records was not enough to make a definitive diagnosis i.e. clinical findings were available but with no supporting evidence from neuro-imaging or post mortem.
- Patients who had traumatic aetiology for intracerebral haemorrhage, Sub-dural haematoma and Extra-dural haematoma

6.6 Sample Size Determination

Every patient meeting the inclusion criteria admitted or on follow up at Kenyatta National Hospital between the specified time periods was included in the sample.

Due to lack of such studies a definite sample size could not be calculated. However, from a preliminary review done at the health records department the estimated minimum sample size for the study was set at one hundred (100). Forty (40) patients were admitted with cerebral vascular diseases in 2014, extrapolated to 80-100 patients for the study period. Using the estimated sample size, the estimated precision of the study was determined as follows:

Using data from the Great Ormond Street Hospital, London study by Ganesan et al: ¹⁷

$$\bullet \quad n = \frac{z^2 p(1-p)}{d^2} \quad d = \sqrt{\frac{z^2 p(1-p)}{n}}$$

- n = estimated minimum sample size
- z = standard normal deviate for 95% confidence interval (= 1.96)
- p = percentage of those with disability from Great Ormond Street Hospital, London study (60%)
- d = degree of precision
- $100 = \frac{1.96 \times 1.96 \times 0.6(1-0.6)}{d^2}$

$$\bullet \quad d = \sqrt{\frac{1.96 \times 1.96 \times 0.6(1-0.6)}{100}} = \mathbf{0.096 \sim 0.1 (10\%)}$$

The degree of precision would vary depending on the sample size achieved as in Table 1.

Table 1: Sample Size Chart

Estimated sample size	60	80	100	120	140	160	180	200
Degree of precision	0.16	0.107	0.096	0.088	0.081	0.076	0.072	0.068
	16%	10.7%	9.6%	8.8%	8.1%	7.6%	7.2%	6.8%

For this study, the minimum sample size was set at 80.

6.7 Patient Recruitment Procedure

Files of patients with CVDs were retrieved from Health Records Department. These were identified using appropriate International Classification of Diseases (ICD) 10 codes for CVDs. ICD-10 codes are indicated in Appendix 2. Retrieval of the files was done by the staff members at the health records department.

Synonyms for CVDs were also used to ensure maximal identification of patients and also capture those patients with CVDs but not classified as having CVD. These included stroke, cerebrovascular accident, intracranial bleed, cerebrovascular insult, hemiparesis and hemiplegia.

Mortality files were also retrieved. These are stored in a different section at the health records department, separate from those of inpatients or outpatients.

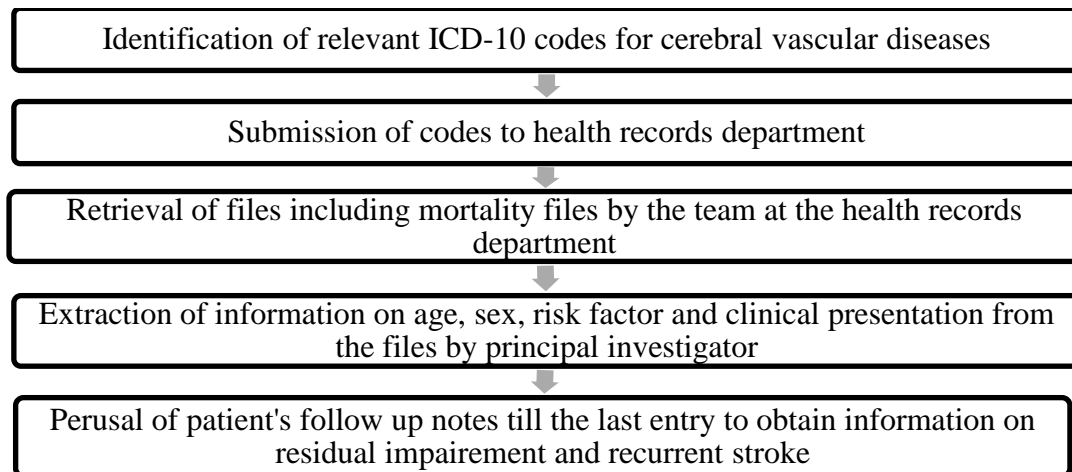
The appropriate codes were then submitted to the health records department.

Once the files were retrieved, information on age, sex, risk factor and clinical presentation was extracted from all the files using the data collection tool in Appendix 3. Information on time from admission to diagnosis was obtained by noting the date of admission and the date when neuro-imaging was performed. For those who were alive, the files were perused until the last entry during follow-up after discharge to obtain information on residual impairment or history of any repeat stroke. Information on residual impairment was obtained from the clinicians notes recorded during the follow-up visits.

Retrieval of this information was done at the Health Records Department in a particular room allocated to researchers. Data abstraction was carried out by the Principal Investigator.

To ensure protection of records, files were not allowed to be removed from the health records department. Files were retrieved in small batches of between ten (10) to twenty (20) files to minimise disruption of services for active patients. The above process is represented as a flowchart in Figure 3.

Figure 3: Patient Recruitment Procedure



6.8 Data Management and Analysis

After retrieving the files from the Health records Department at KNH, the relevant information was collected by the principal investigator using the data collection sheet (Appendix 3). Data was then coded and entered in Statistical Products and Service Solutions (SPSS) version 21.0 software for analysis. The profile of the population was described using demographic, presenting and risk factor characteristics. Clinical outcomes of cerebral vascular event was measured using mortality rate, length of hospital stay in days and time from admission to diagnosis. Diagnosis was based on clinical features and neuro-imaging results demonstrating cerebral vascular disease. Categorical data was summarized into percentages while continuous variables analysed and presented as means or medians where applicable. Chi square test was used to associate mortality with the type of stroke. Statistical tests were interpreted at 5% level of significance (p value less or equal to 0.05). Study findings were presented in form of tables, graphs and charts.

7. ETHICAL CONSIDERATION

Permission to conduct this study was sought from the Department of Paediatrics and Child Health, University of Nairobi. Ethical approval was then sought from Kenyatta National Hospital and University of Nairobi Ethics and Research Committee (KNH/UON-ERC). Given the retrospective nature of this study, individual consent was not required and waiver for individual consent from KNH/UON-ERC was exempt because information was being

collected from secondary data (reviewing of patients' files). Questionnaires were coded to protect patients' privacy.

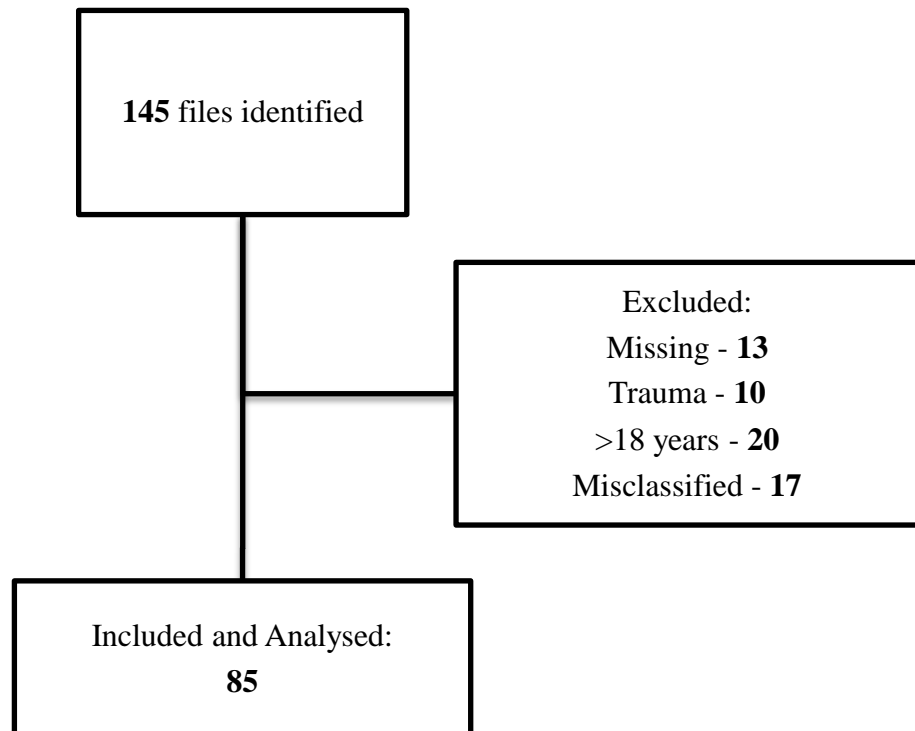
8. RESULTS

Using the ICD-10 codes for CVD, a list of 145 files was identified. A total of 60 files were excluded as follows:

- Seventeen (17) files were misclassified as CVD. The misclassification was based on errors in inputting the codes during computerization of the records. This information was relayed to the team at the health records department and the codes were rectified.
- Ten (10) were excluded due to traumatic aetiology of CVD
- Twenty (20) did not fit the inclusion criteria for age. They were all above 18 years
- Thirteen (13) files were missing

Eighty five (85) met the inclusion criteria and data from these files was extracted and analysed. Given the obtained sample size, the degree of precision for this study was 10.4%. The above process is represented as a flowchart in Figure 4:

Figure 4: Study procedure



8.1 Baseline Characteristics

Table 2: Baseline Characteristics of Children with Cerebral Vascular Disease

Variable	Frequency (%)
Gender	
Male	47 (55.3)
Female	38 (44.7)
Age	
1 month-1year	11 (12.9)
2-4 years	19 (22.4)
5-9 years	33 (38.8)
10-14 years	13 (15.3)
15-18 years	9 (10.6)
Median age (IQR)	6.0 (3.1-10.0)
Initial presentation	
Seizures	37 (43.5)
Weakness	35 (41.2)
Headache	18 (21.2)
Altered consciousness	18 (21.2)
Nausea and vomiting	8 (9.4)
Irritability	3 (3.5)
Crania nerve palsy	3 (3.5)
Visual disturbance	2 (2.4)
Lethargy	1 (1.2)
Aphasia	1 (1.2)

Table 2 represents the baseline characteristics of children with CVDs. The median age of those included in the study was 6 years (Inter-quartile range 3.1-10.0) with a slight male predominance, 47 (55.3%) compared to 38 (44.7%) females. The male to female ratio was 1.24:1. Children aged between 5 and 9 years made the largest proportion of those with CVDs.

The initial clinical presentations were varied. The majority of patients presented with seizures at 43.5% (37 out of 85 patients) followed closely by weakness at 41.2% (35 out of 85 patients). Headaches and altered consciousness were also relatively common both at 21.2% (each with 18 out of 85 patients). Of the 35 who presented with weakness, 2 had monoplegia, 1 had paraplegia, 8 had hemiparesis and 24 had hemiplegia.

The less common presentations included the following: 8 had nausea and vomiting (9.4%), 3 with irritability (3.5%), 3 with cranial nerve palsies (3.5), 2 with visual disturbance (2.4%), 1 with lethargy (1.2%) and 1 with aphasia (1.2%). Those with cranial nerve palsies all presented with facial nerve palsy. Most of the patients had multiple clinical presentations.

8.2 Noted Risk factors of Children with Cerebral Vascular Disease

Table 3: Risk Factor Profile

Risk Factor	Frequency (%)
Sickle Cell Disease	22 (25.9)
Intracranial Infections	20 (23.5)
Other Cardiac Disease	13 (15.3)
Congenital Heart Disease	9 (10.6)
Other Haematological Disorder	8 (9.4)
Arteriovenous Malformation	8 (9.4)
Other Vascular Disorder	2 (2.4)
No Identified Risk Factor	2 (2.4)
Substance Abuse	1 (1.2)

Table 3 demonstrates the risk factor profile of children with cerebral vascular disease. It was noted that the most common risk factor was Sickle Cell Disease (SCD) at 25.9% (22 out of 85 patients) followed by intracranial infections at 23.5% (20 out of 85 patients)

Of those with intracranial infections, 12 out of 20 had bacterial meningitis (60%), 5 had meningoencephalitis (25%), 1 had tuberculous meningitis (5%) and 2 were classified as having other intracranial infections (10%) – 1 with cytomegalovirus (CMV) encephalitis in the background of HIV and 1 with mastoiditis with intracranial spread.

Those classified as having other cardiac disease comprised 13 of the 85 patients, with majority of them having dilated cardiomyopathy (8/13) and the rest with valvular heart lesions (5/13) which were rheumatic. One patient with Marfan's Syndrome had dilated cardiomyopathy with intracardiac clots which led to a cardioembolic ischaemic stroke.

Patients with congenital heart disease comprised 9 out of the total 85, majority of whom had Tetralogy of Fallot (7/9). Of the other two, one had Double Outlet Right Ventricle and the other had Transposition of the Great Arteries and an Atrial Septal Defect, complicated by Infective Endocarditis which was confirmed on Echocardiography.

Those with other haematological disorders were as follows: 2 had haemophilia, 2 had acute myeloid leukaemia with thrombocytopenia, 1 had idiopathic thrombocytopenic purpura, 1 had Fanconi anaemia, 1 had acute lymphoblastic leukaemia with thrombocytopenia and 1 had pancytopenia whose cause hadn't yet been identified by the time they died. All these 8 patients had haemorrhagic stroke.

The other vascular disorders were both related to hypertension; one was secondary to renal artery stenosis and the second had no identified cause of the hypertension despite being adequately investigated.

Two (2) patients had no identified risk factor for their cerebral vascular disease and one (1) patient had substance abuse as a risk factor – a 17 year old boy who abused alcohol, khat and marijuana and developed spontaneous massive intracerebral bleed.

8.3 Type of Cerebral vascular Disease

Ischaemic stroke was observed to be the most common of the cerebral vascular diseases at 67% (57/85) followed by haemorrhagic stroke at 25% (21/85). The least common were subarachnoid haemorrhage (SAH) and cerebrovenous sinus thrombosis at 7% (6/85) and 1% (1/85) respectively. Figure 5 illustrates the types of CVDs.

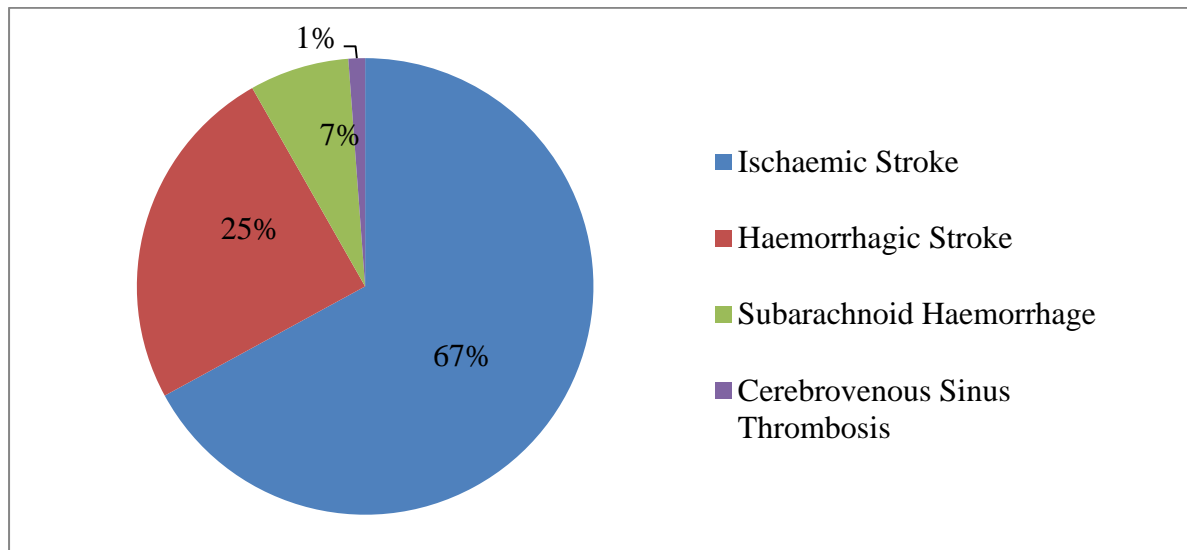


Figure 5: Type of Cerebral Vascular Disease

8.4 Clinical Outcomes of Children with Cerebral Vascular Disease

The clinical outcomes studied included length of hospital stay, duration from admission to diagnosis, presence of residual impairment and mortality. These results are represented in Table 4. Children were admitted in hospital for an average of 15 days (SD) with a median duration of 2 days from admission to diagnosis (inter-quartile range 0-6.5).

Fifteen (15) of the 85 patients died giving a 17.6% mortality. Only 6 (8.6%) had recurrent stroke and all of them had SCD as a risk factor. Five (5) out of the 6 had only 1 repeat stroke but 1 patient had a stroke recurrence 3 times.

In those who were alive, there was residual impairment in 56 of the 70 patients (80%) with most patients having residual weakness (25, 44.6%), convulsions (11, 19.6%) and speech difficulties (10, 17.9%). Out of the 25 with residual weakness, 2 had a monoplegia, 8 had hemiparesis and 15 had hemiplegia.

Table 4: Clinical Outcomes of children with Cerebral Vascular Disease

Variable	Frequency (%)
Mean length of hospital stay in days (SD)	15
Median duration from admission to diagnosis in days (IQR)	2.0 (0-6.5)
Outcome	
Alive	70 (82.4)
Dead	15 (17.6)
History of more than one stroke (n=70)	
Yes	6 (8.6)
No	64 (91.4)
Presence of residual impairment (n=70)	
Yes	56 (80)
No	14 (20)
Residual impairment (n=56)	
Weakness	25 (44.6)
Convulsions	11 (19.6)
Speech difficulties	10 (17.9)
Visual disturbance	8 (14.3)
Difficulty in reading	2 (3.6)
Behaviour change (hyperactivity)	1 (1.8)
Delayed milestones	1 (1.8)
Poor balance	1 (1.8)

8.5 Comparison of Mortality by Type of Cerebral Vascular Disease

Table 5: Mortality by Type of Cerebral Vascular Disease

Variable	Outcome		OR (95% CI)	P value
	Dead	Alive		
Ischaemic	6 (10.5)	51 (89.5)	1.0	
Haemorrhagic	8 (38.1)	13 (61.9)	5.2 (1.5-17.7)	0.008
Sub-arachnoid Haemorrhage	1 (16.7)	5 (83.3)	1.7 (0.2-17.1)	0.652

Table 5 demonstrates a comparison between mortality and type of CVD. A total of 57 patients were recognized to have ischaemic stroke. Six (10.7%) died, with a calculated odds ratio of 1. Having an ischaemic stroke did not affect the odds of mortality. Eight of the 21 patients with haemorrhagic stroke died, with a calculated odds ratio of 5.2 (95% CI = 1.5-17.7). There were increased odds of death with haemorrhagic stroke. Of the total patients with SAH, 1 died, with a calculated odds ratio of 1.7 (95% CI = 0.2-17.1) meaning that there was also increased odds of death with SAH but not as high as it was with haemorrhagic stroke.

Using ischaemic stroke as the baseline, a comparison was made between ischaemic and haemorrhagic stroke and ischaemic stroke vs subarachnoid haemorrhage. Ischaemic vs haemorrhagic stroke had a *p*-value of 0.008 which was significant whereas a comparison between ischaemic stroke vs SAH had a *p*-value of 0.652 which was not statistically significant.

9. DISCUSSION

This study aimed at retrospectively looking at the clinical profiles and outcomes of children with cerebral vascular diseases at Kenyatta National Hospital over a 2.5 year period (between October 2013 and April 2016). The main finding noted was with regard to the risk factors. It was noted during data collection that most of the risk factors were ailments. Only one patient had substance abuse as a risk factor. The predominant risk factor in this study was Sickle Cell Disease at 25.9% (22/85) followed closely by intracranial infections at 23.5% (20/85). In Pakistan, Bibi et al noted intracranial infections as their most prevalent risk factor at 67%¹⁷ while Chung et al from Hong Kong noted that their most prevalent risk factor was Congenital Heart Disease at 30%.¹³ SCD was not noted as a risk factor in either of these studies. This may be due to the fact that SCD is highly prevalent in our set up compared to theirs.

The clinical presentation of children with CVDs at KNH was varied. Although most of the patients had multiple clinical presentations, majority presented with seizures at 43.5% (37/85) and weakness at 41.2% (35/85). Headaches and altered consciousness was also common as a presenting complaint at 21.2% for both (18/85). These findings showed some similarity to those found in the studies done in Pakistan and Hong Kong. Bibi et al from Pakistan had weakness and seizures as their most prevalent presentation at 80% (37 of 46 children) and 60.8% (28 of 46 children) respectively¹⁷. Chung et al noted that their most common presentation was seizures (52%), hemiplegia (34%) and headaches (22%).¹³

Of the 85 patients' files reviewed, the median age was 6 years, with 55.3% and 44.7% being male and female respectively. This gave a male to female ratio of 1.24:1. These findings were similar to those found by Chung et al from Hong Kong in 2004. The mean age of the 50 children they studied over an 11 year period was 5.6 years with a male to female ratio of 1.27:1.¹³

With regard to the clinical outcomes, there was a considerable high mortality of 17.6%, higher than the 12% concluded by the Canadian Paediatric Ischaemic Stroke Registry (CPISR) of 2002. This difference may however be attributed to several factors such as a difference in the risk factors (e.g. SCD more prevalent in Kenya) and possible better quality of healthcare in Canada compared to Kenya. Recurrent stroke was seen in 6 (8.6%). The CPISR reported a 20%-40% chance of stroke recurrence which is much higher than the results we achieved.⁹

Eighty per cent (80%) of patients had residual impairment, majority having residual weakness (25, 44.6%), convulsions (11, 19.6%) and speech difficulties (10, 17.9%). These results were comparable to data obtained by Tham et al from Singapore, who noted hemiparesis in 12 out of 25 children (48%), seizures in 4 (16%) and speech difficulties in 4 (16%).²⁰

Univariate analysis was employed to compare type of stroke versus mortality. Those with ischaemic stroke had the least mortality compared to those with either haemorrhagic stroke or subarachnoid haemorrhage. Those with haemorrhagic stroke had increased odds of death compared to those with ischaemic stroke (OR 5.2; 95% CI 1.5-17.7; *p*-value 0.008). Those with SAH had slightly increased odds of dying compared to those with ischaemic stroke (OR 1.7; 95% CI 0.2-17.1; *p*-value 0.652). This, however, was not statistically significant and may be attributed to the fact that the sample size was small and a very small proportion was found to have SAH.

This study highlighted that cerebral vascular diseases indeed cause significant morbidity amongst children. Sickle Cell Disease and Intracranial infections came up as the most common risk factors. Given this finding, more emphasis should be placed on these children in terms of investigating risks of developing CVDs so as to start treatment early enough in a bid to reduce residual impairment.

10. STUDY STRENGTHS

This study highlighted the presence of cerebral vascular disease in children, a condition thought not to affect children much, and its associated morbidity and mortality.

11. STUDY LIMITATIONS

The following study limitations were encountered:

- This being a retrospective study, a longer study period would have been favourable in order to achieve a good sample size. However, the health information computer system at the Records Department crashed with loss of all computed data between January 2008 and September 2013. This limited the study timeline chosen.
- A large number of files were excluded from the study due to misclassification. This was due to errors during inputting of codes into the health records system noted after files were retrieved. These errors were communicated to the team at the Health Information Department and rectified.
- Several files were missing contributing to a significant amount of missing data which also significantly affected the sample size.
- This being a retrospective study, there was heavy reliance on the availability and accuracy of the medical records.

The exclusion of several files due to misclassification or missing files drastically affected the sample size, with a final sample size of 85. However, efforts were made to reduce these limitations including giving the team at the Health Records Department enough time to go through the generated list to retrieve files that were missed during the first round of retrieval.

12. CONCLUSION

The following conclusions were made following data analysis:

- Sickle Cell Disease was the most common risk factor identified followed closely by intracranial infections, particularly bacterial meningitis.
- Seizures were the most prevalent clinical presentation and weakness was the most common residual impairment identified, particularly hemiplegia.
- The most common type of cerebral vascular disease identified was ischaemic stroke.

- There was relatively high mortality of 17.6% among the children with cerebral vascular disease in this study.

13. RECOMMENDATIONS

- Rigorous screening of all children with Sickle Cell Disease should be considered. This would aim at early detection of those at risk of developing CVD and commencement of appropriate preventive measures.
- Aggressive management of intracranial infections should be done to prevent CVD and its associated morbidity and mortality.
- Accuracy should be observed by the team at the Health Information Department during inputting of disease codes into their records system to avoid errors of misclassification.

14. REFERENCES

1. Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T , on behalf of the participants in the WHO collaborative study on the control of stroke in the community. Cerebrovascular disease in the community: results of a WHO collaborative study. *Bulletin of the World Health Organization*. 1980;**58(1)**:113-130
2. Adams Jr. HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL et al. Classification of subtype of acute ischemic stroke: definitions for use in a multicenter clinical trial. *Stroke*. 1993;**24(1)**:35-41
3. Weisberg LA, Strub RL, Garcia CA. Essentials of Clinical Neurology: Evaluation of Common Neurologic Signs and Symptoms. 2nd Edition. Rockville, Maryland: Aspen Publishers; 1989.
4. Bajzer CT. Cerebral vascular venous drainage. In: Bhatt DL, editor. Guide to Peripheral and Cerebrovascular Intervention. London: Remedica; 2004.
5. Lemke DM, Hacein-Bey L. Cerebral venous sinus thrombosis. *J.Neurosci.Nurs.* 2005; **(5)**:258-264.
6. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, et al. Heart disease and stroke statistics – 2008 update: a report from the American Heart Association statistics committee and stroke statistics subcommittee. *Circulation* 2008; **117(4)**:25-146
7. Lo W, Zamel K, Ponnappa K, Allen A, Chisolm D, Tang M, et al. The cost of pediatric stroke care and rehabilitation. *Stroke*. 2008; **39**:161–5.
8. Lynch JK. Cerebrovascular disorders in children. *Curr. Neurol. Neurosci. Rep.*2004; **4**:129–138
9. Lynch JK, Hirtz DG, DeVeber G, Nelson KB. Report of the national institute of neurological disorders and stroke workshop on perinatal and childhood stroke. *Pediatrics*. 2002; **109 (1)**:116-23
10. Mallick AA, O’Callaghan FJK. The epidemiology of childhood stroke. *Eur. J. Paediatr. Neurol.* 2010;**14(3)**:197-205
11. Al Sulaiman A, Bademosi O, Ismail H, Magboll G. Stroke in Saudi children. *J. Child. Neurol.*1999;**14(5)**:295-8
12. Giroud M, Lemesle M, Gouyon JB, Nivelon JL, Milan C, Dumas R. Cerebrovascular disease in children under 16 years of age in the city of Dijon, France: a study of incidence and clinical features from 1985 to 1993; *J.Clin.Epidemiol.* 1995; **48**:1343–8.

13. Chung B, Wong V. Pediatric stroke among Hong Kong Chinese subjects. *Pediatrics*. 2004;**114**(2):206-12
14. Agrawal N, Johnston SC, Wu YW, Sidney S, Fullerton HJ. Imaging data reveal a higher pediatric stroke incidence than prior US estimates. *Stroke*. 2009;**40**:3415-3421
15. Ogeng'o JA, Olabu BO, Mburu AN, Sinkeet SR. Pediatric stroke in an African country. *J.Pediatr.Neurosci*. 2010;**5**(1): 22–24
16. Tsze DS, Valente JH. Pediatric stroke: a review. *Emerg. Med. Int*.2011: 2011: 734506.
17. Bibi S, Gilani SYH, Shah SRA, Bibi S, Siddiqui TS. Childhood Strokes: Epidemiology, clinical features and risk factors. *J.Ayub. Med. Coll. Abbottabad*. 2011; **23**(2):69-71
18. Ndondo AP, Govender R. Paediatric Stroke.*CME: Your SA Journal of CPD: Paediatric neurology*. April 2011; **29**(4):150-154
19. Ganesan V, Hogan A, Shack N, Gordon A, Isaacs E, Kirkham FJ. Outcome after ischaemic stroke in childhood. *Dev. Med. Child. Neurol*. July 2000; **42**(7):455-61.
20. Tham EH, Tay SKH, Low PS. Factors Predictive of Outcome in Childhood Stroke in an Asian Population. *Ann. Acad. Med. Singapore*. 2009;**38**:876-81

15. APPENDICES

15.1 APPENDIX 1: WAIVER OF CONSENT



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Ref: KNH-ERC/ Mod&SAE/283



KENYATTA NATIONAL HOSPITAL
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27th November, 2017

Dr.Elizabeth Atieno Jowi
Reg. No.H58/68922/2013
Dept.of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Jowi

Re: Approval of waiver of individual consent- Study titled, "Clinical profile and outcomes of children with cerebral vascular disease at Kenyatta National Hospital" (P270/03/2016)

Your communication dated November 13, 2017 refers.

This is to confirm that KNH- UoN ERC approved waiver of individual consent since this was a retrospective study involving review of medical records where no identifiers were collected and met the HIPAA requirements for protection of health information. There was no direct contact with the patients.

Yours sincerely,

A handwritten signature in blue ink, appearing to read "M. L. Chindia", written over a circular scribble.

PROF. M. L. CHINDIA
SECRETARY, KNH- UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Chair, KNH- UoN ERC
The Chair, Dept. of Paediatrics and Child Health,UoN
The Dean, School of Medicine,UoN

Protect to discover

15.2 APPENDIX 2: ICD-10 CODES FOR CEREBRAL VASCULAR DISEASES

Table 6: ICD-10 Codes for Cerebral Vascular Diseases

160	Non-traumatic subarachnoid hemorrhage
161	Non-traumatic intracerebral hemorrhage
162	Other and unspecified non-traumatic intracranial hemorrhage
163	Cerebral infarction
165	Occlusion and stenosis of pre cerebral arteries, not resulting in cerebral infarction
166	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
167	Other cerebrovascular diseases
168	Cerebrovascular disorders in diseases classified elsewhere
169	Sequelae of cerebrovascular disease

15.3 APPENDIX 3: DATA COLLECTION SHEET

STUDY TITLE: CLINICAL PROFILE AND OUTCOMES OF CHILDREN WITH CEREBRAL VASCULAR DISEASE AT KENYATTA NATIONAL HOSPITAL

SECTION 1

Study number _____

Date _____

Age (years) _____

Sex 1. Male 2. Female

Date of admission _____

Date of diagnosis _____

Date of discharge / death _____

Length of stay in hospital (days) _____

Time from admission to diagnosis (days) _____

SECTION 2

1. Age at initial presentation (years) _____

2. Initial presentation

1. Headache	
2. Weakness	
3. Seizures	
4. Altered consciousness	
5. Irritability	
6. Lethargy	
7. Cranial nerve palsy (specify)	
8. Aphasia	
9. Nausea and vomiting	
10. Visual disturbance	
11. Other (specify)	

3. Risk factor

1. Sickle Cell Disease	
2. Congenital Heart Disease	
3. Other Cardiac Disease	
4. Intracranial Infection a. Bacterial meningitis b. Meningoencephalitis c. Tuberculous meningitis d. Other (specify)	
5. Haematological Disorder	
6. Vascular Disorders	
7. Arteriovenous malformation	
8. Other (specify)	

4. Type of CVD

1. Ischaemic stroke	
2. Haemorrhagic stroke	
3. Subarachnoid haemorrhage	
4. Cerebral venous sinus thrombosis	

5. Diagnosis confirmed by

1. CT Scan	
2. MRI	
3. MRA/MRV	
4. Post Mortem	

6. Affected territory (if ischaemic or haemorrhagic stroke)

1. Cerebrum a. Anterior cerebral artery b. Middle cerebral artery c. Posterior cerebral artery	
2. Cerebellum	
3. Brainstem	

7. Outcome

1. Alive

2. Dead

If alive, proceed to Section 3

SECTION 3: OUTCOMES IN PATIENTS WITH STROKE AND ARE ALIVE AT TIME OF STUDY.

1. History of more than one stroke?

a. 1. Yes

2. No

b. If yes, how many?

1

2

3

>3

c. How long after the first episode?

<1 month

1-6 months

6-12 months

>12 months

2. Is there any residual impairment?

a. 1. Yes

2. No

b. If yes, which one?

Weakness

Speech difficulties

Convulsions

Behaviour change


Difficulty in education

Visual disturbance

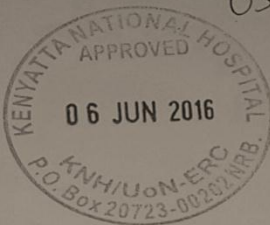
Delayed milestones

15.4 APPENDIX 4: ETHICAL APPROVAL


0569270



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06 JUN 2016
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6th June, 2016

Ref: KNH-ERC/A/193

Dr. Elizabeth Atieno Jowi
H58/68922/2013
Dept. of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Jowi

REVISED RESEARCH PROPOSAL- CLINICAL PROFILE AND OUTCOMES OF CHILDREN WITH CEREBRAL VASCULAR DISEASE AT KENYATTA NATIONAL HOSPITAL (P270/03/2016)

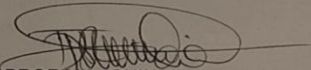
This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and **approved** your above proposal. The approval period is from 6th June 2016 – 5th June 2017.

This approval is subject to compliance with the following requirements:

- Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
- Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
- Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
- Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
- Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
- Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website <http://www.erc.uonbi.ac.ke>

Yours sincerely,


PROF M.L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Assistant Director, Health Information, KNH
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