ANATOMICAL VARIATIONS OF THE VERTEBRAL ARTERY IN A ZAMBIAN INDIGENOUS ADULT POPULATION UNDERGOING COMPUTERISED TOMOGRAPHY ANGIOGRAPHY AT THE UNIVERSITY TEACHING HOSPITALS LUSAKA, ZAMBIA

By

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A dissertation submitted in partial fulfillment of the requirements for the Degree of Master of Science in Human Anatomy

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DECLARATION

I, **Mutalife Fridah,** declare that this dissertation is my own work and that all the sources that I have quoted have been acknowledged by means of complete references. This work has not been submitted before for any other degree at any other university.

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APPROVAL

This dissertation for Mutalife Fridah has been approved as partial fulfillment of the requirements for the award of the Master of Science degree in Human Anatomy at the University of Zambia.

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ABSTRACT

Vertebral artery is an important source of blood supply to the brain. VA variations have a documented incidence ranging between 0.2% to 6.7 % in studies done using autopsy and angiograms in different countries. These variations increase the risks of aneurysms, dissections and leads to vertebrobasilar ischaemia and posterior circulation stroke. Knowledge of variations of the great vessels of the neck is important for endovascular interventionists and diagnostic radiologists, more so in the era of stent placement in the carotid and vertebral arteries and new therapeutic options for intracranial interventions.

This study aims to investigate VA variations in a black Zambian population and determine presence of vascular abnormalities.

A cross-section study was conducted to evaluate 42 Computer Tomography Angiography with various reasons. A data collection form was used to capture information and variations while analysis was done using Statistical Package for Social Sciences (SPSS) version 22.0. Mean and standard deviation were used to describe the variables.

The age ranged from 18 and 81 with mean age of (42.5±) of these 21 were females and 21 males. Of the 42 CTA examined, 11 had abnormalities of which 7 were females and 4 males. Since the VA is paired, each will be described individually. Therefore 84 arteries were examined for any variations and it was found that 16 (19.05%) vessels presented with some unusual features and 68(80.95%) were normal. 81(96.4%) VAs had a normal origin from the subclavian artery while 3 (3.6%) left VA originated from the aortic arch. On variations2 (2.4%) right VAs had fenestrations, 10 (11.9%) VAs had dual origin both right and left sided and 1 (1.2%) left VA was hypoplastic.

The study found that there are variations in the vertebral artery in our country and duplication is more prevalent. Therefore, further studies should be done to determine whether there is an association between the variations and development of cerebrovascular disorders.

Key words *vertebral artery, duplication, fenestrations and hypoplasia*

DEDICATION

This document is dedicated to God almighty for his mercy and favour having given me the privilege to acquire this knowledge.

To my family and husband for allowing me pursue this program and to all frien

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ACRONYMS

VA	Vertebral artery
VAH	Vertebral Artery Hypoplasia
NCD	Non Communicable Diseases
CTA	Computed Tomography Angiography
CVD /A	Cerebrovascular Disorders / Accidents
IQR	Interquartile Range
SD	Standard Deviation
RVA	Right Vertebral Artery
LVA	Left Vertebral Artery
SPSS	Statistical Package for Social Sciences
UNZA	University Of Zambia
UTH	University Teaching Hospital
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION

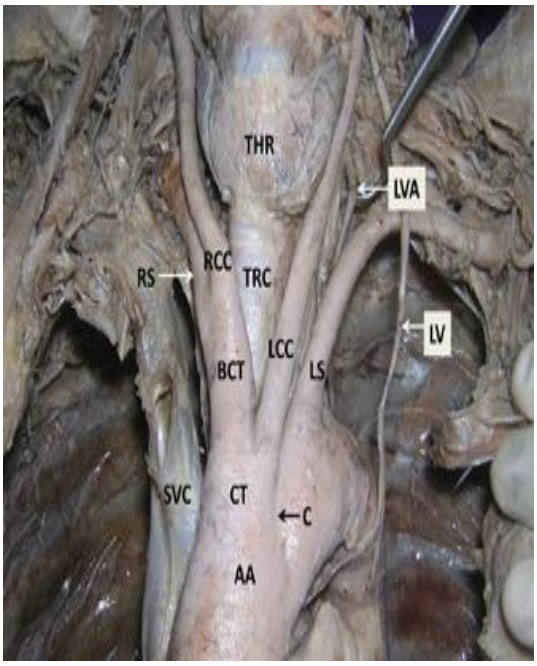
The vertebral artery (VA) originate from the first part of the subclavian artery and unite to form the basilar artery which is the primary blood supply for infratentorial brain structures such as the mesencephalon, pons, medulla oblongata and cerebellum. VA pathologies, including anomalous origin and course, duplication, fenestration and aneurysm formation implicate typically in cerebrovascular events as it is a source of blood supply of posterior circulation (Polguj *et al*., 2013). There are a number of congenital variations of the vertebral arteries and the commonly encountered variations in routine cadaveric dissections and during imaging procedures include *abnormal origin, asymmetry, duplication, fenestration* and *hypoplasia* (Komiyama *et al*., 1999; Polguj *et al*., 2013). These variations increase the risks of aneurysms, dissections and leads to vertebrobasilar ischaemia and posterior circulation stroke.

Vertebral artery variations have a documented incidence ranging between 0.2% to 6.7 % in studies done using autopsy and angiograms in different countries. With the increase in the rate of cardiovascular diseases in developing countries and Sub-Saharan Africa (WHO, 2011), knowledge of the normal and possible variations of the vertebral arteries is indispensable and imperative in diagnosis, treatment and implementation of interventional measures.

Normally, the VA starts above the first rib plane, accounting for 97.1% while in a few cases, its origin is below the first rib plane and some start in the thorax accounting for 2.94%. A study reported that 94.2% of left VA *originated* from left subclavian artery *(Figure 1a)* and entered the *foramen transversarium* at C6 in nearly all cases and 6.3% of left VA originated from the aortic arch (Meila *et al.,* 2012). The origin of the left vertebral artery from the arch of aorta has been documented by different authors with a range of 3.1%–8.3% (Singla *et al*., 2010) *(Figure 1b).*

The *duplication* of the VA has been identified in 0.72% of cadavers (Polguj *et al*., 2013). Prevertebral duplication may occur when a portion of the primitive dorsal aorta persists along with two intersegmental vessels connected to the true VA. A *duplicated*

VA is a significant predisposing factor of vertebrobasilar cervical artery dissection due to significant haemodynamics alterations (Melki *et al*., 2012).



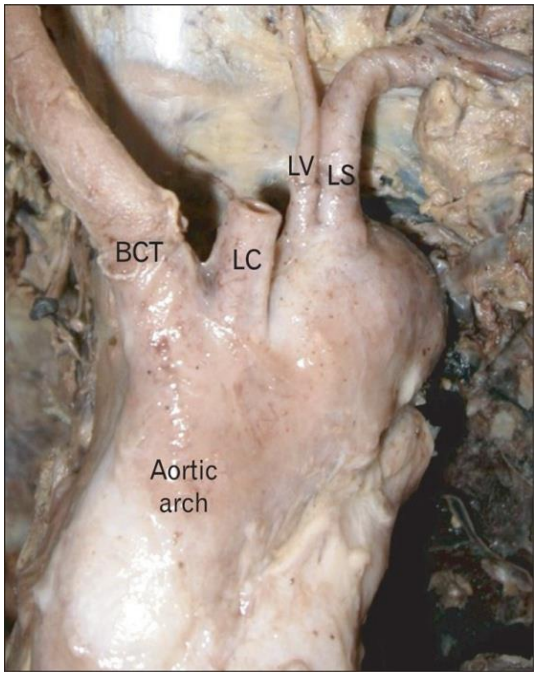


Fig 1a Origin of VA from subclavian artery Fig 1b Origin of VA from arch of aorta

Source; www.researchgate.net. Fig 1a AA: aortic arch, C: common origin of brachiocephalic & common carotid arteries, CT: common trunk, SVC: superior vena cava, BCT: brachiocephalic trunk, LCC: left common carotid, LS: left subclavian, LV: left vagus, RS: right subclavian, RCC: right common carotid, TRC: trachea, THR: thyroid gland, LVA: left vertebral artery
Fig 1b BCT: brachiocephalic trunk, LC: left carotid, LV: left vertebral, LS: left subclavian.

In approximately 60% cases, the arteries are unequal (*asymmetry*) in size. The left vertebral artery is often larger in size than the right. A study in Taiwan revealed that congenital vertebral artery *hypoplasia* is an uncommon embryonic variation of posterior circulation. The frequency of this congenital variation was reported to be 2-6.7% from autopsy and angiograms (Chuang *et al.,* 2006). In another study the VAs on both sides were equal in diameter in 23.3% patients. The right VA was larger in 30% patients and the left VA was larger than the right in 46.6% patients (Dodevski *et al*., 2012).

In the Sub-Saharan African countries scanty information has been found on the variations of the VA. A study done in Kenya investigated the pattern of vertebral artery hypoplasia in an adult black population. Ogeng'o et.al revealed that vertebral artery hypoplasia occurs in about 30% of black Kenyans studied, higher than in most other

populations studied (Ogeng'o et al., 2014). Another study by Park et al demonstrated a 28.9% prevalence of VAH, higher than 2.34–26.5% reported for most Caucasian and Indo-Asian populations (Park *et al*., 2007, Chuang *et al*., 2009)

In a black Zambian population there is no documentation of such variations. Therefore, this study aims to investigate VA variations and compare the findings with what is described in the literature.

1.1 Statement of the problem

Current global mortality from non-communicable diseases (NCDs) remains unacceptably high and is increasing (WHO, 2014). A factor in this increase could be intracranial and extracranial vascular anomalies. There are a number of congenital variations of the vertebral arteries and the commonly encountered variations in routine autopsy and during imaging procedures include *abnormal origin, asymmetry, duplication, fenestration* and *hypoplastic vertebral* arteries (Komiyama *et al*., 1999; Polguj *et al*., 2013). These variations increase the risks of aneurysms, dissections and leads to vertebrobasilar ischaemia and posterior circulation stroke. VA is an important source of blood supply to the brain (Vikram *et al.,* 2013) but there is paucity of information in the regional literature on the morphology of the vertebral vasculature in the black Zambian population.

Accurate knowledge of normal and variant arterial anatomy of the VA is important to neurosurgeons, head and neck surgeons who operate on the neck and radiologists who perform diagnostic investigations on the neck. Detailed knowledge and variations helps to avoid complications and iatrogenic injuries. Such a study was done by Kubikova et.al to emphasize the importance of detailed knowledge of the origin, course and variations of prevertebral segment of the vertebral arteries to prevent surgical complications especially in the era of carotid and vertebral artery stentings and new therapeutic options for intracranial interventions (Kubikova *et al*., 2008).

Geetharani and others concluded that understanding and reporting of the vertebral artery variants is essential to create awareness that can aid in various surgical and radiological procedures (Geetharani *et al.,* 2016).

Various types of anomalies exist in different populations, but the anomalies of the vertebral artery in black Zambian population have not been reported or documented. The findings obtained from this work will be useful for ultrasonographists, surgeons and radiologists by improving their diagnostic; operating and interventional skills and for anatomists in enhancing their knowledge base.

1.2 Significance of the study

The basic knowledge of vertebral artery variations is essential in diagnosis, treatment as well as in educating and training. In cases of occlusion of an internal carotid artery, the principal source of blood supply is through the vertebrobasilar system. For example vertebral *asymmetry* can cause insufficiency in the posterior circulation, which results in vertebrobasilar ischaemia. Asymmetrical vertebral arteries are also considered to be one of the risk factors for pontine infarction (Perren *et al*., 2007). A study of this nature which determines the anatomy and variations found in a black Zambian population can enhance in the reduction of iatrogenic injuries, bleeding and blockages and in the process reduce mortality and morbidity rate of cerebrovascular disorders / stroke patients. If the vertebral arteries are not identified in their normal position, this finding can be misinterpreted as the vessels being congenitally absent (Patasi *et al*., 2009).

Furthermore, knowledge of variations of the great vessels of the neck is important for endovascular interventionists and diagnostic radiologists, more so in the era of stent placement in the carotid and vertebral arteries and new therapeutic options for intracranial interventions.

The findings of this study would be of help to radiologists and surgeons especially with the installation of a catheter laboratory at the UTH as it will provide important clinical information to radiologists and vascular surgeons. Furthermore, such information is essential in a training program which will produce the future generation of specialists for the country.

1.3 Study question

What are the anatomical variations of the vertebral artery in a black Zambian adult (18 years and above) population undergoing computerised tomography angiography at the University Teaching Hospitals Lusaka, Zambia?

1.4 General objective

To investigate the types of anatomical variations of the vertebral artery

1.5 Specific objectives

1. To determine the origin of the vertebral artery.
2. To establish the presence of *duplication, fenestration, hypoplasia, dissections and any other anomalies detected in the stud*y.

CHAPTER TWO

LITERATURE REVIEW

The vertebral artery (VA) originates as the first branch of the first part of the subclavian artery at the base of the neck. The vessel takes a vertical posterior course to enter into the foramen transversarium of the sixth cervical vertebra. The vertebral arteries on both sides pass through the foramina transversaria of the first six cervical vertebrae, penetrate the posterior atlanto-occipital membrane and enter the cranial cavity through the foramen magnum (Standring *et al*., 2005). Both the right and left vertebral arteries merge to form the single midline basilar artery in a complex called the vertebrobasilar system. The system supplies blood to the posterior part of the Circle of Willis as well as a significant portion of the brain in the posterior cranial fossa (Arthur *et al*., 2010).

It divides into 4 segments: the Prevertebral (V1), Vertebral (V2), Atlanto-occipital (V3) and Intracranial (V4) segments *(Figure 2a and b)*. The segment of the artery from its origin at the subclavian artery to its respective transverse foramen is the pretransverse or prevertebral segment (Matula *et al.*, 1997).

Vertebral Artery segments

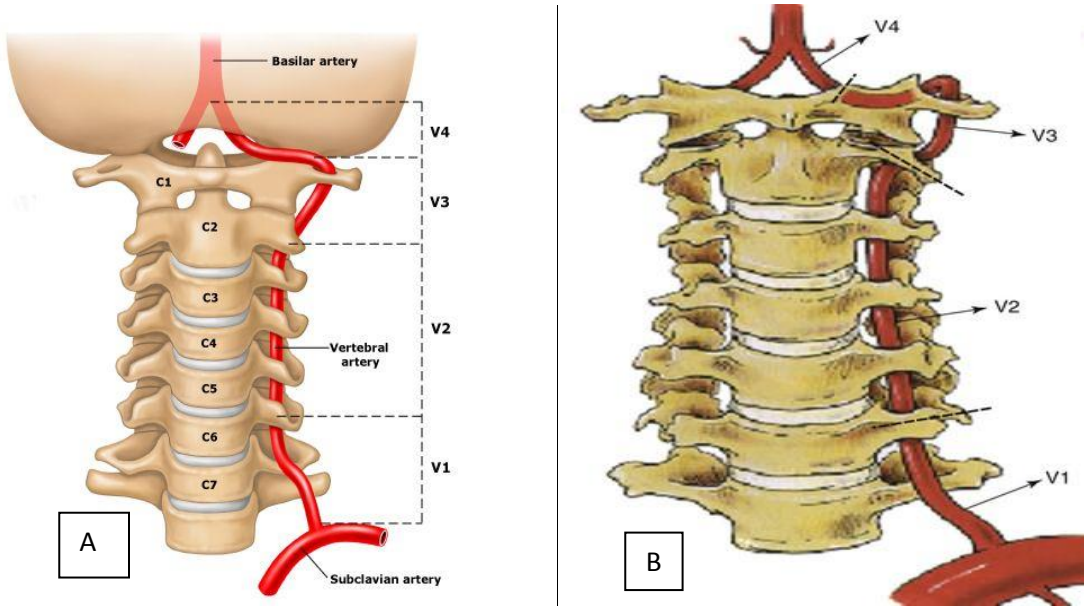


Figure 2a and b V1-prevertebral, V2-vertebral, V3- antlanto-occipital, V4-intracranial segments.
Source; www.cambridge.org.

2.1 Embryology of the VA

To understand anomalies of the great vessels and their branches, one must first understand embryologic development of the aortic arch. The development of vertebral arteries takes place between day 33 and 55 of intra-uterine life. The embryo develops 6 sets of matched aortic arches (Williams, 1995). These arches undergo selective apoptosis and the residual branch vessels constitute the aortic arch and great vessels. According to Sadler, *aortic arches* are paired arteries that arise from the aortic sac embedded in the mesenchyme of the pharyngeal arches and terminate in the right and left dorsal aortae (Sadler, 2012).While *intersegmental arteries* are sets of arteries arising from the embryonic dorsal aorta which supply blood to each somites and its derivatives *(Figure 3).*

Aortic arches

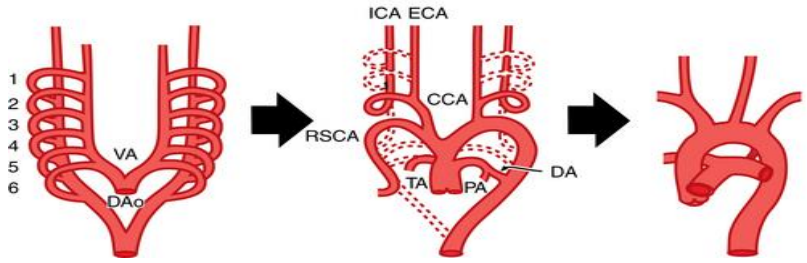


Figure 3 VA- Ventral aorta, DAo- Dorsal aortae, ICA/ECA- Internal & External carotid arteries, CCA- Common carotid artery DA- Ductus arteriosus, PA- Pulmonary artery and TA-Truncus arteriosus
Source; Langman's Medical Embryology text book (2012)

During this process of development, anatomic variants can form. The 1st and 2nd aortic arches (I and II) regress. The paired 3rd arches (III) form the 1st part of the internal carotid artery bilaterally. The proximal right 4th arch (IV) persists as the right subclavian artery while the left 4th arch forms part of the arch of the aorta. The 5th arch involutes and the 6th arch on the right becomes the pulmonary artery and on the left persists during intrauterine life as the ductus arteriosus. The left subclavian artery is derived from the 7th cervical intersegmental artery (Sadler, 2012). The vertebral artery is formed by the development of longitudinal anastomoses that link the cervical intersegmental arteries, which initially originate from each of the paired dorsal aorta. Intersegmental arteries eventually regress (5th and 6th) except for the 7th, which becomes the left subclavian artery and includes the point of origin of the vertebral artery (Sadler,

2012). Anomalous origins may lead to altered haemodynamics and predispose the patient to intracranial aneurysm formation.

Cerebrovascular disorders are one of the leading ailments affecting the modern mankind with high incidence of mortality rates and high levels of disabilities among those who survive cerebrovascular accidents (Voljevica *et al*., 2005). The Vertebral artery system shows a high incidence of variations. Variations of the VA may precipitate to the development of cerebrovascular diseases viz., stroke and aneurysms (Patasi *et al*., 2009). Variations in the form of *hypoplasia* and *duplications* are often prevalent. Asymmetry of vertebral arteries is quite common, but the amount of blood reaching the basilar artery remains constant due to the contralateral large VA (Gillilan, 1975). VA *hypoplasia* or *asymmetry* is frequently associated with posterior circulation stroke (Park *et al*., 2007).

The V3 segment of the VA is the most vulnerable source of blood supply for organs of the posterior cranial fossa (Dodevski and Tosovska-Lazarova, 2012). Due to significant dilation during the head rotation, the V3 became a favorable area of sudden *dissections* (Arthur *et al*., 2010). This segment of the VA possesses number of bends and loops those increase the resistance of blood flow generating target places for arteriosclerosis, thrombosis and wall calcification. Chronic ischaemia in the dependent on VA areas clinically leads to imbalance, disruption of motor coordination, dizziness and disturbance of vision. Dissection of the VA as well as its iatrogenic damage often results in the basilar stroke which has an unfavorable outcome (Cacciola *et al*., 2004).

Anatomical variation is defined as the "normal flexibility in the topography and morphology of body structures" (Satti *et al*., 2007). Many or most variations are totally benign some are errors of embryologic developmental timing or persistence of normally obliterated structures. The knowledge about the variations of the vertebrobasilar arterial complex is important for surgeons operating at the skull base, craniocervical junction, cervical region and for clinicians interpreting the imaging of this region (Poonam *et al*., 2010).

Vertebral artery hypoplasia (VAH) was described in the 19th century. Congenital vertebral artery *hypoplasia* is an uncommon embryonic variation of posterior circulation. The frequency of this congenital variation was reported to be 2-6% from autopsy and angiograms (Rameshbabu *et al*., 2014). The question raised is, could *hypoplasia* be a congenital risk factor for ischaemic stroke? VAH with caliber discrepancies of more than 1:1.7, were observed in up to 10% of normal individuals. There is no general agreement as to the definition of VAH. Operational definitions of VAH vary between diameters of less than 2 to less than 3 mm or an asymmetry ratio of equal or greater than 1:1.7 (Chuang *et al*., 2006). A study was done in Taiwan to find the association between vertebral artery *hypoplasia* and stroke and the results indicated higher incidence of VAH with brainstem/cerebellar ischaemic stroke of about 72%. Another study reported VAH in 13% of patients with posterior circulation strokes. The variant was more common in posterior circulation strokes as compared to matched controls with anterior circulation strokes (Perren *et al*., 2007). Moreover, the majority of posterior circulation strokes affected the brainstem and cerebellum. Park and others also investigated the frequency and clinical relevance of *hypoplastic* vertebral artery in patients with ischaemic stroke with or without vertebral artery territory and in normal healthy people. They found that 35.2% of the cohort had bilateral *hypoplastic* vertebral arteries (Park *et al*., 2007).

Vertebral artery *hypoplasia* has been known to be associated with regional hypoperfusion and complex neurovascular consequences that can lead to vestibular neuronitis and migraine pathogenesis (Campos, 2015). In another study the relationship between a *hypoplastic* vertebral artery and posterior circulation cerebral ischaemia was reviewed. The study revealed reduced blood flow in the *hypoplastic* vertebral artery which could have resulted in local cerebral hypoperfusion and subsequent focal neurological symptomatology. They concluded that risk of cerebral ischaemia is related to the severity of the *hypoplasia (*Katsanos *et al*., 2013)

Variations of the *origin* and course of the vertebral arteries are uncommon but extremely important to recognize in the diagnostic neuroradiology and for surgical and interventional procedures for treatment of patients suffering with cerebrovascular

disease. In a study done by Bergman and others the vertebral arteries presented with a number of variant positions. The presence of a vertebral variant must be considered in patients in whom the normal position of the VA cannot be detected (Bergman *et al*., 2012). Anomalous origin affects haemodynamics and may be associated with intracerebral malformations. However, there is no conclusive evidence that these variants predispose patients to cerebrovascular accidents. Nevertheless, theoretically, altered haemodynamics cause turbulence, which may predispose the patient to *aneurysm* formation and therefore, increase the risk of a cerebrovascular accident.

It has been suggested that *duplicated origin* of the VA may lead to altered haemodynamics and may be associated with cerebrovascular pathologies such as *aneurysm, dissection, kinking and arteriovenous malformation*s. Furthermore, duplication has significant clinical and surgical implications during endovascular interventional and neurosurgical reconstructive procedures. Failure to recognize such vascular variants might result in misdiagnosis leading to unwarranted and avoidable therapeutic interventions (Kim, 2009; Komiyama *et al*., 2001).

Unilateral *duplication* of the VA is rare with a reported incidence of 0.72% (Ionete & Omojola, 2006). Bilateral *duplication* of the VAs is extremely rare with two cases reported in literature. The dual *origin* of the VA has been found which usually remains silent with no clinical expression. But it is also reported that the altered haemodynamics of the anomalous origin may predispose a patient to certain cerebrovascular pathologies like aneurysm and dissection (Mordasisni *et al*., 2008). Another study reported an incidental observation of bilateral *duplication* which is one of the rarest anomalies of the extracranial segments of the vertebral artery (Polguj *et al*., 2013).

The term *"duplication"* is strictly applied to a vertebral artery that has two origins, a variable course and fusion level in the neck. *Duplication* occurs due to failure of involution of some embryonic vessels. Dual *origin* of the VA was first reported in 1844, and till 1999, only about 26 cases have been reported in literature (Harnier *et al*., 2008). All these cases were unilateral *duplication* of either right or left vertebral arteries involving the V1 segment. Bergman and others noted the presence of dual *origin* of vertebral arteries in 5 out of 693 studied specimens (0.72%) and incidentally all were

left-sided (Bergman *et al.,* 2012). Unilateral *duplication* of the vertebral arteries was extensively reviewed (Lemke, 1999) and a total of about 52 cases have been reported in the published literature till date. Unilateral *duplication* of left VA was observed in 27 cases and right VA in 25 cases, suggesting that this anomaly is more common on the left side. *Origin* of both limbs of a VA from the ipsilateral subclavian artery is more commonly observed on the right side. The limbs of the *duplicated* right VA originated from the right subclavian artery and others arose from brachiocephalic trunk, aorta, or thyrocervical trunk (Bruneau, 2006). The pattern of origin of one limb directly from the aortic arch and the second from the subclavian is more commonly observed on the left side. Another study claimed that *duplication* is a predisposing risk factor for dissection (Melki *et al*., 2012). Another study stated that development of the *duplication* is due to a portion of the primitive dorsal aortae which may not have regressed along with one or two intersegmental arteries that are connected to the vertebral artery (Sim *et al.,* 2001). In short duplication of the VA results from failure of controlled regression of the right or left fourth, fifth, or sixth intersegmental artery *(Figure 4)*.

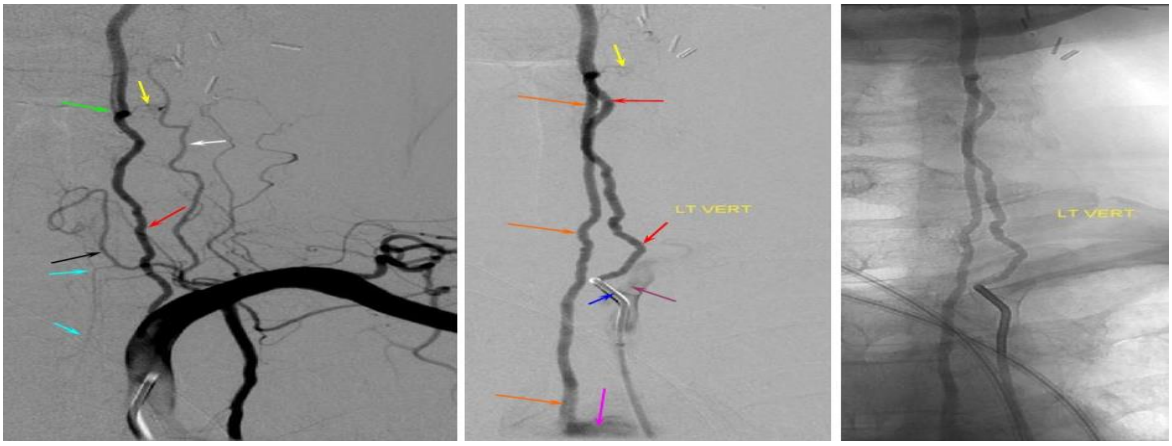


Figure 4. Duplication of the vertebral artery
Source; www.ijav.org

Another vertebral artery variant is *fenestration* which occurs when the vessel lumen is divided into two separate channels that eventually fuse, forming the primary vessel. Autopsy and angiographic studies suggest that the incidence of vertebral artery *fenestration* is 0.23%-1.95%. Although *fenestration* of the VA can occur either intra or extracranially, extracranial *fenestration* at the upper cervical level is more commonly

reported (Drapkin, 2000). The term *fenestration* has been synonymously used with *duplication* in the literature; however, the two describe different anatomical phenomena (Sim *et al*., 2001). *Duplication* of the vertebral artery refers to a condition where the vertebral artery has two origins that fuse at different levels of the neck where as fenestration occurs when there is a single origin that splits to form two channels that re-fuse distally (Ionete and Omojola, 2006). Although uncommon, vertebral artery *fenestrations* are more prevalent than *duplications*, and the extracranial portion of the left vertebral artery is the most common reported site for fenestration *(Figure 5).*

While the clinical significance of vertebral artery *fenestration* itself remains to be determined, it has been associated with multiple co-morbid vascular malformations. In a study done by Kubo and others demonstrated increased risk of saccular *aneurysm* formation and reported symptomatic intracranial *aneurysm* in 20% of patients with vertebral *fenestration* (Kubo *et al*., 2005). Another study demonstrated a 7% prevalence of vertebral artery *fenestration* in 51 cases with known arteriovenous malformation (Uchino *et al*., 2002). Some studies have reported association with epidermoid cysts, persistent trigeminal neuralgia and agenesis of the corpus callosum. *Fenestrations* are an important anatomical variant to appreciate in order to prevent any iatrogenic injuries while caring for patients undergoing endovascular and invasive intracranial interventions.

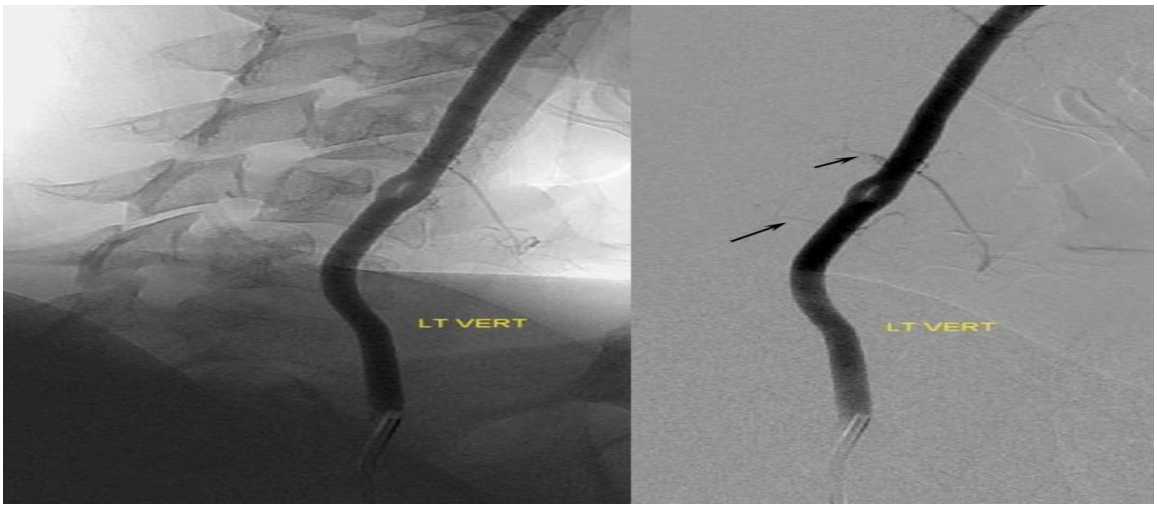


Figure 5. Fenestrated vertebral artery indicated by the arrows.
Source; www.ijav.org

CHAPTER THREE

METHODOLOGY

3.1 Study design

A cross - sectional descriptive study was conducted

3.2 Study setting

Radiology department at the University Teaching Hospitals

3.3.0 Study sample

Male and female adults who underwent computerised tomography angiography at the Radiology department at the University Teaching Hospitals

3.3.1 Inclusion criteria

Male and female adult patients undergoing CT angiography at radiology department UTH

3.3.2 Exclusion criteria

Patients who had traumatic head and cervical injuries undergoing computer tomography angiography (CTA)

Non Zambian patients (non indigenous black Zambian)

3.4 Sample size

The sample size was calculated using the formula $n= Z^2 \times P (1-P) / E^2$

n= sample required

Z= statistic for a given level of confidence = 1.96 when using 95% confidence interval

P = expected prevalence of the condition in the population being studied; prevalence of vertebral artery anomalies worldwide range from 0.2 to 6.6 % (average 3.4%)

E = confidence interval of 0.05 (± 5%)

$n=1.96^2$ x 0.034(1-0.034)/0.0025

3.84 x 0.034 x 0.966 / 0.0025

Sample size =50

3.5.0 Data collection

Date collection was collected and recorded on the data collection sheet. The researcher selected the patients and entered the demographic data on the collection sheet using code numbers, age, sex and diagnosis. Origin and variations of the vertebral artery were recorded by the radiologist.

3.5.1 CT Angiography Protocol

The research assistants (radiographers) followed the CTA protocol as they were getting CT angiography, 50ml of highly iodinated contrast agent was administered intravenously, followed by a saline chaser of 30ml, both with a flow rate of 5ml/s. CT angiography was performed from the aortic arch to the vertex with scan parameters 120kV and 300mA tube voltage and attenuation-based tube current modulation. Axial images were reconstructed with a slice thickness ranging from 0.5- 2.0 mm and an increment of 0.6 mm.

3.6 Data analysis plan

3.6.1 Image Analysis

The obtained axial images from CT angiography were transferred to a workstation for analysis. In addition to the axial source data, post processed multiplanar reformatted and 3D volume-rendering images were evaluated by the radiologist. The anatomic features of the right and left VAs were analysed and anatomical variations were recorded. The presence and origin of the VAs were carefully interpreted. Dual origin, fenestrations and hypoplastic segments in a few cases were also noted.

3.6.2 Statistical Analysis

The data obtained was tabulated and analysed using the Statistical Package for Social Sciences (SPSS) version 22.0 program. The dependent variable is the vertebral artery variations hypoplasia, duplication, fenestration and independent variables are origin, as well as age and gender see Table 1. Age is a continuous variable therefore; mean and standard deviation test would be used where as for the categorical variables Chi-Square would be employed see Table 2. All statistical tests would be performed at 5% significance level or 95% confidence interval with p-value of <0.05 to determine statistical significance.

Table 1. Variables

Independent variables	Scale of measurement	Dependent Variables
Age	Continuous	Vertebral artery variations
Gender	Categorical	
Origin	Categorical	Fenestration Duplication Hypoplasia All are categorical

Table 2. Data analysis plan

Statistical Package for Social Science		
Goals of analysis	Normally distributed	Not normally distributed
Categorical variables	Chi - Square	
Continuous variables	Mean & SD	Median & IQR

3.7 Ethical considerations

Ethical clearance was obtained from ERES converge. Permission was sought from Radiology department at the UTH. Patients spent minimal time in the laboratory to avoid over exposure to radiation since CT emits high radiation and confidentiality was guaranteed. The appropriate personnel were available to take care of the adverse effect of the contrast and any form of emergency. The radiologist took care of patients detected with anomalies.

3.8 Limitations of the Research

In the initial phase of the study due to lack of experience of similar studies in the past at UTH, the technicians assisting the researcher faced some technical difficulties; such as determining the dimensions of CT angiography slices, availability of contrast agent and injection timing.

Moreover the biggest drawback was the continuous breakdown of the CT scan machine which could not allow the researcher to enroll a large sample and delayed the study process.

CHAPTER FOUR

INTRODUCTION

This chapter analyses and presents the study findings which were collected using data collection form. The results are presented in frequency tables, figures, pie and bar charts.

4.1 Presentation of results

The results of the study have been presented according to the sections on the data collection form. Data is grouped according to the variables under discussion. The results are presented using the frequency tables, figures, pie and bar charts to explain the research results. The cross-tabulations have been used to demonstrate relationship between variables.

4.2 Demographic Data and Vertebral Artery Data

The data captured 21 females and 21 males with the age ranging between 18 and 81 years *(Tables 3 and 4).* All were black Zambians.

Table 3. Demographic Characteristics of Data

		Frequency	Percent	Valid Percent	Cumulative Percent
Gender	Male	21	50.0	50.0	50.0
	Female	21	50.0	50.0	100.0
	Total	42	100.0	100.0	

Table 4. Descriptive statistics (Age)

	N	Minimum	Maximum	Mean	Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic
Age	42	18.00	81.00	42.5000	18.52783
	42				

The mean age is 42.5± and SD is 18.53

4.3 Origin of the vertebral artery

All forty two right vertebral arteries took origin from the subclavian and three left VA from the aortic arch *(Table 5 and Figure 6).*

Table 5 Origin – Right VA

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Subclavian	42	100.0	100.0	100.0

Forty two (100%) of the right VA originated from the subclavian artery.

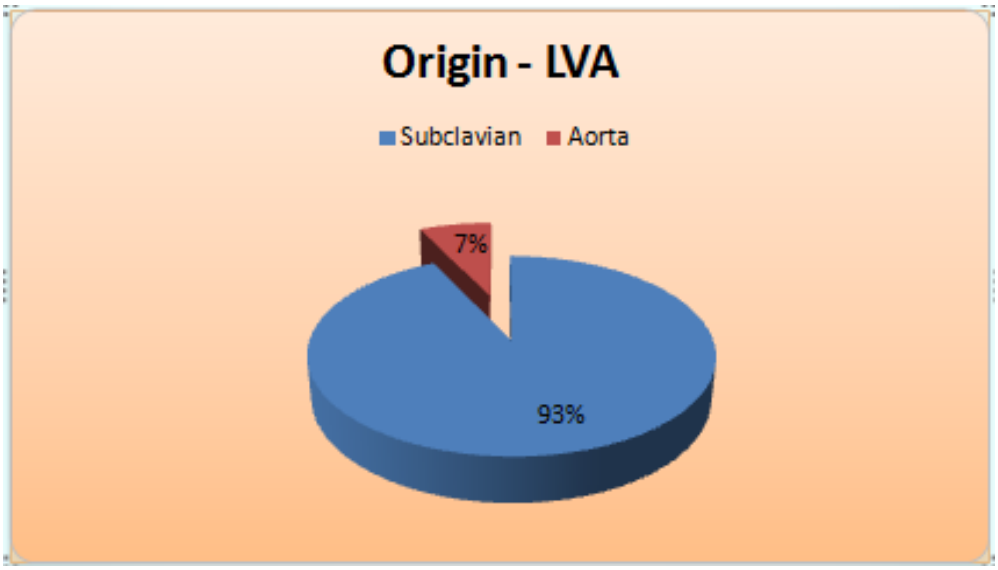


Figure 6. Thirty nine (93%) of the left VA originated from subclavian artery and three (7%) took origin from the aortic arch**.**

4.4 Relationship of the VA variations and the demographic data

Four (19%) were male and seven (33.3%) were females with VA anomalies with a p-value of 0.292 which is considered statistically insignificant *(Table 6).*

Table 6. Relationship of the VA variations and the demographic data

Variable			Variations in Vertebral Artery		Total	Chi - Square	p - value
			Abnormal	Normal			
Gender	Male	Count	4	17	21	1.109	0.292
		%	19.0%	81.0%	100.0%		
	Female	Count	7	14	21		
		%	33.3%	66.7%	100.0%		
	Total	Count	11	31	42		
		%	26.2%	73.8%	100.0%		

4.5 Vertebral artery variations

The variation of the VA was at 26% encountered in the study *(Figure 7).*

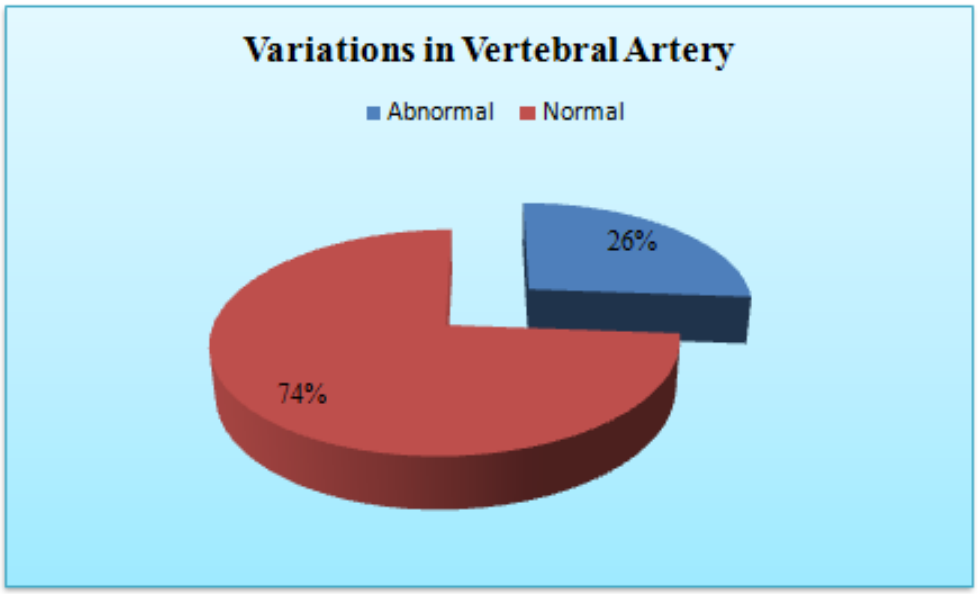


Figure 7. Eleven (26%) VA with abnormalities and thirty one (74%) normal VA

Figure 8a and b show the variations of the right and left vertebral artery.

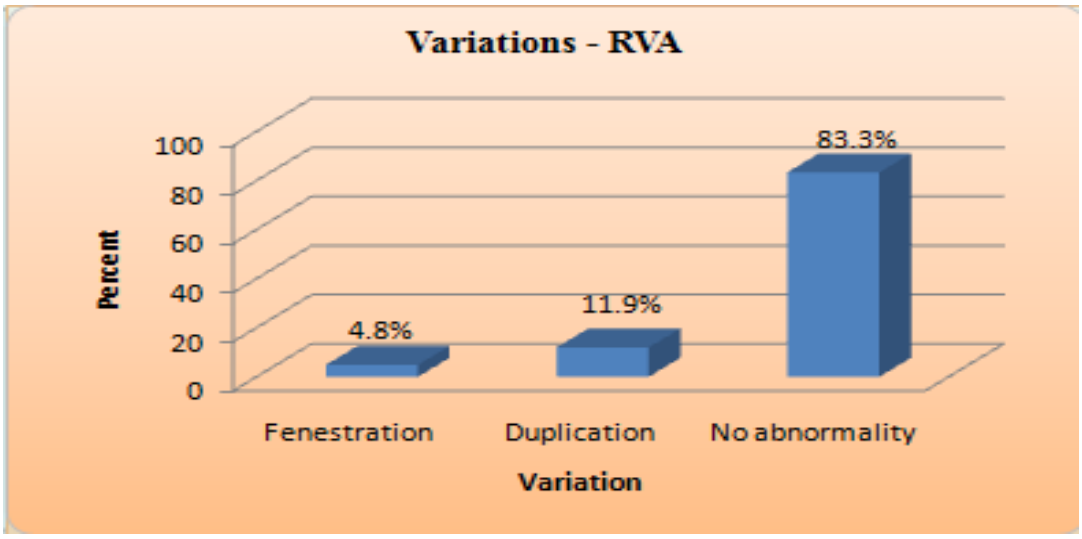


Figure 8a. Variations of the right vertebral artery (RVA) Fenestrations two (4.8%) and duplications five (11.9%) while thirty five (83.3%) had no abnormalities. All took origin from the subclavian artery.

Variations of left VA

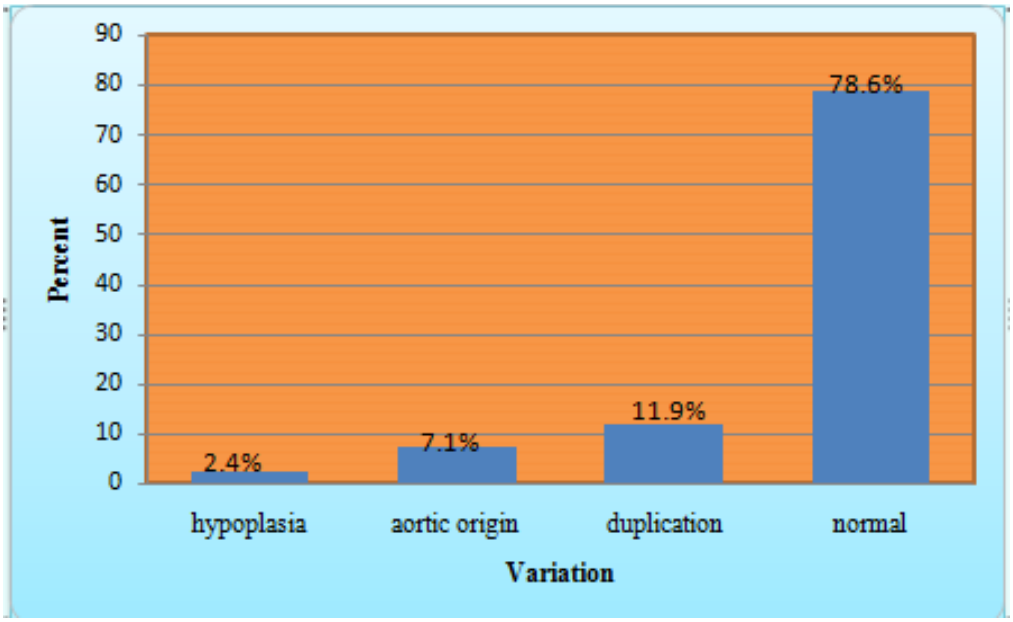


Figure 8b. Variations of the left VA, duplication five (11.9%) and hypoplasia one (2.4%) all took origin from the subclavian artery and three (7.1%) took origin from the aortic arch and thirty three (78.6%) had no abnormalities and took origin from the subclavian artery.

4.6 Vertebral artery variations as revealed on CT angiogram

Vertebral artery variations are common. These are the variations found on CT angiogram in the current study *Figures 9-12*

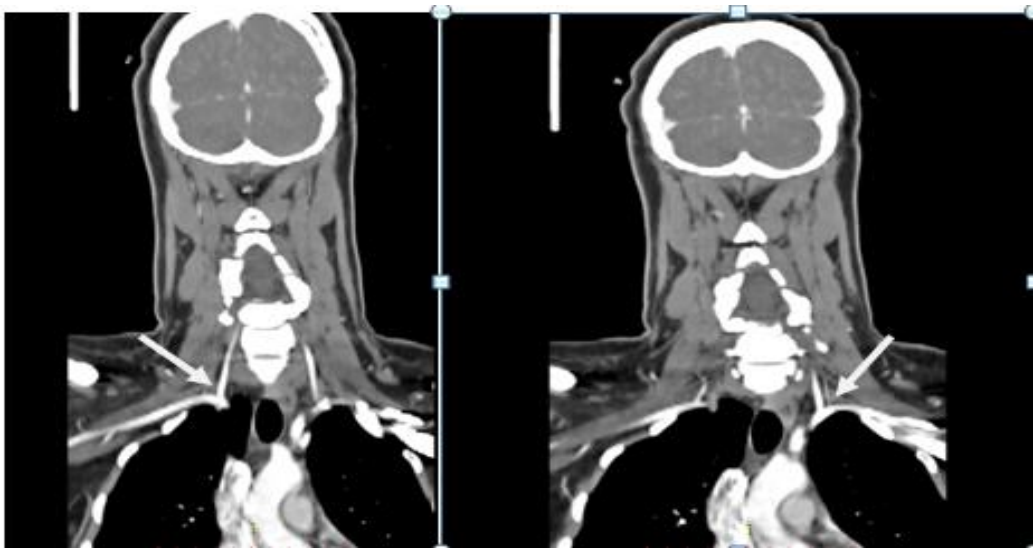


Figure 9: Normal right and left VA origin from the subclavian artery.

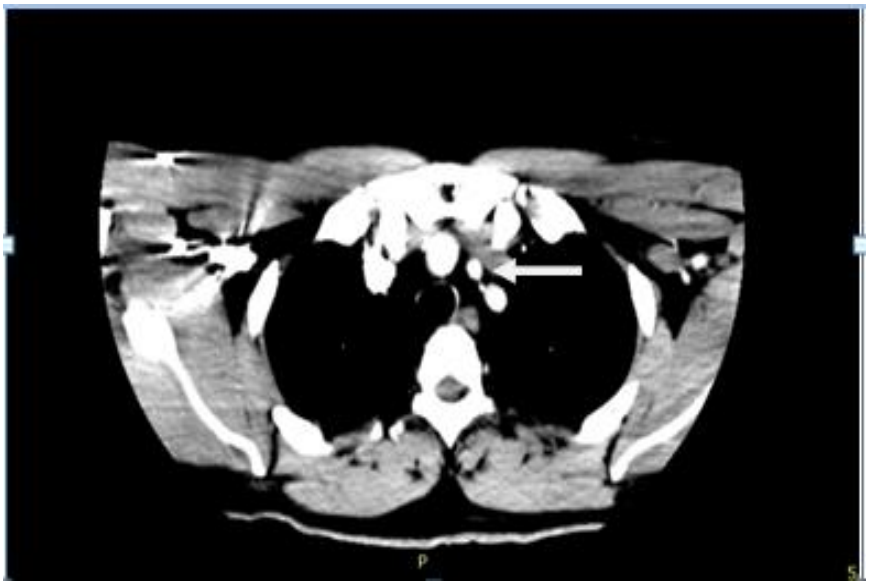


Figure 10: Left aortic VA origin in axial CTA

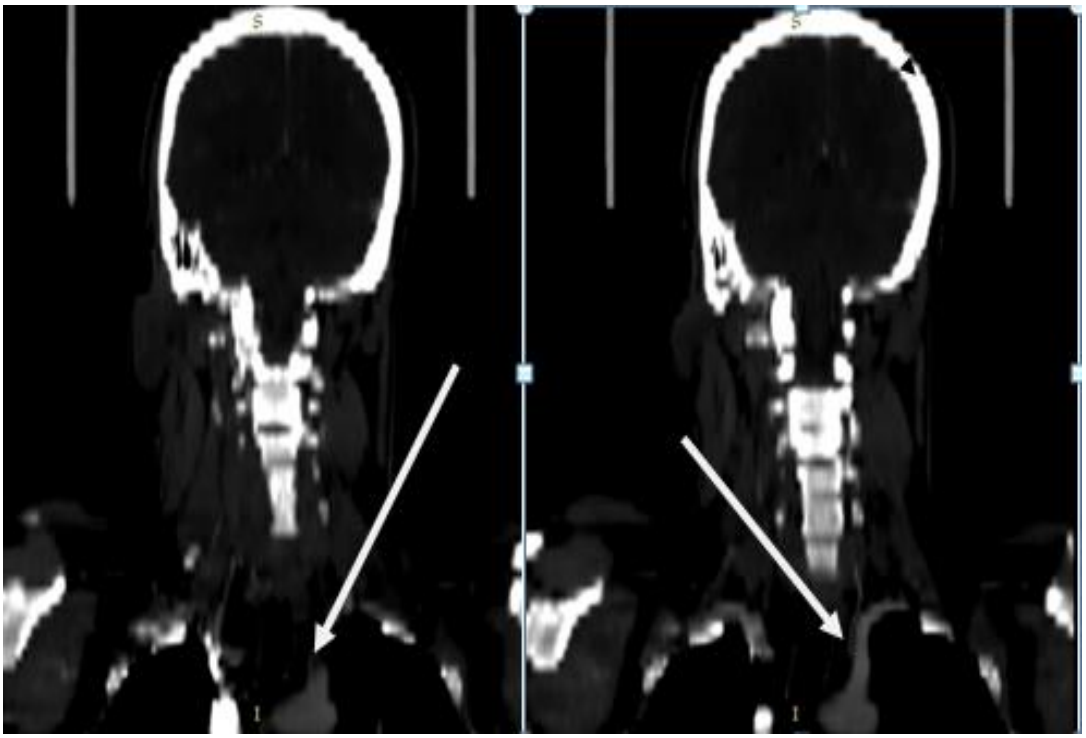


Figure 11: Left VA taking origin from the arch of the aorta running adjacent to the subclavian artery.

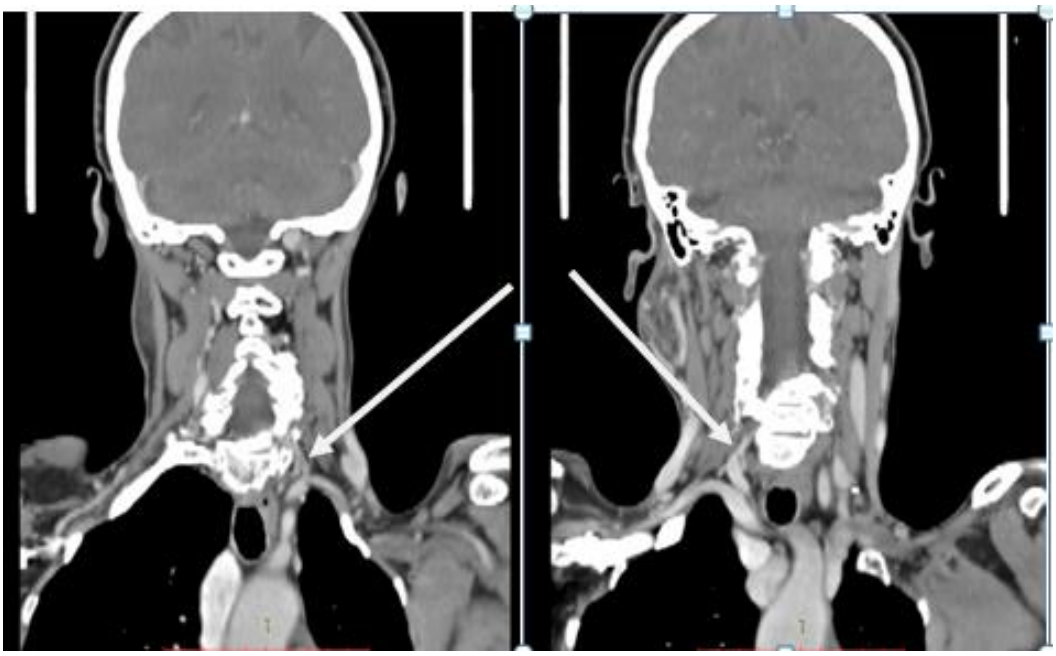


Figure 12: Right and left dual origin of the VA from the subclavian arteries in coronal CTA

CHAPTER FIVE

DISCUSSION

5.1 Vertebral artery variations

Of the CTA examined, eleven (26%) of forty two had abnormalities of which seven were female and four male while thirty one (74%) were normal. Since the VA is a paired blood vessel, each will be described individually. Therefore eighty four arteries were examined for variations and it was found that sixteen (19.05%) vessels presented with some unusual features. Sixty eight (80.95%) VAs were normal. Eighty one (96.4%) arteries originated from the subclavian artery while three (3.6%) took origin from the arch of aorta all were on the left side. Two vessels (2.38%) on the right had fenestrations, ten (11.9%) VAs had dual origin five from right and five from the left sided and one (1.19%) VA on the left was hypoplastic. The study found that variations of VA are consistent with findings from other studies.

5.2 Aortic origin of the Vertebral Artery

The aortic arch normally gives rise to three vessels: the brachiocephalic trunk, left common carotid artery and left subclavian artery. Direct aortic origin of left VA is the most frequent anatomic variant of VA with a prevalence of 2.4-5.8% in several large autopsy series, 2.4-2.5% in patients for cerebral angiography (Al-Okaili & Schwartz, 2007, Komiyama *et al*., 2001). Several aortic arch variations have been previously described including instances where both vertebral arteries originate as additional branches of the aortic arch. The variation examined in our case, report left VA origination in the aortic arch which has been previously reported at varying frequencies (*Figure 10 and 11*), with most studies reporting prevalence between 3% and 8% (Kubikova et al., 2008). We found a frequency of 7.14% (n = 3) which fall within the reported prevalence. In a previous study they recorded 5 out of 6 of their anomalous cadavers as female (Singla *et al*., 2010) where as in this study 2 of 3 are males. Our finding does not support studies done by Singla and friends which suggested that the anomaly is more prevalent in females than males. Perhaps this finding support the suggestion that prevalence of aortic origin in autopsy is higher than in CTA as there is a high chance of missing the anomaly. In comparison with other reports, Yamaki et

al examined the branch of the vertebral artery in 515 Japanese adult cadavers, in thirty (5.8%) left VA originated directly from the aortic arch and 1 right VA from brachiocephalic trunk (Yamaki *et al*., 2006). In another study done in Korean adults two (8%) of 25 examined arch of the aorta revealed that the left vertebral artery was directly originated from the arch of aorta (Shin *et al*., 2008) while Tetiker et al reported that among 76 cases, three (7.9%) of the left VA originated directly from the aortic arch. Such results were comparable to our results which revealed that three (7.14%) of 42 left VA took origin from the aortic arch *(Table 7)*. It is worth noting that the right VA rarely rises from the aortic arch.

Table 7: Comparison of origin vertebral artery with other studies

NO	Studies	No of VA studied	Origin of the VA						
			Subclavian		Aortic arch		Others		%
			Rt	Lt	Rt	Lt	Rt	Lt	
1	Current study	84	42	39		3			
2	Tetiker	76	38	35		3			
3	Melia et al	102	102	96		6			
4	Satti et al	Case report			1				

5.3 Duplication of the Vertebral Artery

Duplicated VA is a rare vascular variant (Bergman *et al*., 1988). It is defined as the VA with two origins which fuse at a variable level of the neck. VA is a result from abnormality of embryologic development of aortic arch and persistence of the intersegmental artery (Polguj *et al*., 2013). Five (11.9%) of the 42 patients who underwent CT angiography had a dual origin of the VA (*Figure 12*). Their age ranged from 20–79 years and 4 were females and 1 was a male. Females were more than male confirming with a study done by Singla *et al* which indicated that dual origin was more common in females than men. All 5 of 42 had bilateral dual origin of the VA. From literature it has been suggested that failure of the primitive dorsal aorta to regress together with the two intersegmental arteries may give rise to duplication of the VA

(Rameshbabu *et al*., 2014). During duplication of the VA, one limb can originate from the subclavian artery, whereas the second limb can originate from the aortic arch, subclavian artery, thyrocervical trunk, or innominate trunk and in this study both limbs were originating from the subclavian artery. Although duplication of the VA is asymptomatic in most cases, clinicians should consider this anomaly during diagnosis and treatment. VA duplication may be encountered unexpectedly during lower cervical anterior surgery and carotid endarterectomy.

5.4 Vertebral Artery fenestration

Vertebral artery fenestration occurs when the vessel lumen is divided into two separate channels that eventually fuse, forming the primary vessel. Autopsy and angiographic studies suggest that the incidence of VA fenestration is 0.23%-1.95% (Drapkin, 2000) these findings are actually incidental. However, in this study two (4.76%) of 42 right VA had fenestration. Ionete *et al*. 2006 reported that failure of the regression of the second intersegmental artery is thought to cause extracranial fenestration (Ionete *et al*., 2006). In another theory it is reported that the plexiform anastomoses fail to involute, leading to extracranial fenestration. VA fenestration has been reported to show some association with multiple co-morbid vascular malformations such as aneurysm and dissections. Kubo and others demonstrated increased risk of saccular aneurysm formation (Kubo *et al*., 2005). A study done by Uchino and others demonstrated a 7% prevalence of vertebral artery fenestration in 51 cases with known arteriovenous malformation (Uchino *et al*., 2002). Although the existence of vascular fenestration in the VAs is of less surgical importance, it may influence the management of intracranial and cervical pathologies by avoiding iatrogenic injury to the vertebral artery.

5.5 Vertebral artery hypoplasia (VAH)

VAH is not rare in the normal population. Although there is no clear definition of VAH, it has been generally defined as the diameter of hypoplastic VA of less than 2 mm or less than 3 mm or where an asymmetry ratio is equal or greater than 1:1.7 between the lateral and contralateral vessel on the luminograms (Park *et al*., 2007). However, probably the most important point is that no consensus exists on how to define VAH. To date, diameters between 2 and 3 mm as well as an asymmetry ratio

threshold >1:1.7 have been used to describe VAH (Perren *et al*., 2007). The published prevalence of VAH varies substantially roughly estimated to range from 1.9% to 11.6% (Katsanos *et al*., 2013). Our study observed one (2.38%) of 42 left VAH. The prevalence reported in our study is still consistent with the rates recently published by others *(Table 8).* A large ultrasound study was done by Park and others where 725 patients with cerebral infarction found a VAH prevalence of 7.4%. Another study described VAH frequency of 35.2% reported within a cohort of 529 patients with stroke and of 26.5% within a cohort of healthy individuals (Park *et al.,* 2007). A study done in Kenya revealed a 28.9% of 346 prevalence of VAH (Ogeng'o *et al*., 2014) higher than prevalence reported in other populations. Although, the VAH frequency observed in the present study is consistent with previous reports, it may not be absolutely comparable because of differences in the approach and definitions applied for its diagnosis. VAH is associated to increase the risk of posterior circulation ischemia, particularly in the territory of the posterior inferior cerebellar artery often due to a relative hypoperfusion to the region. Characteristics of this condition are also important in selection and moulding of catheters during interventional neuroradiological procedures as well as mitigating complications of endovascular treatment and prognostication of cerebrovascular disease.

Table 8: Comparison of VA variations with other studies

No	**Studies**	**No of VA studied**	**Variations of VA**						
			Duplication		**Fenestration**		**Hypoplasia**		**%**
			Rt	**Lt**	**Rt**	**Lt**	**Rt**	**Lt**	
1	Current study	84	5	5	2			1	15.5
2	Ogeng'o *et al*	346					60	40	28.9
3	Uchino *et al*	51			4				7
4	Kim	3386	7	3					0.3

CHAPTER SIX

CONCLUSION

In this study 42 CT angiograms were reviewed and 84 vertebral arteries were analysed, 16 arteries revealed unusual features; varying from aortic origin (n=3), duplication (n=10), fenestration (n=2) and hypoplasia (n=1). No anomalies were detected in the rest (n=68). The duplicated, fenestrated and hypoplastic arteries all took origin from the subclavian artery. This report therefore suggests that awareness of embryology of the VAs can help explain some of the anomalies detected in this study and permits for differentiation of variations from pathological conditions which afflict patients. The result of the present study is expected to provide important information on the vascular anatomy of the vertebral system and its anomalies.

Finally a detailed knowledge of the exact position of vertebral arteries has become more important, given the range of endovascular and surgical interventions available today and the constantly evolving imaging techniques. This calls for further studies on large sample size both CTA and cadaveric to give better insight into VA variations in our country.

6.2 Recommendations

1) A larger study not restricted to the UTH should be carried out to give a better insight of VA variations in our country. Nonetheless, the information from this study can be used as a stimulus and framework upon which further studies can be conducted in the future.
2) Studies should be conducted to investigate the possible association between variations and the development of vascular abnormalities.
3) Studies should be conducted on embalmed cadavers in order to compare the aortic origin of the VA as the detection rate for such an anomaly when cadavers are used is reported to be higher compared to when using CT angiography examination (Al-Okaili & Schwartz, 2007).

6.3 Dissemination of results

Results of this study will be presented to the post-graduate seminar week in August 2018 at the University of Zambia, main campus and to the Department of Surgery, UTH, Lusaka. The research article will be submitted for possible publication in journals such as the Zambian Medical Journal, the E-Journal of Zambia (UNZA) and International Anatomical / Specialised surgical Journals. The researcher will disseminate the results of the study by submitting bound copies of the study documents to the following: University of Zambia Medical library and the Main Campus Library, School of Medicine

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APPENDICES

Appendix 1: Letter of approval from Assistant Dean Postgraduate

UNIVERSITY OF ZAMBIA

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P.O Box 50110
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5 January 2018

Mrs. Mutalife Fridah
Department of Anatomy
University of Zambia
LUSAKA

Dear Mrs. Mutalife

RE: GRADUATE PROPOSAL PRESENTATION FORUM

Following the presentation of your proposal entitled "**Anatomical Variations of the Vertebral Artery in a Zambian Adult Population Undergoing Computerised Tomography Angiography at the University Teaching Adult Hospital Lusaka, Zambia**" your supervisor has confirmed that the necessary corrections to your research proposal have been done.

You can proceed and present to the Research Ethics.

Yours Sincerely

Dr. Lavina Prashar
Assistant Dean, Postgraduate

UNIVERSITY OF ZAMBIA
SCHOOL OF MEDICINE
-5 JAN 2018
ASSISTANT DEAN (PG)
P.O. BOX 50110, LUSAKA.

cc: HOD – Anatomy

Appendix 2: Approval letter from ERES converge

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I.R.B. No. 00005948
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31st January, 2018

Ref. No. 2017-Nov-026

The Principal Investigator
Ms. Fridah Mutalife
The University of Zambia
School of Medicine
Dept. of Human Anatomy
P.O. Box 50110,
LUSAKA.

Dear Ms. Mutalife,

RE: ANATOMICAL VARIATIONS OF THE VERTEBRAL ARTERY IN A ZAMBIAN ADULT POPULATION UNDERGOING COMPUTERISED TOMOGRAPHY ANGIOGRAPHY AT THE UNIVERSITY TEACHING ADULT HOSPITAL, LUSAKA ZAMBIA.

Reference is made to your corrections dated 8th January, 2018. The IRB resolved to approve this study and your participation as Principal Investigator for a period of one year.

Review Type	**Ordinary**	Approval No. **2017-Nov-026**
Approval and Expiry Date	Approval Date: 29th January, 2018	Expiry Date: 28th January, 2019
Protocol Version and Date	Version - Nil	28th January, 2019
Information Sheet, Consent Forms and Dates	• English.	28th January, 2019
Consent form ID and Date	Version - Nil	28th January, 2019
Recruitment Materials	Nil	28th January, 2019
Other Study Documents Questionnaires,	Data Collection Sheet.	28th January, 2019
Number of participants approved for study	-	28th January, 2019

Specific conditions will apply to this approval. As Principal Investigator it is your responsibility to ensure that the contents of this letter are adhered to. If these are not adhered to, the approval may be suspended. Should the study be suspended, study sponsors and other regulatory authorities will be informed.

Conditions of Approval

- No participant may be involved in any study procedure prior to the study approval or after the expiration date.
- All unanticipated or Serious Adverse Events (SAEs) must be reported to the IRB within 5 days.
- All protocol modifications must be IRB approved prior to implementation unless they are intended to reduce risk (but must still be reported for approval). Modifications will include any change of investigator/s or site address.
- All protocol deviations must be reported to the IRB within 5 working days.
- All recruitment materials must be approved by the IRB prior to being used.
- Principal investigators are responsible for initiating Continuing Review proceedings. Documents must be received by the IRB at least 30 days before the expiry date. This is for the purpose of facilitating the review process. Any documents received less than 30 days before expiry will be labelled "late submissions" and will incur a penalty.
- Every 6 (six) months a progress report form supplied by ERES IRB must be filled in and submitted to us.
- ERES Converge IRB does not "stamp" approval letters, consent forms or study documents unless requested for in writing. This is because the approval letter clearly indicates the documents approved by the IRB as well as other elements and conditions of approval.
- Every 6 (six) months a progress report form supplied by ERES IRB must be filled in and submitted to us. Late submission of these will attract a penalty.

Should you have any questions regarding anything indicated in this letter, please do not hesitate to get in touch with us at the above indicated address.

On behalf of ERES Converge IRB, we would like to wish you all the success as you carry out your study.

Yours faithfully,
ERES CONVERGE IRB

Prof. E. Munalula-Nkandu
BSc (Hons), MSc, MA Bioethics, PgD R/Ethics, PhD
CHAIRPERSON

Appendix 3: Letter of permission and approval to conduct research at UTH

THE UNIVERSITY OF ZAMBIA
SCHOOL OF MEDICINE

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH
UNIVERSITY TEACHING HOSPITAL
24 NOV 2017
SENIOR MEDICAL SUPERINTENDENT
PRIVATE BAG RW1X, LUSAKA

To :Dr Clarence Chiluba
The Senior Medical Superintendent
University Teaching Hospital
Lusaka

24 November 2017

Subject: Request for Mrs Fridah Mutalife to undertake an MSc Research Project

Reference: ANATOMICAL VARIATIONS OF THE VERTEBRAL ARTERY WITH REFERENCE TO CEREBORVASCULAR DISORDERS AT THE UNIVERSITY TEACHING HOSPITAL

Dear Dr Chiluba

I would like to introduce Mrs Mutalife who is an MSc Anatomy student in the University of Zambia. In order for her to undertake the chosen research project she will need access to contrast and CT scans in the Department of Radiology.

We request permission for her to come to your hospital on mutually agreed days and times for her to collect the necessary data. She will need permission to access the Department of Radiology.

We look forward to a favourable response to this request.

Yours Sincerely

Approved
27.11.17

Professor Krikor Erzingatsian Hon FRCSI; Hon FCS(ECSA)
Professor of Surgery, Department of Surgery UTH, UNZA
MSc Anatomy Coordinator

Appendix 4: Data collection sheet

Structured questionnaire

TITLE: Anatomical variations of the vertebral artery in a Zambian population undergoing computerized tomography angiography at the University Teaching Adult Hospital, Lusaka Zambia

Instructions

Indicate clearly the answer by ticking (X) or writing in the spaces below.

Study number……

Section A

PERSONNAL PROFILE

1.0 Gender male ( ) female ( )

1.1 What is your age? …….. Years

1.3 What is the diagnosis? ……..

1.4 Do you experience raised blood pressure (hypertension)? Yes ( ) No ( )

1.5 Do you experience raised blood sugar (Diabetes Mellitus)? Yes ( ) No ( )

1.6 Do you take alcohol? Yes ( ) No ( )

1.7 Do you smoke? Yes ( ) No ( )

Section B

Table 1. Origin of VA

VARIANT IN ORIGIN					
SUBCLAVIAN		ARCH OF AORTA		OTHERS	
Right	Left	Right	Left	Right	Left

Table 2. Variations

VARIANTS									
DUPLICATION		FENESTRATION		HYPOPLASIA		ANEURYSM		OTHERS	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left

APPROVED
29 JAN 2018
ERES CONVERGE
P/BAG 126, LUSAKA.

Appendix 5: CT scanner machine