Normal Position of the Cerebellar Tonsils in Relation to the Anteroposterior Diameter of the Foramen Magnum in Individuals of Different Age Groups

By

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DECLARATION

I, Patience Namakau Buumba, declare that this Dissertation is my own work and that all the sources I have cited have been indicated and acknowledged using complete references. I further declare that this Dissertation has not been previously submitted for a diploma, degree or for any other qualifications at this or any other university. It has been written according to the guidelines for Master of Science in Human Anatomy Degree dissertations of the University of Zambia.

Signature:…………………………………… **Date:**…………………………

CERTIFICATE OF COMPLETION OF DISSERTATION

I, Professor Erzingatsian Krikor, having supervised and read this dissertation is satisfied that this is the original work of the author under whose name it is being presented. I confirm that the work has been completed satisfactorily and is ready for final submission.

Signature…………………………………………… **Date**………………………

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CERTIFICATE OF APPROVAL

This dissertation of Patience Namakau Buumba has been approved in partial fulfillment of the requirements for the award of the Degree of Master of Science in Human Anatomy by the University of Zambia.

Examiner I

Signature:…….………………………… … **Date:**…………………….….

Examiner II

Signature: ……………………………. **Date**…………...…………

Examiner III

Signature……………………………… **Date**………………………

ABSTRACT

BACKGROUND: The cerebellar tonsils are part of the nervous system which is the chief controlling and coordinating system of the body. Their functional role is not yet known but are believed to coordinate skilled and learned movements. The cerebellar tonsils are prone to herniation through the foramen magnum in conditions causing increased intracranial pressure. If increased pressure compresses important brain structures, it can lead to serious, permanent problems or even death. Determining the normal position of cerebellar tonsils and its relationship with the Anteroposterior diameter of the foramen magnum in the Zambian population could provide guidance on considerations which need to be taken into account when making a possible diagnosis of individuals with cerebellar tonsillar herniation as well as in formulation of treatment objectives.

OBJECTIVE: The objective of the study was to determine retrospectively the relationship between the normal position of the cerebellar tonsils and the anteroposterior diameter of the foramen magnum in individuals of different age groups.

METHODS: A cross sectional study design was used which analysed, retrospectively, patient digital records of MRI scans of the brain taken at the Cancer Diseases Hospital in Lusaka from the year 2012 to 2014. Computer software tools, which included rulers, were used to measure lengths of the anteroposterior diameter of the foramen magnum by drawing a line from the Basion to the Opisthion (Basion-Opisthion reference line) and the position of the tonsils by drawing a perpendicular line from the inferior most point of the tonsils to the Basion-Opisthion reference line. Data analysis was performed using the Stata version 12 statistical software package.

RESULTS: From a sample of 127, 67 (52.8%) were female and 60 (47.2%) were male. The median age was 28 years (Inter Quartile Range 1 - 75). The average anteroposterior diameter of the foramen magnum and cerebellar tonsillar position were 36.5mm (range; 23.4mm - 47.6mm) and 0.5mm (range; -14.5mm – 13.1mm) respectively. Trends in the means of the position of the cerebellar tonsils showed that the tonsils were below the foramen magnum from ages 1-4 years ascending to a position above the foramen magnum by age 5years and reaching their highest point between 12-17 years then gradually descending again. Trends in the means of the AP diameter of the foramen magnum showed an increase in the size of the foramen magnum up to the beginning of adolescence at which point it remains almost constant. One unit (1mm) increase in the diameter of the foramen magnum resulted into a significant lowering of 0.13mm in the position of the cerebellar tonsils.

CONCLUSION: The study showed an association between cerebellar tonsillar position and the anteroposterior diameter of the foramen magnum with 1mm increase in the AP diameter of the foramen magnum causing a descent of 0.13mm of the cerebellar tonsils.

KEY WORDS: Cerebellar Tonsils, Anteroposterior Diameter, Foramen Magnum, age groups.

DEDICATION

To my baby Thabo

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DEFINITIONS OF TERMS USED

Basion	-	The median point of the anterior border of the foramen magnum of the occipital bone.
Basion-Opisthion Reference Line	-	A straight line drawn from the Basion to the Opisthion of the foramen magnum.
Chiari Malformationa	-	Congenital disorder that involves malformation of the skull and downward displacement of the cerebellar tonsils through the foramen magnum.
Foramen Magnum	**-**	An opening at the base of the skull which transmits the spinal cord.
Herniation	-	Abnormal protrusion of an organ or other body part through a defect or natural opening in a covering, membrane, muscle, or bone into another space.
Intracranial Pressure	-	The pressure that is exerted on the brain by both internal and external forces such as cerebral spinal fluid and blood.
Opisthion	-	The median point of the posterior border of the foramen magnum of the occipital bone.

LIST OF ABBREVIATIONS

ANOVA	**-**	Analysis of Variance
AP	**-**	Anteroposterior
CDH	**-**	Cancer Diseases Hospital
CNS	**-**	Central Nervous System
CSF	**-**	Cerebrospinal Fluid
CT	**-**	Cerebellar Tonsils
CTE	**-**	Cerebellar Tonsillar Ectopia
ICP	**-**	Intracranial Pressure
IQR	-	Interquartile Range
MRI	**-**	Magnetic Resonance Imaging
PNS	**-**	Peripheral Nervous System
RTA	**-**	Road Traffic Accident
UTH	**-**	University Teaching Hospital

CHAPTER ONE

INTRODUCTION

The cerebellar tonsils are part of the nervous system which is the chief controlling and coordinating system of the body. The nervous system adjusts the body to the surroundings and regulates all bodily activities both voluntary and involuntary (Chaurasia, 2010). Chaurasia describes the nervous system as having been divided into the Central Nervous System (CNS) and the Peripheral Nervous System (PNS). The CNS comprises the brain and spinal cord whereas the PNS comprises 12 pairs of cranial nerves and 31 pairs of spinal nerves.

The brain is the part of the central nervous system contained in the cranial vault (Fix, 2008). It is composed of the cerebrum, the cerebellum and the brain stem which is further subdivided into mid brain, pons and medulla (Moore and Agur, 1995). Moore and Agur have further described the brain as consisting of : two cerebral hemispheres which form the largest part of the brain occupying the anterior and middle cranial fossae of the skull; the diencephalon forming the central core of the brain; the midbrain (rostral part of the brain stem) which lies at the junction of the middle and posterior cranial fossae; the pons (middle part of the brain stem) which lies in the anterior part of the posterior cranial fossa; the medulla oblongata (caudal part of the brain stem) which lies in the posterior cranial fossa and is continuous with the spinal cord; and the cerebellum which is placed posterosuperior to the pons and medulla and lies beneath the tentorium cerebelli in the posterior cranial fossa.

The cerebellum as described by Standring (2008) is divided by numerous curved transverse fissures, the deepest fissures divide it into lobes and lobules. The deepest fissure in the vermis is the fissure prima, which curves ventrolaterally around the superior surface of the cerebellum to meet the horizontal fissures; it appears early in embryological development and marks the boundary between the anterior and posterior lobes.

On the posterior lobe are the tonsils which are the most prominent hemispheric structures of the sub-occipital surface (Figure 1), located inferomedially (Ramos et al, 2012). Ramos and others go on to describe the tonsils as being ovoid structures, which have a vertical average size of 13.5 mm, but may range from 10 to 18 mm, and a width average size of 7.8 mm which may range from 5 to 10 mm. Standring (2008) further explains that the nodule and attached flocculi constitute a separate flocculonodular lobe, which is separated from the uvula and tonsils by the deep posterolateral fissure.

Furthermore, Ramos et al (2002) pointed out that the tonsils are anterosuperiorly related to the inferior medullary velum and telachorioidea, laterally to the biventral lobule, superolaterally to the tellovelotonsillar cleft, posteriorly and inferiorly to the cisterna magna. These features can easily be seen on sagittal section of the brain (Figure 2).

The functional role of the cerebellar tonsils is not yet known but they are believed to coordinate skilled and learned movements. According to Marvridis (2014), the cerebellar tonsils belong to the neocerebellum (also called the pontocerebellum) which comprises the posterior lobe (except the uvula and pyramids) and is the largest portion of the cerebellum.

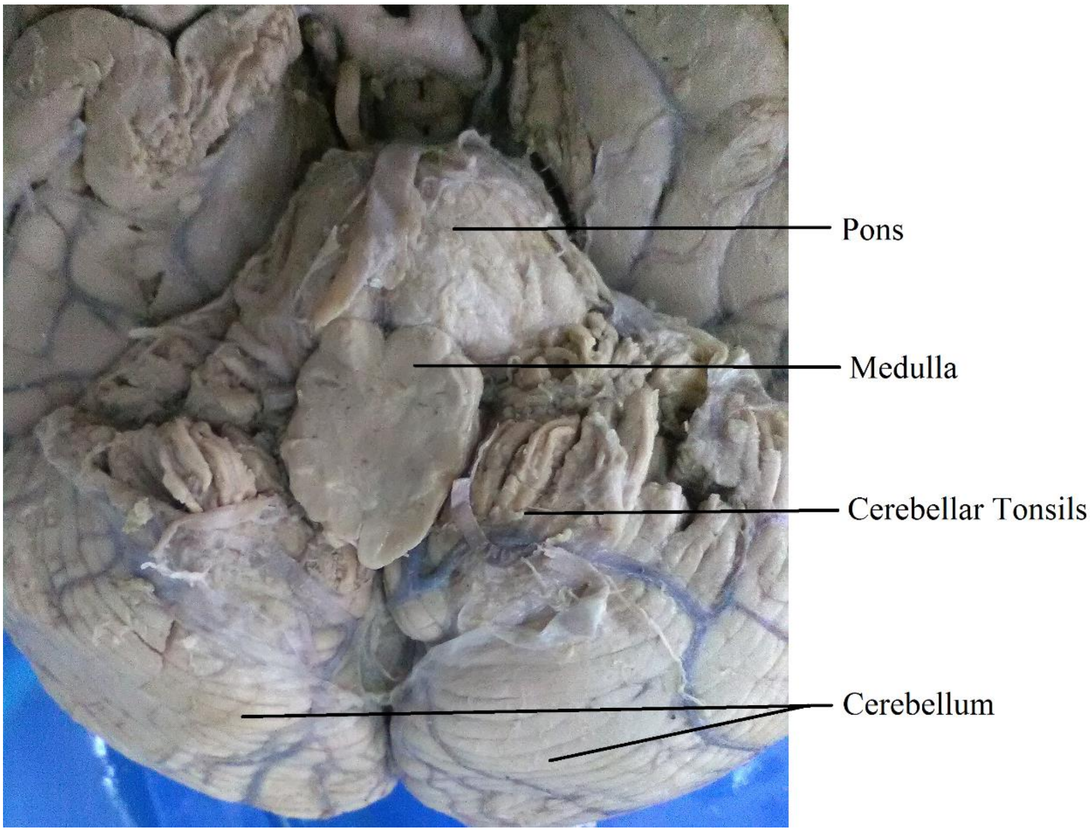

Figure 1.1: Inferior view of the cerebellum and the position of the tonsils on the inferior aspect of each of the cerebellar hemispheres taken at the dissection laboratory, University of Zambia, School of Medicine.

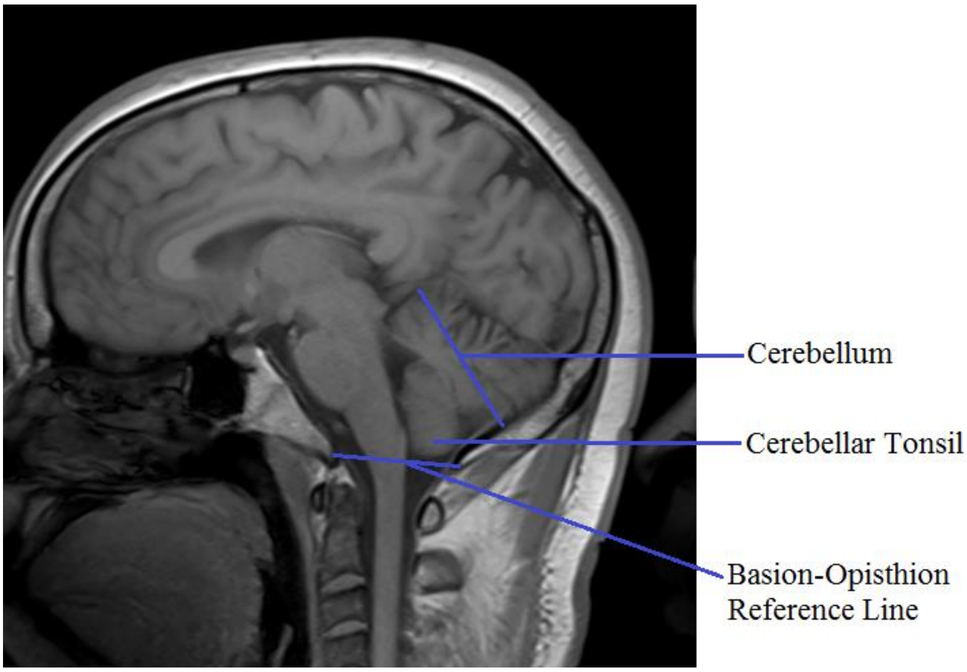

Figure 1.2: MRI sagittal section through the brain showing the cerebellar tonsil taken at Cancer Diseases Hospital, Radiology Department.

The cerebellar tonsils are prone to herniating through the foramen magnum (an opening at the base of the skull which transmits the spinal cord) (Figure 3), this can involve one or both tonsils, particularly in the instance of a Chiari malformation, a disorder that may be congenital or acquired.

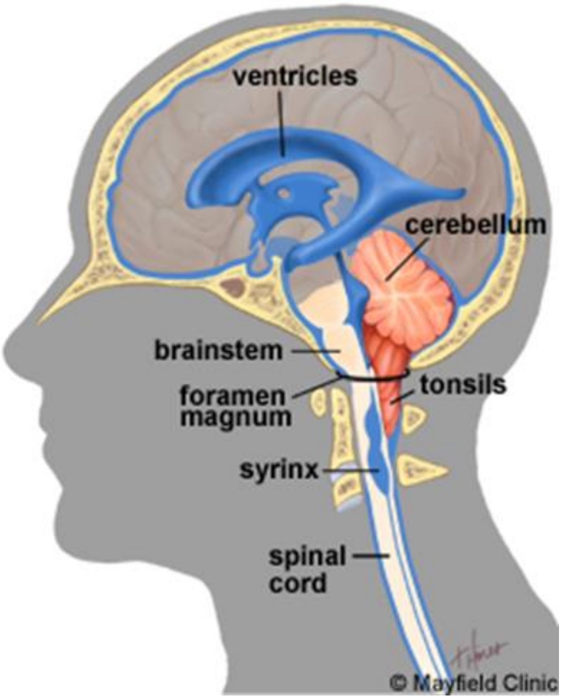

Figure 1.3: Showing Cerebellar Tonsillar Ectopia (Mayfieldclinic.com)

Tonsillar herniation can also occur in conditions that cause a rise in Intra-Cranial Pressure (ICP). Medical procedures such as lumbar puncture could cause a sudden drop in icp in the presence of raised intracranial pressure causing sudden death (Hoffman, 2015). This is corroborated by Mokri (2000), who indicated that abnormalities demonstrated on head MR imaging studies in patients with sudden CSF volume depletion include sinking or sagging of the brain and descent of the cerebellar tonsils sometimes mimicking Chiari I malformation.

Sudden increased ICP is a serious and often life threatening condition. If increased ICP compresses brain structures and blood vessels, it can lead to serious, permanent disability or mortality (Kantor, 2015). Causes of increased ICP as outlined by Dunn (2002) include; localised mass lesions (traumatic haematomas; extradural, subdural, intracerebral), neoplasms (glioma, meningioma, metastasis), abscesses, focal oedema (secondary to trauma, infarction, tumour), disturbance of CSF circulation, obstruction of major venous sinuses, defuse brain oedema (encephalitis, meningitis, diffuse head injury) and idiopathic intracranial hypertension.

An increase in ICP is a serious medical problem. The Michigan State University module for Increased ICP of 2007 explains that since the brain is enclosed in a rigid cranium, the free space to expand is limited. When the mass of the intracranial contents increases in the presence of disease, ICP increases. When ICP exceeds a critical point, displacement of organs or organ parts near a potential space(s) occurs, and herniations occur. The nature of herniation is determined by the location of the lesion. The pressure can damage the brain or spinal cord by pressing on important brain structures and by restricting blood flow into the brain (A.D.A.M. Medical Encyclopedia, 2003). Cerebellar tonsillar herniation through the foramen magnum can occur with increased ICP and could cause compression of the brainstem and upper cervical spinal cord as they exit the skull. This could result in dysfunction of respiratory and cardiac centres in the brain.

The position of the cerebellar tonsils can be measured with reference to a straight line drawn from the Basion to the Opisthion of the foramen magnum (Figure 4). This line also represents the Anteroposterior (AP) diameter of the foramen magnum (O'Connor et al, 1973). The Basion and Opisthion of the foramen magnum can easily be identified on sagittal section of the MRIs of the head.

Figure 1.4: sagittal section through the brain showing a line drawn from the Basion to the Opisthion of the foramen magnum taken at Cancer Diseases Hospital, Radiology Department

To measure properly the position of the cerebellar tonsils, Magnetic Resonance Imaging (MRI) is used. MRI scan is a non-invasive test used to evaluate the brain, spinal cord, and surrounding CSF (Mayfield clinic, 2013). Mayfield clinic further goes on to say that, herniation may reach the level of the first two vertebrae (C1 or C2) of the cervical spine and that herniation of the tonsils is often measured in millimetres (mm) below the foramen magnum. It has been observed that it is not enough to measure herniation of the tonsils below the foramen magnum. The normal position of the tonsils should be considered in order to determine the true extent of their displacement. This is so because many other studies, Mikulis et al (1992), Lakshmi (2015) and others, have confirmed the existence of variations in the position of the cerebellar tonsils in individuals of different age groups. These results have differed from study to study. Furthermore, it is important that the size of the foramen magnum be considered when determining the position of the cerebellar tonsils.

1.1 Statement of the Problem

Several studies carried out in various places around the world have indicated that there is no standard normal position of the cerebellar tonsils. This has been attributed in part to variations due to ethnicity of the study subjects. Since results of the studies done on the subject have been different every time, there is need to carry out a study on the Zambian population in order to have a proper reference range for diagnosis in our patients. Furthermore, researchers from around the world have looked at the normal position of the cerebellar tonsils in relation to age of the individual; gender; pathological conditions such as Chiari 1 Malformation; and the size and shape of the skull. To date there is no documented data about the normal position of the cerebellar tonsils in the Zambian population, or literature detailing the relationship of the size of the foramen magnum to the position of the cerebellar tonsils.

1.2 Study Objectives

1.2.1 Main Objective

The main objective of this study was to determine the relationship between the normal position of the cerebellar tonsils and the size of the foramen magnum in individuals of different age groups.

1.2.2 Specific Objectives

I. To determine the position of the cerebellar tonsils in individuals of different age groups.

II. To determine the anteroposterior diameter of the foramen magnum in individuals of different age groups.

III. To determine the correlation of the position of the tonsils to the AP diameter of the foramen magnum.

IV. To correlate the position of the cerebellar tonsils in individuals on demographic characteristics including gender.

1.3 Research Questions

1. What is the normal position of the cerebellar tonsils in individuals of different age groups in the Zambian population?

2. Is there a correlation between the size of the foramen magnum and the position of the cerebellar tonsils?

1.4 Significance of the Study

This study was aimed at finding out the normal position of the cerebellar tonsils in different age groups of the Zambian population as well as how the position of the tonsils is affected by the size (AP diameter) of the foramen magnum. Apparent herniation of the cerebellar tonsils into the foramen magnum is a frequent normal variation and can be misleading when interpreting the MRI scans conducted on patients. Therefore, determining the normal position of cerebellar tonsils in the Zambian population could provide guidance on considerations which need to be taken into account when making a possible diagnosis of tonsillar herniation.

Tonsillar herniation is a problem that arises due to increase in Intra-Cranial Pressure (ICP). This can be caused by many factors including space occupying lesions and traumatic head injuries. Traumatic brain injury accounts for up to half of trauma related fatalities worldwide (Winter et al, 2005). In fact, Faul et al (2010) have referred to traumatic head injury as a silent epidemic. The Global Burden of Disease (2002) predicts that by the year 2020, RTAs will become the third leading cause of death and disability in the developing world.

Recently, in Zambia, there has been an increase in the number of Road Traffic Accidents (RTAs). This therefore entails a high likelihood of people involved in these accidents suffering head injuries which in turn may lead to development of raised intracranial pressure, a risk factor for cerebellar tonsillar herniation.

Simoonga (2009) reported an increase in the number of RTAs in the country between 2004 and 2007. Statistics from the medical records at the University Teaching Hospital showed an increase in the number of people admitted to the hospital following RTAs from 203 in 2012 to 243 (20%) in 2013 and to 323 (33%) in 2014. Therefore, the number of admissions following RTAs has risen from 2012 to 2014 by 59%. These statistics are expected to translate into an increase in the number of patients suffering head injuries with increased intracranial pressure and subsequent cerebellar tonsillar herniation.

Although similar research about CT position has been carried out in some other parts of the world, there have been variations in the results obtained, therefore emphasizing the fact that there is no standard position of the cerebellar tonsils that is universally applicable. Various factors do affect the position of the cerebellar tonsils such as the shape of the face and the size of the skull base in different ethnic groups (Flanagan, 2010). It is possible that such differences can be expected in the Zambian population and the region. However, no information, during the study, was found within the region on the subject, hence the importance of carrying out the study.

Furthermore, it is recognized that the age groups that were considered by many of the other authors had a wide distribution implying that age had not been considered as a possible factor contributing to the differences. For this reason the researcher used a narrower age range in order to take into consideration rapid growth spurt especially between the ages 1 to 17 years.

Relating the position of the cerebellar tonsils to the size of the foramen magnum is one of the objectives of this study as there is paucity of information on the subject in the literature. Information on this subject could provide an explanation as to why some people can have their cerebellar tonsils below the foramen magnum and remain asymptomatic whereas in others cerebellar tonsillar ectopia causes severe symptoms. Such knowledge can help with early diagnosis of pathological conditions; improve options for management and determine patient prognosis.

To the best knowledge of the researcher, such a study has not been performed in Zambia.

1.5 Ethical Considerations

Ethical approval was sought from Excellence in Research Ethics and Science (ERES) CONVERGE IRB and authorization was obtained from the Cancer Diseases Hospital in order to utilise the Magnetic Resonance Imaging facilities which the hospital offered. The information obtained from the study was used strictly for this research project. To guarantee confidentiality of the information obtained, the data collection forms which were used were coded and did not reveal the names of the patients.

This study was retrospective and posed no risk to the patient as there was no direct contact.

CHAPTER TWO

LITERATURE REVIEW

A number of similar studies have been carried out on the subject, most of them comparing the position of the tonsils in normal subjects to those of individuals with a firm diagnosis of Chiari malformation. Some of the studies have related the position of the cerebellar tonsils to the age of the patient, gender as well as shape and size of the skull.

A study was carried out by Lakshmi (2015) on 515 patients during MRI investigation over a period of 8 months in India. It looked at the position of cerebellar tonsils with reference to the level of the foramen magnum. Results of the study showed that the highest number of cerebellar tonsillar ectopia was seen in the fifth decade of life while a rise in the position of the tonsils was seen in the seventh decade in both sexes. In children less than a year old and in old age, the position of tonsils was found to be above the foramen magnum.

Another study was carried out in the United States of America by Barkovich et al (1986) where the position of the cerebellar tonsils was measured with respect to the inferior aspect of the foramen magnum in 200 normal patients and in 25 patients with an established diagnosis of Chiari I malformation. Barkovich and his colleagues found the mean position of the tonsils to be 1 mm above the foramen magnum with a range from 8 mm above the foramen magnum to 5 mm below the foramen magnum. They also found that 14% of normal patients had tonsils extending slightly below the foramen magnum. The researchers observed that a small degree of herniation of the cerebellar tonsils on MRI was of debatable significance. Furthermore, Barkovich et al, in their study used manual callipers to measure distances from the hard copies of the MRI, which was done to the nearest millimetre. It has been noted that this method of measuring the position of the cerebellar tonsils may be inaccurate and unreliable. This is because as compared to digital measurements, those of manual vernier callipers are interpreted subjectively from the scale by the user and this may not completely eliminate bias.

Mikulis et al (1992), in the United States of America, observed tonsillar elevation with increasing age and therefore considered the following as criteria for determining ectopia. In the first decade of life, 6 mm; in the second and third decades, 5 mm; in the fourth to eighth decades, 4 mm; and in the ninth decade, 3 mm. Mikulis et al (1992) came to the conclusion that a single reference standard that shows the normal distance of the cerebellar tonsils from the foramen magnum is unsuitable unless age is considered. Smith et al (2013), also based in the United States of America, found that the position of the tonsils in normal participants was 7.5 mm below the foramen magnum for ages 0–10 years, 4 mm for 11–20 years, 5 mm for 21–30 years, 4 mm for 31–40 years, 4 mm for 41–50 years, 3 mm for 51–60 years, 2.5 mm for 61–70 years, and 2 mm for 71 years and older. These figures somewhat contradict the results by Mikulis and his colleagues in that what was considered ectopia by Mikulis et al in 1992 was actually in the normal range in a study conducted by Smith and his colleagues. Smith and colleagues further observed a trend in their study where the mean position of the tonsils lowered slightly with increasing age into young adulthood and ascended gradually with advancing age in adulthood.

In a study carried out by O'Connor et al in 1973, they described the normal position of the cerebellar tonsils as measured from the inferior most point to the Basion-Opisthion reference line which always lay virtually at the same level bilaterally and was above the reference line in all cases, the ages of the participants however were not specified in this particular study. The average distance from the tonsils to the reference line in 100 cases was 6 mm (+/-2 mm).

Cheng et al (2003) in China used MRI to compare quantitatively the position of the cerebellar tonsils in age matched neurologically normal adolescents with that found in idiopathic scoliosis patients. In the healthy subjects, results showed that the inferior most point of the cerebellar tonsils was at an average of 2.8 mm above the basion-opisthion reference line, with a range from 0 to10mm above the foramen magnum.

Freeman et al (2010) carried out a study in four groups of patients, two of the groups were non traumatic (recumbent or upright) and the other two groups had history of trauma (recumbent or upright). In the non-traumatic group, Cerebellar Tonsillar Ectopia (CTE) was found in 5.7% (recumbent) and 5.3% (upright) groups. They reported rare cases of CTE of 5mm and more.

In a study carried out by Acer et al (2006), the researchers measured the volumes of 28 human skulls and the cross-sectional area of the foramen magna, results showed that the skulls with bigger volume had bigger foramen magna. They mentioned that because of this, the consequences of nervous tissue displacement can be highly variable. However, they did not mention whether this affects the position of the tonsils.

Huang et al (2013) carried out a study that compared cranial dimensions between patients diagnosed with Chiari 1 Malformation and normal controls. They found that the factors that were assessed in the study suggest underdevelopment of the occipital bone in patients with Chiari 1 Malformation whereas in in the normal controls, the occipital bone and hindbrain were normally developed. They also found that the shape of the posterior cranial fossa in the group with Chiari 1 Malformation resembled a narrow funnel.

From the studies that have been reviewed so far it is safe to conclude that there is no particular standard that has been exhibited as to what the position of the cerebellar tonsils should be in normal individuals. Many factors including age, gender and the shape and size of the skull have been attributed to the differences in the position of the tonsils by different authors. For the aforementioned reasons, the researcher undertook this study with particular reference to the level of the tonsils and to the AP dimensions of the foramen magnum.

CHAPTER THRE

METHODOLOGY

3.1 Study Design

The study design that was used in this research was a cross sectional study design which analysed retrospectively patient records of MRI scans of the brain taken at the Cancer Diseases Hospital in Lusaka from the year 2012 to 2014. The study endeavoured to determine whether or not there was a relationship between the position of the cerebellar tonsils and the size of the foramen magnum.

3.2 Study Site

The study was conducted in the Radiology Department at the Cancer Diseases Hospital in Lusaka. This study site was chosen because the radiology department offers MRI facilities and also receives referrals to the facility from all over the country including the University Teaching Hospital which is the largest referral hospital in Zambia.

3.3 Study Population

The study population included all MRI records of patients, 1 year and older, who had MRI brain scans taken at the CDH in Lusaka from the year 2012 to 2014.

3.4 Criteria

3.4.1 Inclusion criterion

All MRI brain scans of patients, 1 year and older, taken at the CDH between the years 2012 and 2014 that had been certified by a qualified radiologist as having no pathology.

3.4.2 Exclusion Criteria

All MRI brain scans of patients, 1 year and older, taken at the CDH between the years 2012 and 2014 that had been certified by a qualified radiologist as having pathology were excluded.

All MRI brain scans which had no record of the patient’s age and gender were also excluded from the study.

3.5 Sample Size

A census was used in this study. That is to say, all MRI brain scans that fit the inclusion criterion within the period under review were included in the study. The CDH on average takes 2000 scans each year, among these, half (1000) of them are brain scans. The reason a census was chosen for this particular study was because while there are several (an average of 1000) MRI brain scans taken at the CDH each year, patients who are referred to the MRI facility are suspected of having pathology, therefore, there may not be many MRI brain scans certified as being normal by the consultant radiologist. It was for this reason that all the MRI brain scans that fit the inclusion criterion were considered in order to have a sample size that would yield significant results.

3.6 Data Collection Instruments

The researcher used digital records of MRI scans of the brain that fit the inclusion criterion.

Computer software tools including rulers were used to measure lengths for the position of the cerebellar tonsils as well as the AP diameter of the foramen magnum.

A data collection form (appendix 10.5) was formulated and was used to record the information collected from the digital MRIs. This information included; a code by which to identify the patient, the age of the patient which was vital in this study since the researcher was considering the age groups of individuals, the AP dimensions of the foramen magnum (measured from the Basion to the Opisthion) as well as the lengths from the inferior most point of the tonsils to the Basion-Opisthion reference line (representing the position of the cerebellar tonsils).

3.7 Data Collection Procedure

Data collection began with retrieval of the hard copies of patients' MRI reports and selecting those that fit the inclusion criterion. These copies were then used to find digital MRI brain scan records on the computer hard drive making sure all the scans chosen fit the inclusion criterion. Individual patients' digital MRI brain scans were then transferred on to compact discs (CDs). The discs were then individually analysed and measurements were taken using computer software tools. All the images were corrected for magnification before any measurements were taken, this is to say that all images were set to the same magnification before measurements were taken, to avoid bias. The AP diameter of the foramen magnum was measured from the Basion to the Opisthion of the foramen magnum on mid-sagittal section of the MRI brain scans to permit accuracy of measurements. The measurements of the cerebellar tonsillar position were then carried out from the inferior most point of the cerebellar tonsils to a line that was drawn from the Basion to the Opisthion of the foramen magnum, this was also done on the mid-sagittal section of the scans for the same reasons. The data collected was then recorded on the data collection form.

3.8 Research Variables

Dependent Variable

Position of the cerebellar tonsils

Independent variable

Age

Gender

AP diameter of the foramen magnum

3.9 Data Management

3.9.1 Data Analysis Instruments and Procedures

Data analysis was performed using the Stata version 12 statistical software package, and results were summarised on tables and graphs.

The Stata package was used to determine the proportions of demographic characteristics of the sample. The data was then grouped according to different age groups and the mean positions of the cerebellar tonsils and the AP diameter of the foramen magnum for each age group were determined. The age groups that were used were according to Medlej (2014) but slightly modified and were as follows:

Toddler (1 to 4 years)

Child (5 to 11 years)

Adolescent (12 to 17 years)

Young adult (18 to 39 years)

Middle age (40 to 59 years)

Old age (60 and older)

The one-way Analysis of Variance (ANOVA) was used to compare mean values in the position of the cerebellar tonsils among the different age groups. Linear regression was used to determine factors associated with the position of the cerebellar tonsils as well as the anteroposterior diameter of the foramen magnum. All statistical tests were performed at 5% significance level or 95% confidence interval with p-value of <0.05 to determine statistical significance.

CHAPTER FOUR

RESULTS AND INTERPRETATION

4.1 0verview

The study investigated retrospectively the relationship between the normal position of the cerebellar tonsils and the Anteroposterior diameter of the foramen magnum in individuals of different age groups. The study also considered the patients' gender as one of the demographics that were likely to alter the results. A sample of 127 was collected, out of which 67 (52.8%) were female and 60 (47.2%) were male. The median age was 28 years (IQR 1 - 75). The average anteroposterior diameter of the foramen magnum was 36.5mm (range; 23.4mm - 47.6mm) and the cerebellar tonsillar position in the participants was 0.5mm (range; -14.5mm – 13.1mm).

4.2 position of the Cerebellar Tonsils and anteroposterior diameter of the foramen magnum in different age groups

Table 1, illustrates the means and interquartile ranges of Cerebellar tonsillar position and anteroposterior diameter of the foramen magnum in different age groups measured in millimetres (mm).

Table 4.1: CT position and AP diameter of the foramen magnum for different age groups

Age group (years)	Mean CT position (IQR)	Mean AP diameter (IQR)
1 - 4yrs	-0.6 (-4.5 to 4)	31.6 (23.4 to 39.1)
5 - 11yrs	0.3 (-12.7 to 4.9)	36.6 (27.8 to 47.0)
12 - 17yrs	1.0 (-3.1 to 6.4)	36.0 (26.3 to 39.8)
18 - 39yrs	0.7 (-14.5 to 13.1)	36. 9 (26.3 to 47.6)
40 - 59yrs	0.4 (-2.7 to 5.7)	37.4 (32.0 to 44.2)
60 - 75yrs	-0.5 (-3.6 to 1.3)	37.2 (34.2 to 43.2)

Abbreviations: CT; Cerebellar tonsils, IQR; interquartile range, AP; anteroposterior

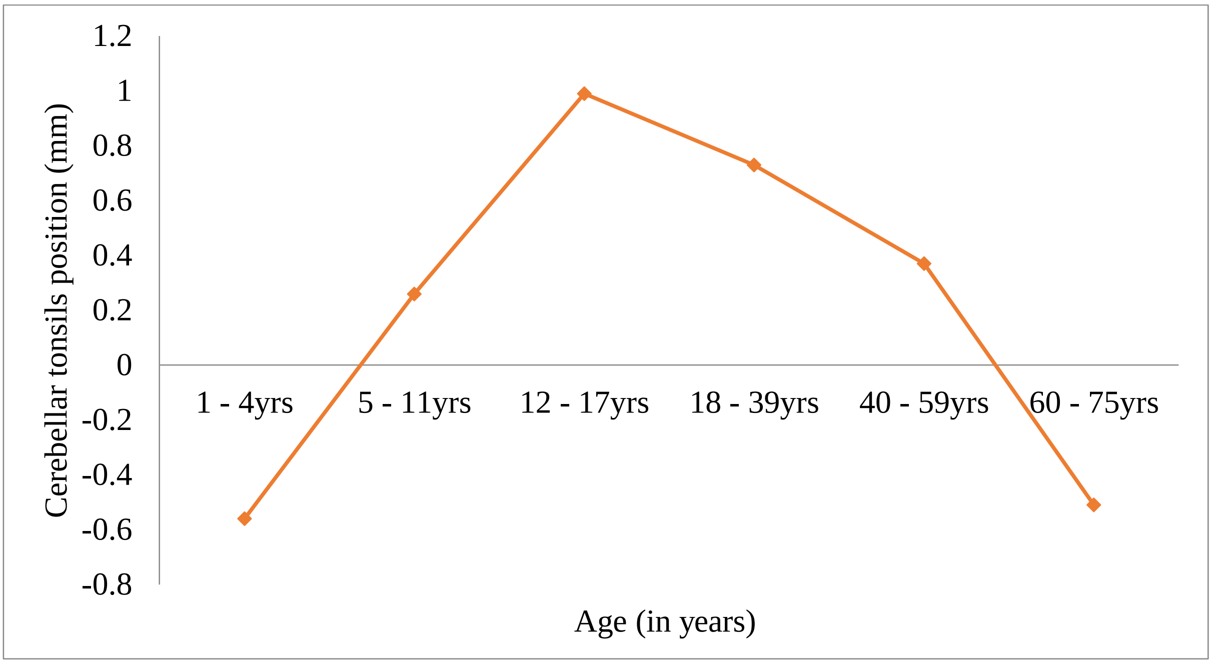

Figure 4.1: Mean position of the cerebellar tonsils in different age groups

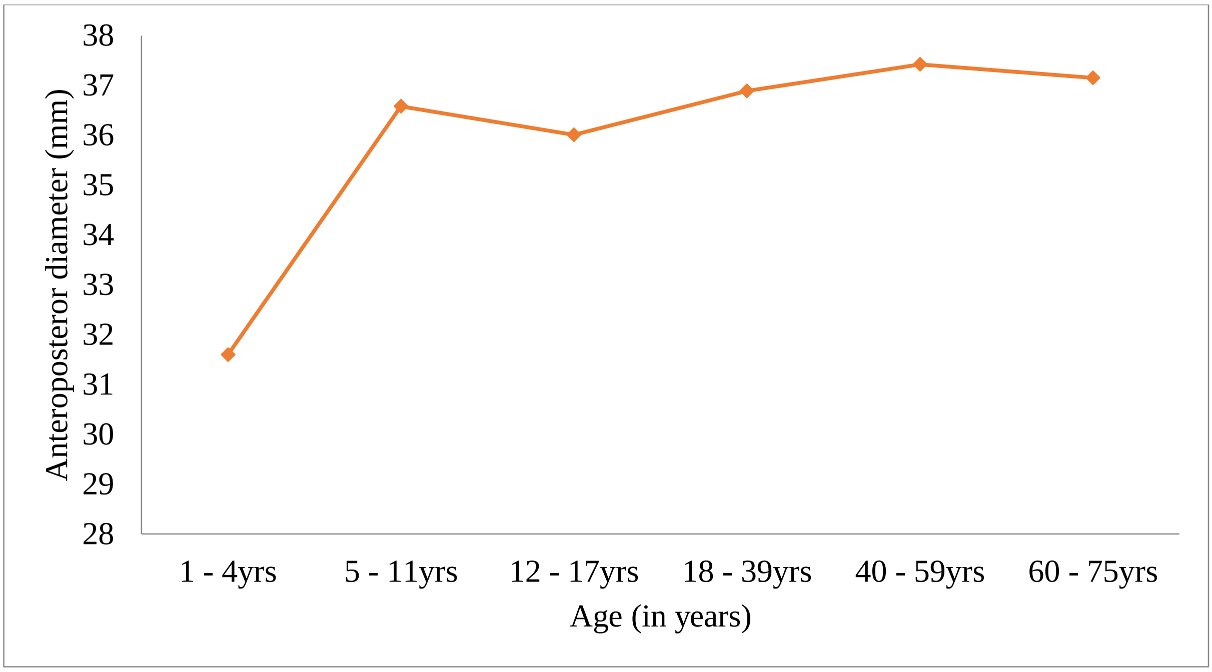

Figure 4.2: Mean Anteroposterior diameter of the foramen magnum in different age groups

4.3 Comparing the different means of CT position and AP diameter with respect to age groups

The results of the differences in means of the cerebellar tonsillar (CT) position and AP diameter for different age groups are shown in Table 2. Overall, there was no evidence of a statistical difference in the means of CT position (p = 0.8196) and AP diameter (p = 0.0608) for the different age groups. However, comparing each age group for AP diameter was able to show that the means for those aged 1-4yrs and 40-59yrs were statistically different (p = 0.033).

Table 4.2: Difference in means of CT position and AP diameter for age groups

Age category (in years)	Frequency	Mean CT position	P-value	Mean AP diameter	P-value
1 - 4yrs	7	-0.6	0.8196[aCT]	31.60	0.0608[aAP]
5 - 11yrs	20	0.3		36.58	
12 - 17yrs	15	1.0		36.01	
18 - 39yrs	54	0.7		36.89	
40 - 59yrs	23	0.4		37.42	0.033[bAP]
60 - 75yrs	8	-0.5		37.15	

Abbreviations: CT- cerebellar tonsils; AP- anteroposterior; aCT- overall p-value for CT position means; aAP- overall p-value for AP diameter means; bAP- p-value for the difference in means between age group 1 – 4yrs and 40 – 59yrs.

4.4 Factors associated with cerebellar tonsillar (CT) position

Table 3 below shows factors that are related to the position of the cerebellar tonsils. Univariate analysis showed that, one year increase in age lowered the CT position by 0.01mm (95% CI -0.4, 0.02), although the findings were statistically insignificant (p = 0.648). When compared to males, females had insignificantly lower CT position by 0.76mm (95% CI -1.89, 0.37; p = 0.186).

One unit increase in AP diameter of the foramen magnum significantly lowered the CT position by 0.13mm (95% CI -0.26, -0.01; p = 0.041). Hence, AP diameter is the predictor variable for CT position because it was the only variable that was still significant during multivariate analysis (Table 3).

Table 4.3: Predictors of cerebellar tonsils (univariate and adjusted analysis)

	Univariate		Adjusted	
Characteristics	**Coef (95%CI)**	**P-value**	**Coef (95%CI)**	**P-value**
Age	-0.01 (-0.4, 0.02)	0.648	-0.00 (-0.03, 0.03)	0.882
Gender				
Male	0.00	0.00	0.00	0.00
Female	-0.76 (-1.89, 0.37)	0.186	-0.89 (-2.01, 0.23)	0.120
AP diameter	-0.13 (-0.26, -0.01)	0.041**	-0.14 (-0.27, -0.01)	0.032**

Abbreviations: CI- confidence interval; AP- anteroposterior; **p-value <0.05

4.5 Factors associated with anteroposterior (AP) diameter

Univariate analysis (Table 4) showed that, as the age of a person increases by one year, anteroposterior diameter is increased by 0.04mm (95% CI 0.00, 0.08), however the findings were not statistically significant (p = 0.069). Females compared to their male counterparts had a reduced anteroposterior diameter by 0.89mm (95% CI -2.43, 0.64). This finding had no statistical evidence (p = 0.253). Cerebellar tonsil (CT) position was seen to be significantly associated with the reduction of the AP diameter of the foramen magnum by 0.24 (95% CI -0.48, -0.01, p = 0.041). During multivariate analysis (Table 4), the other variables apart from CT position were still not significant. Hence, CT position was a significant predictor of AP diameter.

Table 4.4: Predictors of anteroposterior diameter (univariate and adjusted analysis)

	Univariate		Adjusted	
Characteristics	**Coef (95% CI)**	**P-Value**	**Coef (95% CI)**	**p-value**
Age	0.04 (0.00, 0.08)	0.069	0.04 (- 0.01, 0 .08)	0.085
Gender				
Male	0.00	0.00	0.00	0.00
Female	-0.89 (-2.43, 0.64)	0.253	-1.06 (-2.57, 0.45)	0.170
CT position	-0.24 (-0.48, -0.01)	0.041**	-0.25 (-0.49, -0.02)	0.032**

Abbreviations: CI- confidence interval; CT- cerebellar tonsils; **p-value <0.05

CHAPTER FIVE

DISCUSSION

5.1 Position of the Cerebellar Tonsils in different Age Groups

According to the results that were obtained from the sample collected in this study, the trends in the means of the cerebellar tonsils in different age groups showed that the tonsils were generally below the foramen magnum from ages 1-4 years ascending to a position above the foramen magnum by age 5 and reaching their highest point between 12-17 years and then gradually descending again. Therefore, there was elevation of the tonsils with increasing age until adolescence after which there was a gradual decent. This finding could have been due to the fast rate at which the brain grows between ages 1-4years. According to the Centre on the Developing Child (2009,) about 700 new nueronal connections are formed every second in the first few years of life. This and the accumulation of neuroglia in the early years could cause an increase in the size of the brain in a still expanding skull causing herniation of neuronal structures. Later in life, brain matter begins to decrease while skull volume remains the same. This can be proven thought a study by Ge et al in 2002 where results showed a significant linear decrease in Both grey matter and white matter with age with a greater rate beginning only in adult midlife. This phenomenon could explain why the tonsils in individuals over the age of 60 years have lower lying tonsils. The brain volume decreases while the skull remains the same size causing the brain to sag and consequently herniate.

There were some similarities in trends between this study and studies from other regions. Mikulis et al in 1992 for example found in a study they carried out that there was an elevation in the position of the tonsils with age. Smith and colleagues in a study in 2013 observed lowering of cerebellar tonsillar position with increasing age into young adulthood and from then on an elevation into adulthood. Lakshmi (2015) found the largest number of cerebellar tonsillar ectopia was concentrated in the fifth decade of life and thereafter a rise in the position in the seventh decade in both genders. The position of the cerebellar tonsils in infancy and old age was found to be above the foramen magnum. This was contrary to what was observed in this study where tonsillar ectopia was seen in children from 1-4 years and adults over 60 years.

The mean positions of the cerebellar tonsils of different age groups were compared using a one way analysis of variance (ANOVA). This was done in order to find out whether there were any significant differences in the cerebellar tonsillar positions of the different age groups. Results showed that even though there were differences from group to group in the position of the tonsils, these differences were not statistically significant with p-value of 0.8196. However, there were no studies found to compare these findings.

5.2 Anteroposterior Diameter of the Foramen Magnum in Individuals of Different Age Groups

The average anteroposterior diameter of the foramen magnum was found to be 36.5mm with a range from 23.4-47.6mm. These results were similar to those of other studies, for instance a study by Lakshmi (2015) in India, found the mean value of the AP diameter of the foramen magnum to be 35.57 with a range from 15-45mm. Osunwoke et al (2012) in a study in Nigeria found the average length of the AP Diameter of the foramen magnum to be 36.11mm.

Radhika et al (2014) in India also did a morphometric study of the foramen magnum and results showed an average anteroposterior diameter of 35.3mm with a range from 27mm to 43mm. The studies by Osunwoke et al and Radhika et al however only involved adults.

The means of the anteroposterior diameter of the foramen magnum were also compared using the one way ANOVA. When all measurements were compared against each other, the differences were seen to be statistically insignificant with P-value of 0.0608. However, when the means of age groups 1-4 years and 40-59 years were compared, there was a significant difference seen with P-value of 0.033. This difference could have been as a result of the fact that in the 1- 4 years age group, the skull is still growing and is much smaller Compared to the 40-59 years age group where maximum growth has been achieved and fusion of the skull bones has already taken place. The current study as well as other studies like the one carried out by Lakshmi (2015) have shown an increase in the diameter of the foramen magnum with increasing age. This could explain the significant difference in the said age groups. However, there were no studies found to compare these results with.

Trends in the means of the AP diameter of the foramen magnum in the different age groups seen in this research showed an increase in the size of the foramen magnum up to the beginning of adolescence (defined in this research as 12 years) at which point it remains almost constant. In a study by Lakshmi (2015) results showed an increase in the size of the foramen magnum up to the age of 14 after which the size remains constant.

The study also showed that the AP diameter of the foramen magnum was smaller in females compared to males. The anteroposterior diameter of the foramen magnum in females was less by 0.89mm though this finding was not statistically significant. This was similar to results seen in other studies like one by Lakshmi (2015), in which the AP diameter of the foramen magnum was found to be larger in males compared to females. This has also been confirmed by Muralidhar et al (2014), Ukoha et al (2011) and many others.

5.3 Association of the Cerebellar Tonsillar Position and Anteroposterior Diameter of the Foramen Magnum

A univariate analysis of the position of the cerebellar tonsils against the anteroposterior diameter of the foramen magnum showed that one unit (1mm) increase in the diameter of the foramen magnum resulted into a significant lowering of 0.13mm in the position of the cerebellar tonsils. Therefore, of all the variables that were analysed against the position of the cerebellar tonsils, the anteroposterior diameter of the foramen magnum is the one that was statistically seen to be a predictor of cerebellar tonsillar position because it was the only one that was statistically significant with P-value of 0.041.

5.4 Factors Associated with Cerebellar Tonsillar Position

Linear regression was done to determine factors that affect the position of the cerebellar tonsils. Position of the cerebellar tonsils was analysed against two (2) other factors that could affect cerebellar tonsillar position including the age of the patient and their gender.

With respect to age, univariate analysis showed that an increase in the age of the patient by one year caused lowering in the position of the cerebellar tonsils by 0.01mm. This was done at 95% confidence interval. In a study by Bartholomeusz et al (2002), they observed that in early childhood, there is an increase in both head circumference and brain volume, and from adolescence onwards, brain volume decreases while head circumference does not. However, there was no indication of the rate of increase of the circumference of the skull in relation to that of the volume of the brain. Finding out the rate of increase of both head circumference and brain volume could give reasons as to why there is ectopia in the early years of life observed in this study.

When analysed with reference to the gender of the patient, females showed a lower cerebellar tonsillar position by 0.76mm in comparison to their male counterparts, although this difference was statistically insignificant. This difference could be due to the difference in the size of the brain between males and females. Studies have shown differences in brain size between males and females with males having larger brains. Research carried out by Dekaban and Sadowsky (1978), shows that from birth the female brain is slightly smaller compared to the male brain.

This finding is comparable to that seen in the study by Lakshmi (2015) where they observed lower position of the cerebellar tonsils in females compared to males. The study by Smith et al (2013) also established that females have, on average, a lower tonsil position compared to males.

5.5 Limitations

This study was meant to be a population survey (census) where the researcher was to include all the eligible samples to the study but the mode of data collection involved did not allow for this. Therefore, this might have caused distortion of the results obtained since the largest number of participants was between ages 18-39 years.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

A statistically significant relationship was observed between the size of the foramen magnum and the position of the cerebellar tonsils. It was observed that the larger the anteroposterior diameter of the foramen magnum, the lower the position of the cerebellar tonsils.

i. The position of the cerebellar tonsils changes with increasing age, with the tonsils situated below the foramen magnum between ages 1-4 years and gradually ascending to a position above the foramen magnum reaching their maximum position at about 17 years then gradually descending.
ii. The study showed an increase in the anteroposterior diameter of the foramen magnum with age until about 12years after which it became somewhat constant
iii. The study showed an association between cerebellar tonsillar position and the Anteroposterior diameter of the foramen magnum with 1mm increase in the AP diameter of the foramen magnum causing a descent of 0.13mm of the cerebellar tonsils.
iv. Based on the results of the study, females had lower cerebellar tonsillar position compared to males, this trend was seen in all age groups.

6.2 Recommendations

i. It is recommended that other similar studies be carried out perhaps on larger samples sizes and over a longer period of time to confirm the findings of this study.
ii. It is recommended that in future studies on cerebellar tonsillar ectopia, age should be taken into consideration.
iii. Studies should be carried out to correlate the size of the foramen magnum with progression of symptoms in conditions involving cerebellar tonsillar ectopia.

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APPENDICES

10.1 Approval Letter from Assistant Dean (Postgraduate)

THE UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

Telephone : +260211252641
Telegram: UNZA, Lusaka
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P.O Box 50110
Lusaka, Zambia

20th March, 2015

Ms Patience Namakau Buumba
Department of Anatomy
School of Medicine
UNZA
LUSAKA

Dear Ms. Buumba,

RE: GRADUATE PROPOSAL PRESENTATION FORUM

Following the presentation of your dissertation entitled **"A Retrospective Study to Determine the Normal Position of the Cerebellar Tonsils in Individuals of Different Age Groups at the Cancer Diseases 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 faithfully,

Dr. S.H. Nzala
ASSISTANT DEAN, POSTGRADUATE
CC: HOD, Anatomy

UNIVERSITY OF ZAMBIA
SCHOOL OF MEDICINE
23 MAR 2015
ASSISTANT DEAN (PG)
P.O. BOX 50110, LUSAKA

10.2 Approval Letter from Eres Converge

33 Joseph Mwilwa Road
Rhodes Park, Lusaka
Tel: +260 955 155 633
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Email: eresconverge@yahoo.co.uk

I.R.B. No. 00005948
F.W.A. No. 00011697

8th September, 2015

Ref. No. 2015-May-007

The Principal Investigator
Ms. Patience Namakau Buumba
The University of Zambia
School of Medicine
Dept. of Anatomy
P.O. Box 50110,
LUSAKA.

Dear Ms. Buumba,

RE: AN MRI INVESTIGATION AT CANCER DISEASES HOSPITAL OF THE NORMAL POSITION OF THE CEREBELLAR TONSILS IN RELATION TO THE ANTEOSTERIOR DIAMETER OF THE FORAMEN MAGNUM.

Reference is made to your corrections dated 11th August, 2015. The IRB resolved to approve this study and your participation as principal investigator for a period of one year.

Review Type	**Ordinary**	Approval No. **2015-May-007**
Approval and Expiry Date	Approval Date: 8th September, 2015	Expiry Date: 7th September, 2016
Protocol Version and Date	Version-Nil	7th September, 2016
Information Sheet, Consent Forms and Dates	• N/A.	7th September, 2016
Consent form ID and Date	Version-Nil	7th September, 2016
Recruitment Materials	Nil	7th September, 2016
Other Study Documents	Data Collection form.	7th September, 2016
Number of participants approved for study	1,000 (Patient records)	7th September, 2016

Where Research Ethics and Science Converge

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.

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

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

10.3 Letter of Permission to Conduct Research

THE UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

To : Dr Kennedy Lishimpi
Senior Medical Superintendent
Cancer Diseases Hospital
Lusaka.

11 February 2015

Sub. : Ms Patience Buumba. Research project & Radiology

Dear Dr Lishimpi

I wish to introduce to you Ms Buumba a second year MSc Anatomy student who is to undertake a research project on the radiological dimensions of cerebellar tonsils in relation to the foramen magnum.

I would very much appreciate if you could give her permission to collect data from the MRI unit in your Department.

With kind regards and best wishes
Yours Sincerely

Professor Krikor Erzingatsian FRCSI: Hon FCS(ECSA)

cc : Dean SOM

10.4 Letter of Approval to Conduct Research

All Correspondence should be addressed to the
Executive Director
Tel/Fax: +260 1 257706

In reply please quote:

No............................

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH
CANCER DISEASES HOSPITAL

P. O. Box Rw 51337
LUSAKA

4th May, 2015

Buumba Patience Namakau
University of Zambia
School of Medicine
Department of Anatomy
P.O Box 50110
Lusaka.

Dear Buumba Patience N. Student No. 512807109

RE: PERMISSIOM TO CARRY OUT RESEARCH

In response to your letter dated 11th February, 2015, permission is hereby granted to you to carry out your research project from the Cancer Diseases Hospital, Radiology Department, titled: **Normal Position of the Cerebellar Tonsils in Individuals of Different Age Groups at the Cancer Diseases Hospital, Lusaka, Zambia.**

Yours sincerely,

Dr Kennedy Lishimpi – **BSc MB ChB MMed FC Rad Onc (SA)**
SENIOR MEDICAL SUPERINTENDENT

10.5 Data Collection Form

Data Collection Form

Patient code number:

Hospital ID number:

Age of the patient (years)/Gender

AP diameter of the foramen magnum (measured from the Basion to the Opisthion of the foramen magnum (mm)):

Position of the cerebellar tonsils (Distance measured from the inferior most point of the cerebellar tonsil to the Basion-Opisthion reference line (mm)):

APPROVED
0 8 AUG 2015
ERES CONVERGE
P/BAG 125, LUSAKA.