بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Evaluation of Cerebral White Matter Changes for Sudanese Hypertensive Patients Using Magnetic Resonance Imaging

تقويم تغيرات المادة البيضاء للمخ لدى مرضى إرتفاع ضغط الدم السودانيين بإستخدام التصوير بالرنين المغناطيسي

A Thesis Submitted for Partial Fulfillment of Requirements of M.Sc Degree in Diagnostic Radiologic Technology

Prepared by:

Rania Mohammed Elhassan Awadallah Mohammed Ali Murad

Supervisor:

Associate prof. Ikhlas Abdelaziz Hassan Mohamed

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{الآية}

بِسْمِ اللهِ الرَّحْمَنِ الرَّحِيمِ

قال تعالى:

" قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَآ إِلاَّ مَا عَلَّمْتَنَآ إِنَّكَ أَنْتَ العَلِيمُ الحَكِيمُ (32) "

(سورة البقرة)

Dedication

This research is lovingly dedicated to:

My first teacher; who taught me the meaning of the word "science", and she guided me towards the excellence.

(My mother)

The soul of the dear person; who had been my constant source of inspiration, and he left fingerprints of grace in my life.

(My father)

The joy and fun makers; who given me an endless care, love, support and encouragement.

(My brothers)

The gorgeous persons; who supported me, and they sweetened the taste of my life.

(My family)

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At first, all the praises and thanks are to Allah. Then thanks and gratitude must go to the supervisor Dr.Ikhlas Abdelaziz Hassan; for her guidance, patience, and wise advices throughout the time it took me to complete this research. I need to express my gratitude and appreciate as well to the staff of the modern medical center and Asia hospital; who had generously given their time and expertise to better my work. Thanks are also due to my gorgeous friends who gave me an unconditional assistance and continuous encouragement. Finally; I would like to acknowledge the professors, colleagues, librarians, volunteers, and everyone who unflaggingly helped, contributed or supported my thesis.

Abstract

The aim of this study was to evaluate the cerebral white matter changes for Sudanese hypertensive patients using magnetic resonance imaging. The sample consisted of thirty subjects randomly chosen from modern medical center and Asia hospital, they divided into control group and hypertensive group, both underwent magnetic resonance scans for the brain by (1.5T or 0.2T) machine using comparable protocols included (T1, T_2 and Fluid Attenuated Inversion Recovery pulse sequences), a semi-quantitative visual rating scale (Fazekas) was used to assess the changes of cerebral white matter. The data analyzed by (SPSS) and the *p* value was (0.05). The study found that; the hypertensive group had more white matter changes than the control group, there was a statistically significant difference between them for periventricular white matter changes (19.20 _ 11.80, $p = 0.014$), while no significant difference for deep white matter changes was present (17.90_13.10, $p = 0.055$). Regarding the control status of hypertension; the patients who had controlled blood pressure got either none, mild or moderate changes whereas uncontrolled one had severe white matter changes, the differences between them for periventricular and deep white matter changes were (4.94_11.50, $p = 0.003$) and (7.12_ 9.00, $p = 0.355$) respectively. The duration of hypertension showed a statistically significant high negative correlation ($^{-}0.743$, $p= 0.001$) with periventricular white matter changes, and insignificant weak negative correlation ($^{-}0.230$, $p= 0.409$) with deep white matter changes. Cerebral white matter changes appeared as a normal finding for aging process in control group, while in hypertensive group they tend to occur earlier in life and appear to be more severe, this may indicate that; hypertension can accelerate brain aging.

الخلاصة

الهدف من هذه الدراسة هو تقييم تغيرات المادة البيضاء للمخ لدى مرضى إرتفاع ضغط الدم السودانيين بإستخدام التصوير بالرنين المغناطيسي. تكونت العينة من ثلاثين شخصا أُختيروا عشوائياً من المركز الطبي الحديث و مستشفى آسيا و قسموا إلى مجموعة تحكم و مجموعة مريضة بالضغط، كلتا المجموعتين أجرت مسحاً للدماغ بالرنين المغناطيسي بواسطة جهاز قوته (1.5 أو 0.2) تسلا وبإستخدام بروتوكولات متماثلة تضمَّنت المتسلسلات النبضية ($ت_1$ و $ت_2$ و إسترداد الإشارة المنعكسة بعيار الزمن الثاني)، و تم إستخدام مقياس نظري شبه كمي (فازيكاس) لتقييم التغيرات في المادة البيضاء للمخ. حُللت البيانات بطريقة (إس بي إس إس) و كانت القيمة الحرجة (0.05). وجدت الدراسة أن المجموعة المصابة بالضغط لديها تغيرات في المادة البيضاء أكثر من مجموعة التحكم، و كان هنالك فرق إحصائي مهم بينهما في التغيرات الموجودة في المنطقة حول البطين المخي من المادة البيضاء (19.20_11.80، ب = 0.014)، بينما لم يكن الفرق مهما في حالة التغيرات في المنطقة العميقة من المادة البيضاء (17.90_ 13.10، ب = 0.055). فيما يتعلق بمدى ضبط مرض الضغط؛ فإن المرضى الذين كان ضغطهم منضبطاً كانت التغيرت لديهم إما منعدمة أو خفيفة أو متوسطة، في حين أن ذوي الضغط غير المنضبط كانت لديهم تغيرات شديدة في المادة البيضاء، و كانت الفروقات بينهما في المنطقة حول البطين المخي والمنطقة العميقة من المادة البيضاء هي (4.94_ 11.50، ب = 0.003) و (7.12_ 9.00 ، ب = 0.355) على التوالي. أظهرت فترة مرض الضغط إرتباطاً عكسيا قوياً و مهماً بالنسبة للتغيرات في المنطقة المحيطة بالبطين المخي (-0.743، ب = 0.001)، وإرتباطاً عكسياً ضعيفاً وغير مهم بالنسبة للتغيرات في المنطقة العميقة (-0.230، ب = 0.409). تغيرات المادة البيضاء للمخ ظهرت عند مجموعة التحكم كنتيجة طبيعية لعملية التقدم في السن، أما في مجموعة الضغط فإنها كانت تميل للحدوث في عمر مبكر و بصورة أكثر حدة مما قد يشير إلى أن مرض الضغط بإمكانه أن يعجِّل من شيخوخة الدماغ.

List of abbreviations

Abbreviation	Meaning
AHA	American Heart Association
AICA	Anterior Inferior Cerebellar Artery
ARIC	Atherosclerosis Risk in Communities Study
ARWMC/L	Age Related White Matter Changes/ Lesions
CI	Confidence Intervals
CNS	Central Nervous System
CSF	Cerebro-Spinal Fluid
CT	Computed Tomography
DWMC/L	Deep White Matter Changes/ Lesions
DTI	Diffusion Tensor Imaging
FLAIR	Fluid-Attenuated Inversion Recovery
HTN	Hypertension
MRI	Magnetic Resonance Imaging
PCA	Posterior Cerebral Artery
PD	Proton Density
PICA	Posterior Inferior Cerebellar Artery
PVWMC/L	Peri-Ventricular White Matter Changes/ Lesions
SCA	Superior Cerebellar Artery
SPSS	Statistical Package of Social Sciences
WMH	White Matter Hyperintensities
WML	White Matter Lesions

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Chapter one

Introduction

Chapter one

Introduction

1.1 Prelude:

Worldwide, raised blood pressure is estimated to cause 7.5 million deaths, about 12.8% of the total of all deaths (World Health Organization, 2012). The incidence of hypertension has increased rapidly in the Sudan in the last few years (Babiker et al., 2013). A formal survey reported that; Sudanese hypertensive patients compromise 24.8% from all population; this initiates the need to detect the potential effects of hypertension throughout the body especially on vital organs such as the brain (Federal ministry of health, 2015).

The brain lies within the cranial cavity and is composed of the cerebrum, the brain stem, and the cerebellum (Dean and West, 1987). The cerebrum as a whole has many critically important functions including thought, judgment, memory, and discrimination. It consists of gray matter which contain neuron cell bodies and white matter which composed mainly of myelinated axons. White matter contains fibers that create pathways for the transmission of nerve impulses to and from the cortex; the site of processing (Kelley and Petersen, 1997).

In elderly people, cerebral white matter develops lesions referred to as age-related white matter changes (ARWMC); their prevalence varies considerably across studies depending on the population studied and the technique used (Launer et al., 2005). Between a thirty and eighty percent of magnetic resonance scans done in persons over the age of sixty five; cerebral white matter changes were shown (Wong et al., 2002).

White matter changes are frequently seen on computed tomography (CT) and magnetic resonance imaging (MRI) scans. They appear as ill-defined hypodensities on computed tomography; whereas on magnetic resonance imaging, they appear as hyperintensities on T_2-weighted, proton density, and fluid-attenuated inversion recovery (FLAIR) images (Pantoni, 2010). Due to their bright appearance on magnetic resonance imaging white matter changes are also called white matter hyperintensities (Debette and Markus, 2010).

White matter lesions were found to influence mental and physical function (Kim et al., 2008). Many studies have shown that white matter changes were associated with a host of poor outcomes, including cognitive impairment, dementia, gait disturbances, and increased risk of stroke and death (Xiong and Mok, 2011). Researches were conducted and found an association between white matter lesions and hypertension, but others said that; there was no significant association.

1.2 Statement of problem:

The high percentage of hypertension in Sudanese population initiates the need for assessing the suspected effects of this fatal disease on vital organs; i.e. the brain. It was noticed that; many hypertensive patients had diminished levels of cognitive performance; this may be an indicator of having severe cerebral white matter changes. Previous studies have found an association between hypertension and age-related white matter changes but their results were controversial, also they were conducted almost exclusively on elderly individuals.

1.3 Objectives:

1.3.1 General objective:

The general objective of this study was to evaluate the cerebral white matter changes in Sudanese hypertensive patients using magnetic resonance imaging.

1.3.2 Specific objectives:

The specific objectives of this study were:

- To determine the location of white matter lesions.
- To assess the shape of white matter lesions.
- To measure the size of white matter lesions.

1.4 Over view:

The study consisted of five chapters; the first was a brief introduction, the second was a theoretical background as well as the previous studies, and the third considered with materials and methods. Chapter four showed the results whereas chapter five included the discussion of the results, conclusion, recommendations and limitations. At the end references were cited, and appendices were added.

Chapter two

Literature review

Chapter two

Literature review

2.1 Theoretical background:

2.1.1 Anatomy and physiology:

The central nervous system (CNS) is composed of the brain and spinal cord (Dean and West, 1987). The brain regulates and coordinates many critical functions from thought processes to bodily movements. Morphologically the brain consists of meninges, ventricles, cerebrum, brain stem, cerebellum, and cerebral vascular system (Kelley and Petersen, 1997). Figure (2.1) shows the cerebrum, brain stem, and cerebellum which considered the major parts of the brain (Dean and West, 1987).

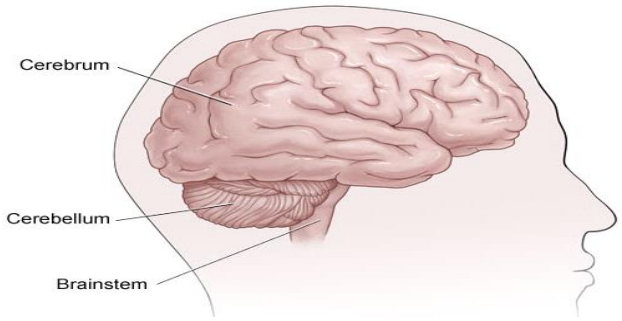

Figure (2.1) shows the major parts of the brain (Giovannoni, 2015).

2.1.1.1 The meninges:

The brain was surrounded and protected by three membranes called meninges. The outermost membrane, the dura matter, is the toughest; this double-layered membrane is continuous with the periosteum of the cranium, between the layers of the dura matter are meningeal arteries and dural sinuses. The dura matter has folds

that help to separate the structures of the brain include the falx cerebri, tentorium cerebelli, and the falx cerebelli (Kelley and Petersen, 1997).

The middle membrane, known as the arachnoid membrane, is a delicate, transparent membrane that is separated from the dura matter by a potential space called the subdural space. The inner layer, or pia matter, is a highly vascular layer that adheres closely to the contours of the brain. The subarachnoid space separates the pia matter from the arachnoid matter; this space contains cerebrospinal fluid (CSF) that circulates around the brain and spinal cord. Figure (2.2) shows the meninges of the bain (Kelley and Petersen, 1997).

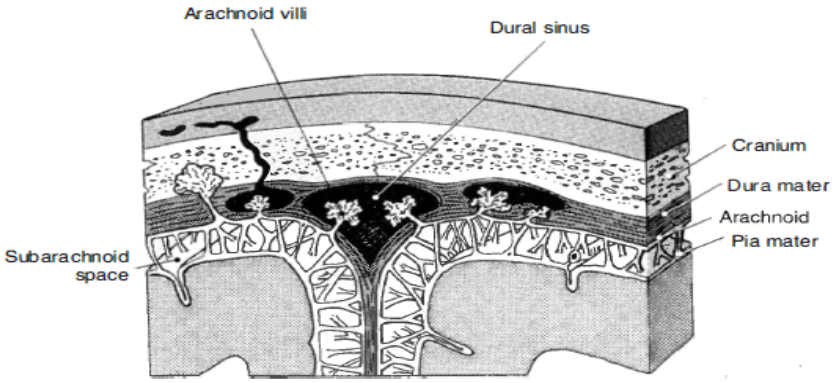

Figure (2.2) shows the meninges of the brain (Kelley and Petersen, 1997).

2.1.1.2 The ventricles:

The ventricular system provides a pathway for the circulation of the cerebral spinal fluid throughout the central nervous system. A major portion of the ventricular system is composed of four fluid-filled cavities (ventricles), located deep within the brain. The right and left lateral ventricles lie within each cerebral hemisphere and separated at the midline by the septum pellucidum, they consist of a central body and three extensions; the frontal, occipital, and temporal horns. The lateral ventricles open into the third ventricle through the paired interventricular

foramen (Kelley and Petersen, 1997).

The third ventricle is located midline just inferior to the lateral ventricles, it communicates with the fourth ventricle via the cerebral aqueduct. The fourth ventricle is a diamond shaped cavity located anterior to the cerebellum and posterior to the pons, its lateral angles extend to form the lateral apertures, while the inferior angle of it has a median aperture continues with the central canal of the spinal cord. The apertures allow for the passage of cerebro spinal fluid between the ventricles and the subarachnoid space. Figure (2.3) shows the ventricles of the brain (Kelley and Petersen, 1997).

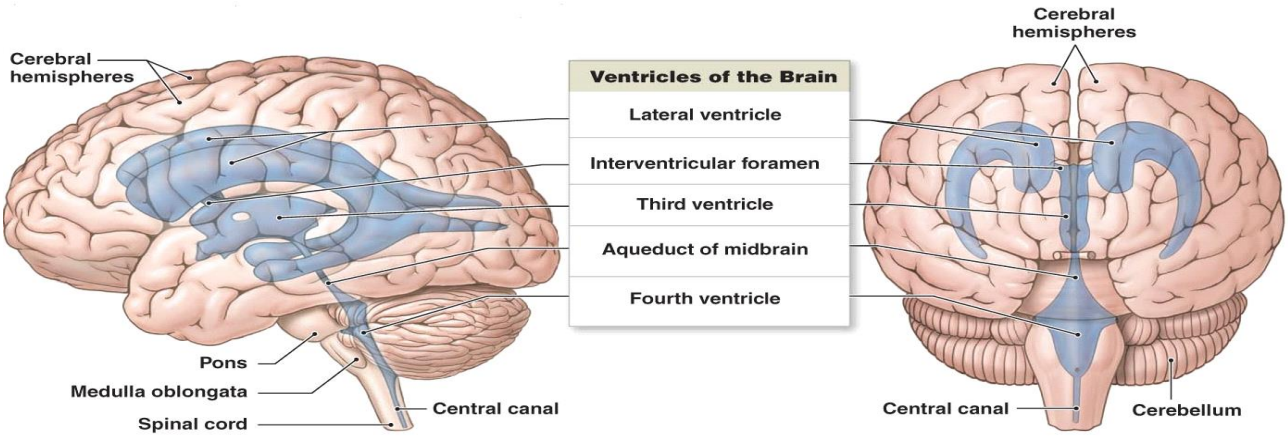

Figure (2.3) shows lateral (left image) and anterior (right image) views for the ventricles of the brain (Giovannoni, 2015).

2.1.1.3 The cerebrum:

The cerebrum is the largest portion of the brain, and is composed of the right and left cerebral hemispheres which are connected by a mass of white matter called corpus callosum, and are otherwise partly separated by the median longitudinal fissure which contain the falx cerebri. As shown in figure (2.4) the hemispheres consist mainly of cortical gray matter (neuron cell bodies) and white matter

(myelinated axons) (Ryan et al., 2004).

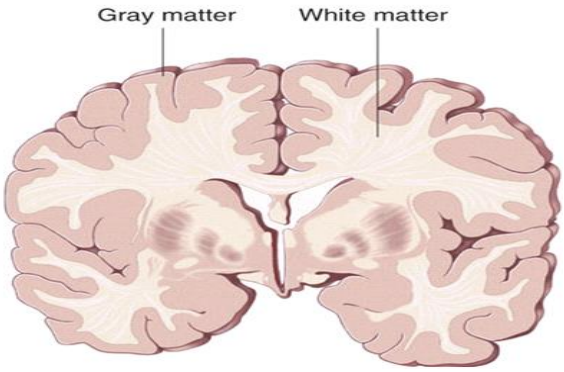

Figure (2.4) shows a coronal view for gray and white matter of the brain (Giovannoni, 2015).

2.1.1.3.1 Cerebral cortex:

The cortex, the outermost portion of the cerebrum, is composed of gray matter (neuron cell bodies) approximately three to five millimeter thick; its surface is arranged in a number of folds called gyri separated by sulci or fissures. The cerebral cortex of each hemisphere can be divided into four individual lobes; frontal, parietal, occipital, and temporal; figure (2.5) demonstrate lobes of the brain. Each lobe has critical regions, with specific functions (Kelley and Petersen, 1997).

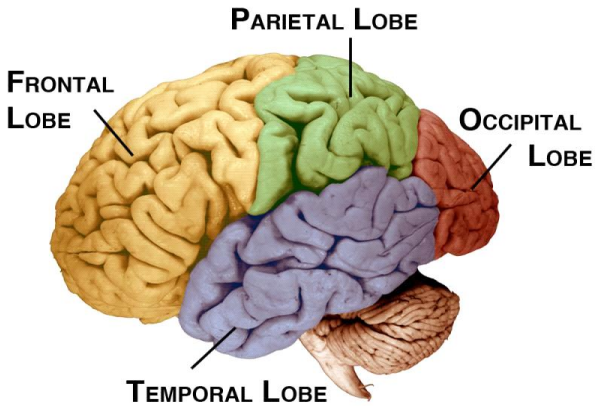

Figure (2.5) shows the frontal, parietal, temporal, and occipital lobes of the brain (Giovannoni, 2015).

The largest of the four lobes is the frontal lobe, which generally concerned with personality and voluntary motor activities. The parietal lobe is concerned with peripheral sensations, the occipital lobe is concerned with vision, and the temporal lobe deals with sensations of smell, taste, and hearing, figure (2.6) illustrate the function of each cortical lobe (Kelley and Petersen, 1997).

The main sulcus of the brain is the central sulcus, which divides the precentral gyrus of the frontal lobe and postcentral gyrus of the parietal lobe. The precentral gyrus is considered the motor strip of the brain and the postcentral gyrus is considered the sensory strip of the brain; as shown on figure (2.6). The cortex receives sensory input; it also sends instructions to the muscles and glands for control of bodily movement and activity (Kelley and Petersen, 1997).

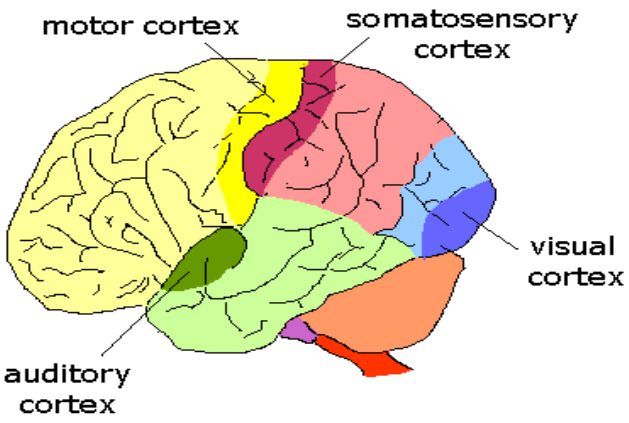

Figure (2.6) shows the functions of the cortical lobes (Giovannoni, 2015).

2.1.1.3.2 Cerebral white matter:

Deep to the cortex is the white matter; as explained in figure (2.4); which consists of nerve fibers (axons) that create pathways for the transmission of nerve impulses to and from the cortex (Kelley and Petersen, 1997). Most of these axons are surrounded by a type of sheath called myellin which gives the white matter its

color (Douglas, 2008). It also protects the nerve fibers from injury and improves the speed of transmission of all nerve signals (Klein and Thorne, 2007).

There are three types of fibers within the cerebral hemispheres; they are the commissural fibers; which connect corresponding areas of the two hemispheres, association fibers; which connect different parts of the cortex of the same hemisphere, and projection fibers; which join the cortex to lower centers (Ryan et al., 2004).

Commissural tracts cross from one cerebral hemisphere to the other through bridges called commissures. The great majority of commissural tracts pass through the large corpus callosum and a few tracts pass through the much smaller anterior and posterior commissures (Saladin, 2012). The corpus callosum forms the roof of the lateral ventricles, and consist of four parts; the rostrum, genu, body, and splenium; this is illustrated on figure (2.7) (Kelley and Petersen, 1997).

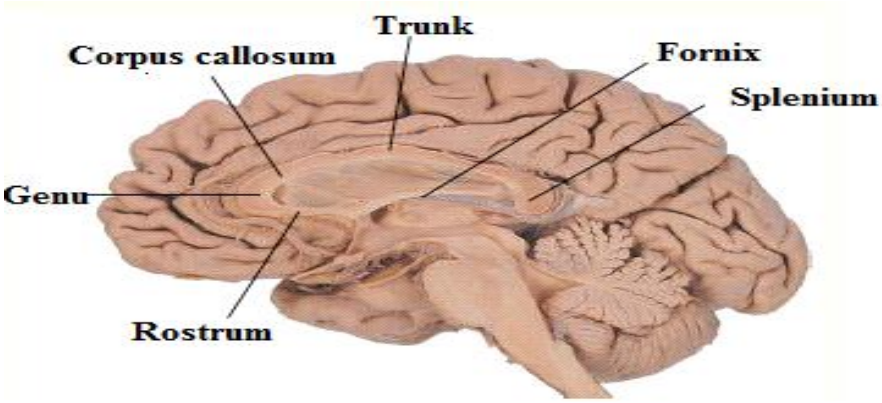

Figure (2.7) shows the parts of the corpus callosum (Corpus callosum. 2011).

Projection fibers join the cerebral cortex to lower centers. They are called the internal capsule, where they lie lateral to the thalamus and the corona radiata as they fanout between the internal capsule and the cerebral cortex (Ryan et al., 2004). Association tracts connect different regions within the same hemisphere of

the brain. Long association fibers connect different lobes of a hemisphere to each other whereas short association fibers connect different gyri within a single lobe (Saladin, 2012).

Unlike gray matter, which peaks in development in a person's twenties, the white matter continues to develop, and peaks in middle age (Sowell et al., 2003). In general, men have approximately 6.5 times the amount of gray matter than women, and women have nearly 10 times the amount of white matter than men. The gray matter represents information processing centers in the brain, while the white matter represents the networking of these processing centers (Calif, 2005).

Aggregates of gray matter such as the basal ganglia, the thalamus, and the hypothalamus are located within the cerebral white matter. The fluid-filled cerebral ventricles are also located deep within the cerebral white matter as shown on figure (2.8) (Marner et al., 2003).

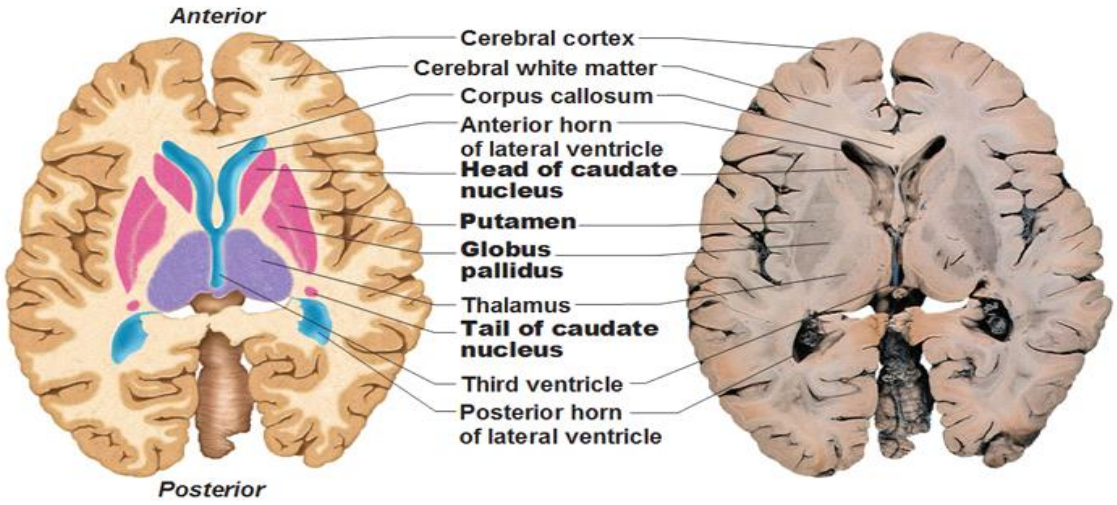

Figure (2.8) shows axial view of the brain cortical gray matter, white matter, and aggregations of gray matter such as thalamus, qaudate nucleus, putamen, and globus pallidus (Giovannoni, 2015).

2.1.1.4 The brain stem:

The brainstem is a relatively small mass of tissue packed with motor and sensory nuclei, making it vital for normal brain function. Its major segments are the midbrain, pons, and medulla oblongata; mentioned on figure (2.9). The brain stem connects the cerebral hemispheres with the spinal cord (Kelley and Petersen, 1997).

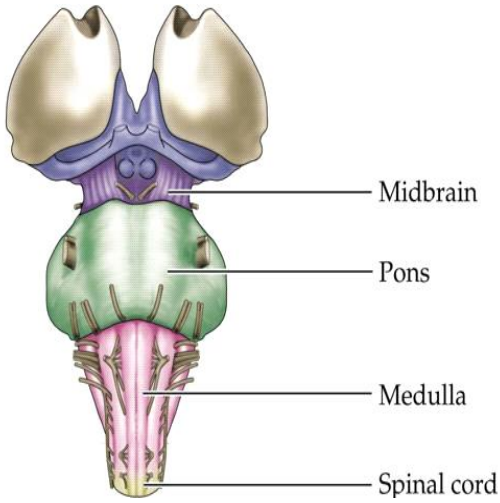

Figure (2.9) shows an anterior view for the brain stem and its divisions mid brain, pons, and medulla oblongata) (Antranik 2011).

2.1.1.5 The cerebellum:

The cerebellum lies in the posterior cranial fossa behind the pons and medulla oblongata as expressed on figure (2.10). It is composed of two hemispheres which are joined across the midline by a narrow strip called the vermis. Like the cerebrum the cerebellum is composed of an outer cortex of gray matter and has white matter in its interior. The cerebellum is concerned with the maintenance of balance and posture, and coordination of voluntary muscular movement (Dean and

Weast, 1987).

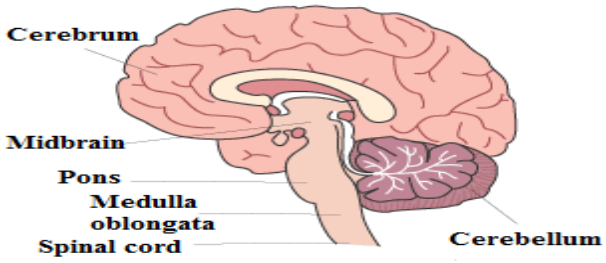

Figure (2.10) shows the cerebellum of the brain (Casanova, 2013).

2.1.1.6 The cerebral vascular system:

2.1.1.6.1 Arterial supply:

The brain receives arterial blood from the internal carotid and vertebral arteries.

2.1.1.6.1.1 Internal carotid arteries:

The internal carotid arteries supply the frontal, parietal, and temporal lobes of the brain; they enter the skull through the carotid canals of the temporal bones. When the internal carotid artery runs lateral to the optic chiasm it branches into the middle cerebral artery which supplies much of the lateral surface of the cerebrum, and anterior cerebral artery which in turn supply the anterior frontal lobe and the medial aspect of the parietal lobe (Kelley and Petersen, 1997).

The anterior cerebral arteries meet in the midline to form a short anterior communicating artery. This important vessel creates an anastomosis between the left and right cerebral hemispheres of the brain. Another small vessel, the posterior communicating artery, connects the internal carotid artery to the posterior cerebral artery (Kelley and Petersen, 1997).

2.1.1.6.1.2 Vertebral arteries:

The two vertebral arteries enter the cranium through the foramen magnum; they unite ventral to the pons to form the basilar artery. The vertebral and basilar arteries give rise to several pairs of smaller arteries that supply the cerebellum, pons, and inferior and medial surfaces of the temporal and occipital lobes. The four major pairs of arteries are listed in order from inferior to superior; posterior inferior cerebellar (PICA), anterior inferior cerebellar (AICA), superior cerebellar (SCA), and posterior cerebral (PCA) (Kelley and Petersen, 1997).

2.1.1.6.1.3 Circle of willis:

The circle of Willis, is a critically important anastomosis among the four major arteries (two vertebral and two internal carotids) feeding the brain. The circle of Willis is formed by the anterior and posterior cerebral, anterior and posterior communicating, and the internal carotid arteries. The circle is located mainly at the base of the brain. Figure (2.11) shows the circle of willis. The circle of Willis functions as a means of collateral blood flow from one cerebral hemisphere to another in the event of blockage (Kelley and Petersen, 1997).

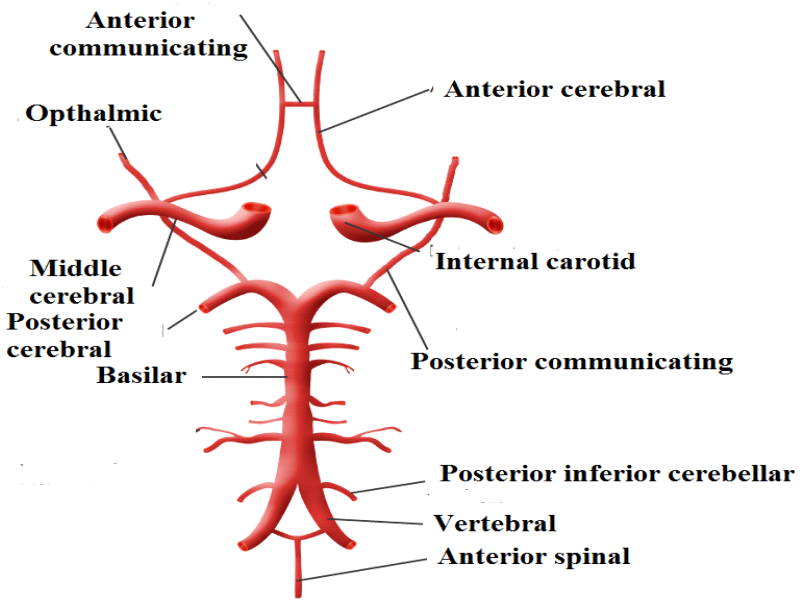

Figure (2.11) shows the circle of willis (Circle of Willis- Isolated “Labeled”. 2010).

2.1.1.6.2 Venous drainage:

The venous system of the brain and its coverings is composed primarily of the dural sinuses, superficial cortical veins, and deep veins of the cerebrum. The dural sinuses are very large veins located within the dura matter of the brain. The major dural sinuses include superior and inferior sagittal, straight, transverse, sigmoid, cavernous, and petrosal (Kelley and Petersen, 1997).

The superficial cortical veins are located along the surface of each cerebral hemisphere and are responsible for draining the cerebral cortex and portions of the white matter. The deep veins of the cerebrum drain the white matter and include the thalamostriate, septal, internal cerebral, basal (vein of Rosenthal), and great cerebral vein (vein of Galen). All cerebral venous output will eventually drain into one of the dural sinuses and ultimately into the internal jugular veins of the neck. Figure (2.12) shows the main sinuses and veins of the brain (Kelley and Petersen, 1997).

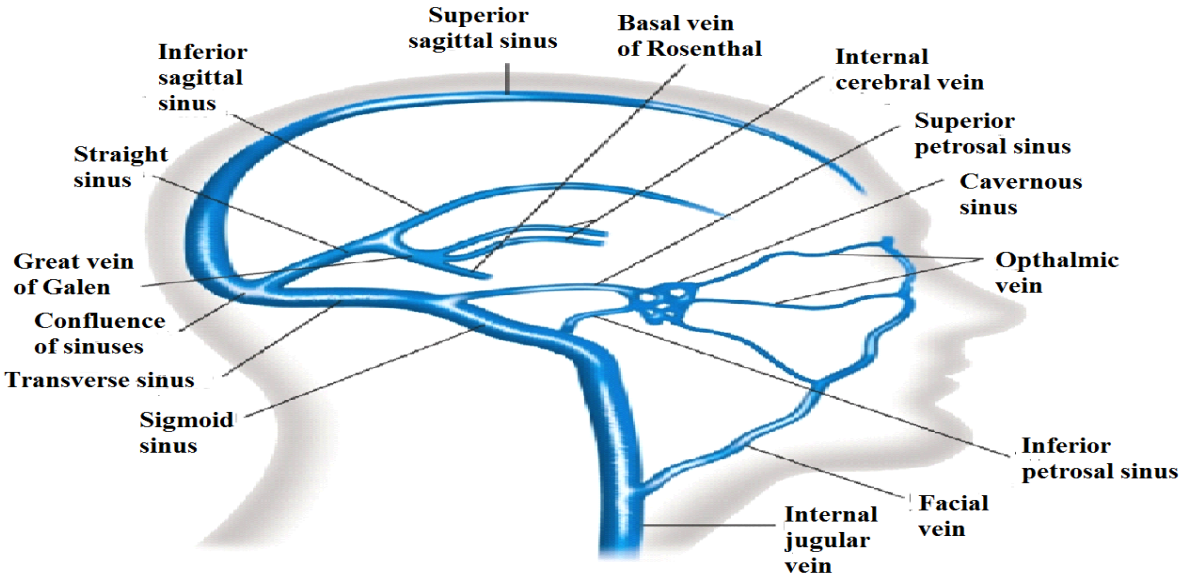

Figure (2.12) shows the venous drainage of the brain (Downes, 2014).

2.1.2 Pathology:

2.1.2.1 Hypertension (high blood pressure):

2.1.2.1.1 Definition:

Hypertension (HTN) is defined as having a blood pressure higher than 140 over 90 mmHg. This means the systolic reading; which is the pressure as the heart pumps blood around the body is over 140 mmHg, or the diastolic reading as the heart relaxes and refills with blood is over 90 mmHg (Gill, 2015). Controlled hypertension is defined as systolic blood pressure less than 140mm Hg and diastolic blood pressure less than 90 mm Hg, among persons with hypertension; otherwise it is considered as uncontrolled (Keenan, 2011).

The American Heart Association (AHA) (2014), defines the following ranges of blood pressure in millimeters of mercury (mmHg); normal blood pressure is below 120 systolic and below 80 diastolic, prehypertension is 120-139 systolic or 80-89 diastolic, stage one hypertension is 140-159 systolic or 90-99 diastolic, stage two hypertension is 160 or higher systolic or 100 or higher diastolic, and hypertensive crisis when blood pressure is above 180 systolic or above 110 diastolic.

2.1.2.1.2 Risk factors and Causes:

There are general risk factors that can be responsible for raising the risk of hypertension, these include; obesity, age, race, sex, and lifestyle. Other risk factors are a family history of the disease and chronic stress.

Depending on its causes; hypertension is divided into primary and secondary. Primary or essential hypertension is unlikely to have a specific cause but multiple

factors, including blood plasma volume and activity of the renin-angiotensin

system, the hormonal regulator of blood volume and pressure. Primary hypertension is affected by environmental factors, including the lifestyle and it is more common than secondary hypertension.

Secondary hypertension has specific causes; it is secondary to another problem such as certain diseases and medications, for example primary aldosteronism, kidney disease, Cushing syndrome, congenital adrenal hyperplasia, and hyperthyroidism. Common reversible causes are use of oral contraceptives, which can cause a slight rise in blood pressure; hormone therapy for menopause is also a culprit (Gill, 2015).

2.1.2.1.3 Symptoms:

High blood pressure itself is usually asymptomatic. It can do its damage silently (Gill, 2015). The effect of high blood pressure can be felt throughout the body. Long term hypertension can lead to many complications on the heart, brain, kidneys, eyes, and even bone. Figure (2.13) illustrate some of the potential effects of hypertension on different body organs (Pietrangelo, 2014).

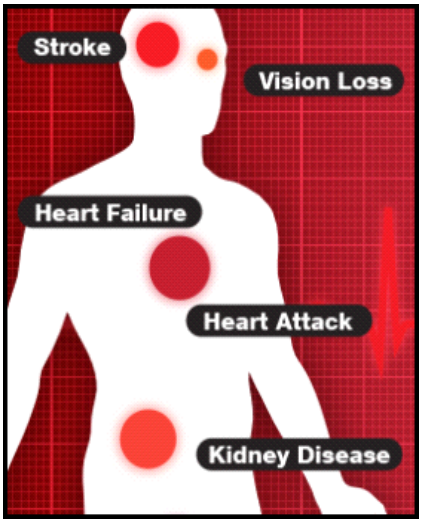

Figure (2.13) shows the side effects of high blood pressure on human body (Pietrangelo, 2014).

2.1.2.1.4 Diagnosis and tests:

Diagnosis of high blood pressure is made by measuring it, over a number of clinic visits, via a sphygmomanometer. An isolated high reading is not taken; rather, diagnosis can be made after measurement on at least three separate days. Other tests also help to identify the cause and determine whether there have been any complications; these may include urine tests, kidney ultrasound imaging, blood tests, electro cardiogram ECG and possibly echocardiography (Gill, 2015).

2.1.2.2 White matter changes (hyperintensities):

2.1.2.2.1 Definition:

White matter changes are commonly referred to as age-related white matter change (ARWMC). As the name implies, they are dependent on the age of patient, it is a condition routinely found in elderly population (Cheng, 2011). These white matter lesions (WML) are also called white matter hyperintensities (WMH), because they appear as areas of high intensities or bright signals on magnetic resonance images of the human brain or that of other mammals (Debette and Markus, 2010).

2.1.2.2.2 Imaging technique:

White matter changes are ill defined hypodensities on computed tomography. On magnetic resonance imaging, which is more sensitive than computed tomography on delineating the lesions, they appear as hypointensities on T_1-weighted imaging and hyperintensities on T_2-weighted imaging, proton density and fluid-attenuated inversion recovery sequences (FLAIR) (Xiong and Mok, 2011).

Fluid-attenuated inversion recovery is the sequence of choice for best disease visualization (Runge et al., 2015). It has the advantage of making cerebrospinal fluid looks dark while the white matter lesion still appears bright. This improves the lesion conspicuity, especially in areas close to the CSF spaces such as periventricular areas (Cheng, 2011).

2.1.2.2.3 Location:

Cerebral white matter changes can be divided into periventricular white matter changes (PVWMC) and deep white matter changes (DWMC) (Xiong and Mok,

2011). There are no widely accepted rules for defining white matter lesions other than the continuity rule; it defined the lesions contiguous with the margins of each lateral ventricle as periventricular and the lesions separate to it as deep. This rule has been applied in most of the visual rating scales fore white matter lesions (Kim et al., 2008).

2.1.2.2.4 Etiology:

The underlying etiology of white matter changes is still unclear (Maniega et al., 2015). Pathological studies had shown that; (PVWMC) were related to disruption of blood brain barrier, whereas the (DWMC) were related to incomplete ischemic arteriosclerosis (Xiong and Mok, 2011). That means (PVWMC) are not ischemic in nature (Gaillard 2008).

2.1.2.2.5 Scales and rating:

As to the assessment of white matter changes, various visual rating scales have been proposed. One of the most popular visual rating scales is Fazekas scale which has been validated histopathologically (Xiong and Mok, 2011). Fazekas scale is a four point scale, it divides the white matter into periventricular and deep, and each is given a grade depending on the size and confluence of lesions (Gillard 2008). It classified the lesions into mild, moderate or severe (Barkhof et al., 2013).

Nowadays, fully automated techniques and semiautomated segmentation methods become increasingly available. Different from the visual rating scales, volumetric measurement is more accurate however; it is more time-consuming with higher requirement of expertise and excellent quality of magnetic resonance imaging, which limits its use for research purpose (Xiong and Mok, 2011).

2.1.3 Magnetic resonance imaging for the brain:

2.1.3.1 Common indications:

Since the early 1980s, magnetic resonance imaging has been shown to be the most sensitive technique for the vast majority of intracranial diseases such as tumors, infarctions, and temporal lobe epilepsy; it is also very sensitive to diseases of the cerebral white matter (Liney, 2006).

2.1.3.2 Equipment:

The equipments needed for brain magnetic resonance imaging are a head coil, immobilization pads, and ear plugs (Westbrook, 2008).

2.1.3.3 Patient positioning:

The patient lies supine on the couch with his/her head within the head coil, the head is adjusted so that; it is straight and the interpupillary line is parallel to the couch. The patient is positioned so that the longitudinal alignment light lies in the midline, and the horizontal alignment light passes through the nasion. Straps and foam pads are used for immobilization (Westbrook, 2008).

2.1.3.4 Conventional technique (protocol):

A scout three planes (axial, sagittal, and coronal) is done. The conventional protocol includes axial T_2-weighted, coronal T_2, and sagittal T_1-weighted images. A saturation slab is used to avoid flow artifact (Westbrook, 2008).

2.1.3.4.1 Axial spin echo/ fast spin echo T_2/ PD:

Medium slices/gaps are prescribed from the foramen magnum to the superior surface of the brain. Slices may be angled so that they are parallel to the anterior

and posterior commissural axis. Proton density (PD) may be replaced by fluid attenuated inversion recovery (FLAIR) (Westbrook, 2008). Figure (2.15) illustrate the method of planning of axial slices on a sagittal view (Moeller and Reif, 2003).

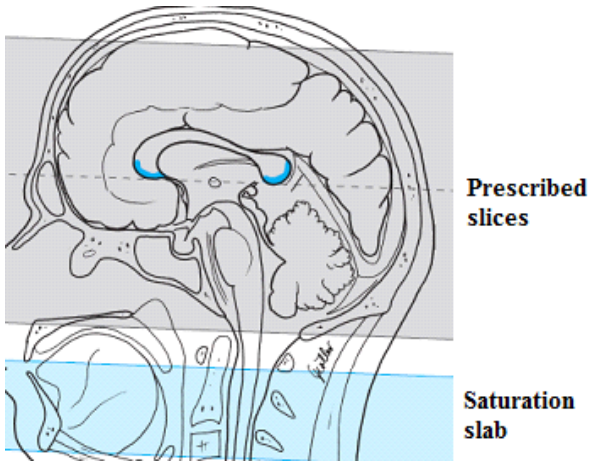

Figure (2.14) shows the planning of axial slices (Moeller and Reif, 2003).

2.1.3.4.2 Coronal spin echo/ fast spin echo T_2/ PD:

At the coronal image the prescribed slices from the cerebellum to the frontal lobe (Westbrook, 2008). Figure (2.16) explain the how to plan the coronal slices on a sagittal view (Moeller and Reif, 2003).

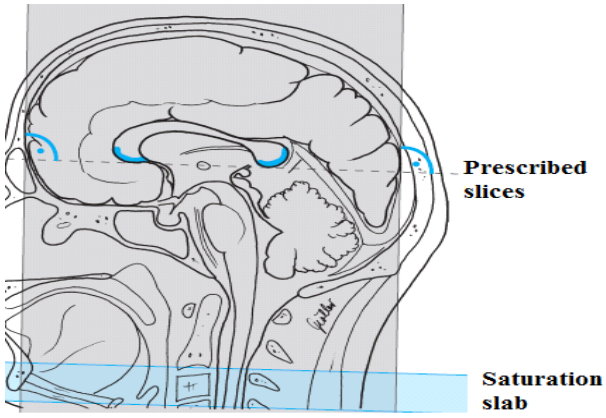

Figure (2.15) shows the planning of coronal slices (Moeller and Reif, 2003).

2.1.3.4.3 Sagittal spin echo/ fast spin echo T_1:

Medium slices/gaps are prescribed on either side of the longitudinal alignment light from one temporal lobe to the other. The area from the foramen magnum to the top of the head is included in the image (Westbrook, 2008). Figure (2.17) demonstrate the planning of sagittal slices on axial view (Moeller and Reif, 2003).

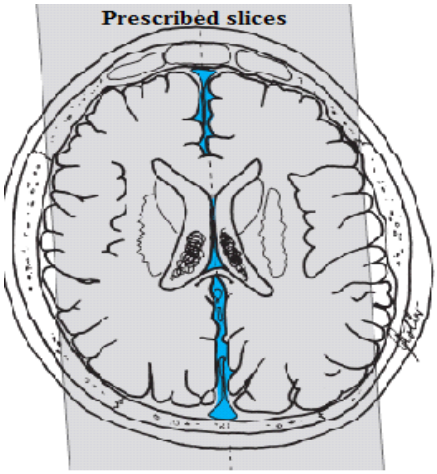

Figure (2.16) shows the planning of sagittal slices (Moeller and Reif, 2003).

2.2 Previous studies:

There were many theses had been done to study the prevalence of white matter hyperintensities and its relationship to high blood pressure.

A study was conducted to assess the association of white matter lesions with blood pressure, hypertension, and its treatment and control. A random sample of 1920 participants aged 55 to 72 years in the Atherosclerosis Risk in Communities Study (ARIC) was examined. Spin-density 1.5-T magnetic resonance imaging scan images were coded from 0 for normal to 9 for most severe white matter lesions. Hypertension was defined as systolic or diastolic pressure ≥140/90 mm Hg or use of antihypertensive medication.

The study used a scale from 0 to 9 based on the visual pattern matching of the participant's scans to reference standards. The reference standards are described as follows; no WMLs (grade 0), discontinuous periventricular rim or minimal dots of subcortical WMLs (grade 1), thin continuous periventricular rim or few patches of subcortical WMLs (grade 2), thicker continuous periventricular rim with scattered patches of subcortical WMLs (grade 3), thicker shaggier periventricular rim with mild subcortical WMLs, may have minimal confluent periventricular lesions (grade 4), mild periventricular confluence surrounding the frontal and occipital horns (grade 5), moderate periventricular confluence surrounding the frontal and occipital horns (grade 6), periventricular confluence with moderate involvement of the centrum semiovale (grade 7), periventricular confluence involving most of the centrum semiovale (grade 8), and all white matter involved (grade 9).

The study found that, the percentages of persons with WMLs grades 0 through 2 and 3 through 9, respectively, were as follows; normotensives, 92.4% and 7.6%,

versus all hypertensive subjects, 83% and 17% (P<.001); and treated controlled hypertensive, 86% and 14%, versus treated uncontrolled hypertensive subjects, 76% and 24% (P=.003). Multivariable adjusted odds ratios (95% confidence intervals) for WMLs grade ≥3 relative to normotensive subjects was 2.34 (1.71 to 3.20) for all hypertensives, 1.99 (1.19 to 3.08) for untreated hypertensives, 1.94 (1.32 to 2.85) for treated controlled hypertensives, and 3.40 (2.30 to 5.03) for treated uncontrolled hypertensives. After additional adjustment for hypertension duration, treatment, and control status, the odds ratios (95% confidence intervals) for a 1 SD increase of systolic and diastolic blood pressure were 1.43 (1.11 to 1.85) and 1.16 (0.94 to 1.43), respectively.

The study concluded; hypertension is associated with increased odds of white matter lesions, and treated uncontrolled hypertensive subjects have greater odds of white matter lesions than those with treated controlled hypertension. The data suggest that the level of blood pressure, especially systolic blood pressure, is related to white matter lesions, additional to the effects of categorically defined hypertension and its treatment and control status (Liao et al., 1996).

Another study reported the frequency distribution of subcortical and periventricular white matter lesions according to age and gender. A total of 1077 subjects aged between 60–90 years were randomly sampled from the general population. All subjects underwent 1.5T MRI scanning; white matter lesions were rated separately for the subcortical region and the periventricular region with a visual rating scale.

The study found that; of all subjects 8% were completely free of subcortical

WMLs, 20% had no PWMLs, and 5% had no WMLs in either of these locations. The proportion with WMLs increased with age, similarly for men and women. Women tended to have more subcortical WMLs than men (total volume 1.45 ml v 1.29 ml; p=0.33), mainly caused by marked differences in the frontal WML volume (0.89 ml v 0.70 ml; p=0.08). PWMLs were also more frequent among women than men (mean grade 2.5 v 2.3; p=0.07). Also severe degrees of subcortical WMLs were more common in women than in men (OR 1.1; 95% confidence interval (95% CI) 0.8–1.5) and PVWMLs (OR 1.2; 95% CI 0.9–1.7), albeit that none of these findings were statistically significant.

The study concluded; the prevalence and the degree of cerebral white matter lesions increased with age. Women tended to have a higher degree of white matter lesions than men. This may underlie the finding of a higher incidence of dementia in women than in men, particularly at later age Leeuw et al. (2001).

A research was done to evaluate prospectively the association of white matter lesions with the duration and treatment of hypertension. A total of 1077 subjects aged between 60 and 90 years from two prospective population based studies were randomly sampled. One half of the study subjects had their blood pressure measured between 1975 and 1978 and the other half between 1990 and 1993. Hypertension was defined as systolic or diastolic pressure ≥160/95 mm Hg or use of antihypertensive medication. All subjects underwent 1.5 Tesla MRI scanning.

White matter lesions were considered to be present if there was hyperintensity on both the proton density (PD) and the T_2 weighted image without prominent hypointensity on the T_1 weighted image, the lesions classified into those in the subcortical and periventricular regions. The number and size of subcortical WMLs was rated on hard copy according to their largest diameter in categories of small

(<3 mm), medium (3–10 mm) and large (>10 mm). In order to calculate the volume of subcortical white matter lesions on hard copy, they were considered to be spherical with a fixed diameter for each size category.

Periventricular white matter lesions were rated semiquantitatively for each region [adjacent to the frontal horns (frontal capping); adjacent to the lateral wall of the lateral ventricles (bands); and adjacent to the occipital horns (occipital capping)] on a four point scale: 0 = no white matter lesions; 1 = pencil thin periventricular lining; 2 = smooth halo or thick lining; 3 = large confluent white matter lesions. The overall amount of PVWMLs was calculated by summing the scores for the three separate regions to give a total in the range 0–9.

The study was proved the following results; subjects with hypertension had increased rates of both types of WMLs. Duration of hypertension was associated with both periventricular and subcortical WMLs. This relationship was influenced strongly by age. For participants with >20 years of hypertension and aged between 60 and 70 years at the time of follow up, the relative risks for subcortical and periventricular WMLs were 24.3 [95% confidence interval (CI) 5.1–114.8] and 15.8 (95% CI 3.4–73.5), respectively, compared with normotensive subjects. Subjects with successfully treated hypertension had only moderately increased rates of subcortical WMLs and PVWMLs (relative risk 3.3, 95% CI 1.3–8.4 and 2.6, 95% CI 1.0–6.8, respectively) compared with normotensive subjects. For poorly controlled hypertensives, these relative risks were 8.4 (95% CI 3.1–22.6) and 5.8 (95% CI 2.1–16.0), respectively.

The study concluded; there was a relationship between long standing hypertension and the presence of white matter lesions. The findings are consistent with the view that; effective treatment may reduce the rates of both types of white

matter lesion. Adequate treatment of hypertension may therefore prevent white matter lesions and the associated cognitive decline (Leeuw et al., 2002).

Dijk et al. (2004) assessed in 10 European cohorts the relation between concurrently and previously measured blood pressure levels, hypertension, its treatment, and severe cerebral white matter lesions. In total, 1805 nondemented subjects aged 65 to 75 years were sampled from ongoing community-based studies that were initiated 5 to 20 years before the MRI.

Images acquired on a 1.0-T or a 1.5-T machine using comparable MRI protocols included T_1, T_2, and proton density-weighted magnetic resonance images. White matter lesions were considered present if visible as hyperintense on proton density-weighted and T_2-weighted images, without prominent hypointensity on T_1-weighted scans.

White matter lesions in the periventricular and subcortical region were rated separately using semi-quantitative measures. Periventricular white matter lesion grades were rated semi-quantitatively (range 0 to 9). For subcortical white matter lesions, a total volume was approximated. Three raters, trained by one neuro-radiologist, scored all images.

They performed logistic regression analyses adjusted for potential confounders in 1625 people with complete data. Concurrently and formerly assessed diastolic and systolic blood pressure levels were positively associated with severe white matter lesions.

The researchers found that; both increases and decreases in diastolic blood pressure were associated with more severe PVWMLs. Increase in systolic blood pressure levels was associated with more severe periventricular and subcortical

white matter lesions. People with poorly controlled hypertension had a higher risk of severe white matter lesions than those without hypertension, or those with

controlled or untreated hypertension. Higher blood pressure was associated with an increased risk of severe white matter lesions.

Vlek et al. (2009) were conducted a cross-sectional study to evaluate associations between blood pressure and white matter lesion in patients with manifest vascular disease. The researchers also examined whether relations between blood pressure and white matter lesions were modified by the localization of the symptomatic site or presence of diabetes.

A total of 1030 patients with vascular disease (cerebrovascular disease (23%), coronary heart disease (59%), peripheral arterial disease (23%), abdominal aortic aneurysm (9%)) from the Second Manifestations of arterial disease study were included. white matter lesions volume was calculated using an automated quantitative volumetric method and subsequently divided into quartiles. Participants had a mean age of 58.7 years. Median volume of white matter lesion was 1.70 ml. Mean blood pressure was 141/82 mmHg and 69% suffered hypertension.

The researchers found that; there were no significant associations between systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP) or hypertension presence, and moderate or large white matter lesion volumes were present. The relation between blood pressure and white matter lesion was not modified by the localization of vascular disease or diabetes presence.

The researchers concluded; among patients with manifest vascular disease, blood

pressure was not associated with the presence of white matter lesion, irrespective of the presence of diabetes or the localization of vascular disease.

Chapter three
Materials and methods

Chapter three

Materials and methods

3.1 Materials:

3.1.1 Patients:

The data needed to conduct this study were collected from modern medical center and Asia hospital at the period from January to March (2016). A total of thirty patients were randomly chosen, fifteen of them had a normal blood pressure without any cardiovascular or other diseases; whereas the others were hypertensives.

All hypertensive patients had an age equal to or greater than forty years old and taking anti-hypertensive medication. The patients with an age less than forty years old or those who had other diseases that could affect their brains were excluded from the sample.

3.1.2 Machines used:

The machines which used were general electric signa excite HD 1.5T magnetic resonance scanner at modern medical center and general electric 0.2T magnetic resonance scanner at Asia hospital. The type of coil which used was a head coil. Immobilization bads were also used.

3.2 Methods:

3.2.1 Data collection:

The study was an analytical case control study, combined a control group of fit

individuals; as well as another group of hypertensives. Hypertension was defined as having a systolic blood pressure more than 140 mmHg, and diastolic blood pressure more than 90 mmHg, or receiving antihypertensive treatment. Height and weight were measured and the body mass index was calculated as weight divided by height squared.

The participant's clinical data were registered on a master data table contained the variables; age, gender, body mass index (BMI) and the duration of hypertension as well as its control. Another type of variables derived from the magnetic resonance images concerned with the location and the grade of severity of white matter changes; were also registered on the table.

3.2.2 Magnetic resonance imaging protocol:

The participants underwent axial T_1 and T_2 spin echo, as well as axial fluid attenuated inversion recovery (FLAIR) weighted magnetic resonance images for their brains. The slices were prescribed from the foramen magnum to the superior surface of the brain. The positioning block was angled so that it was parallel to the line which joins the genu and splenium of the corpus callosum.

3.2.3 Image interpretation and rating scale:

White matter hyperintensities were considered to be present if there were bright signals on both the fluid attenuated inversion recovery (FLAIR) and the T_2 weighted images without a prominent hypointensity on the T_1 weighted image. The images also interpreted by a radiologist for a second opinion. The lesions were rated using a Fazekas visual rating scale to assess their location, size, and shape. Figure (3.1) shows different grades of fazekas scale for periventricular and deep white matter lesions.

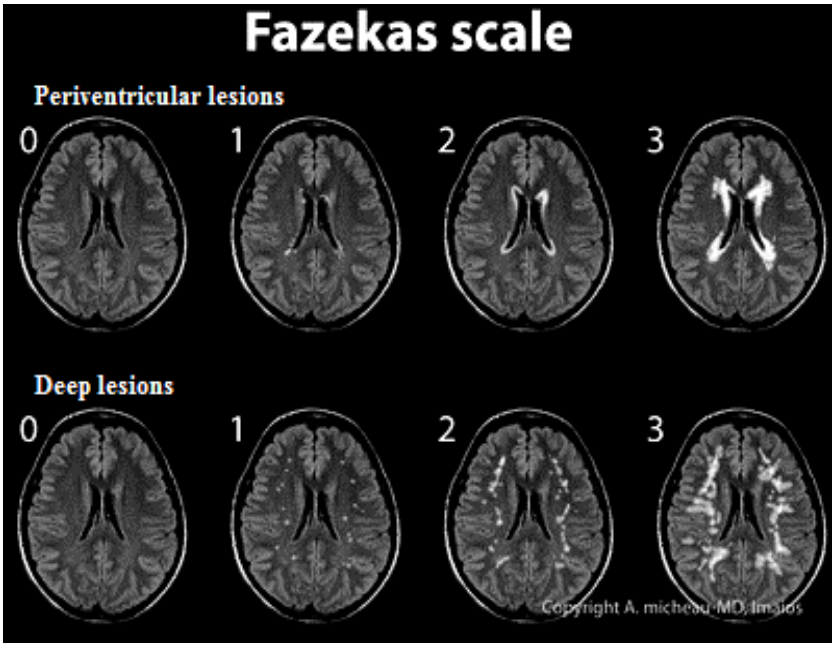

Figure (3.1) shows Fazekas scale for white matter lesion; periventricular (upper row) and deep (lower row) (Micheau, 2008).

For the assessment of the location; white matter lesions were classified into periventricular and deep. The lesions were considered as periventricular when they had an attachment with the ventricles; otherwise they were classified as deep white matter lesions. The size of white matter lesions were rated for the largest one; in categories of small (< 3 mm), medium (3-10 mm), and large (> 10 mm).

For the assessment of the shape and size depending on Fazekas scale, the periventricular white matter lesions were divided into four grades; zero for no lesion, one for caps or thin lining (small), two for smooth halo or thick lining (medium), and three for irregular lesions that extend into deep white matter (large). The deep white matter lesions also classified into four grades; zero for no lesion, one for focal lesions (small), two for beginning confluent (medium), and three for extensively confluent lesions (large).

Fazekas four point scale reflects the severity of white matter lesions according to their grades; grade one correspond to mild, two to moderate and three to sever white matter changes.

3.2.4 Data analysis:

The data were analyzed by (SPSS), and the tests which used were Mann-Whitney U test and Sperman’s rho.

Chapter four

Results

Chapter four

Results

The findings of this study were presented by the following figures and tables:

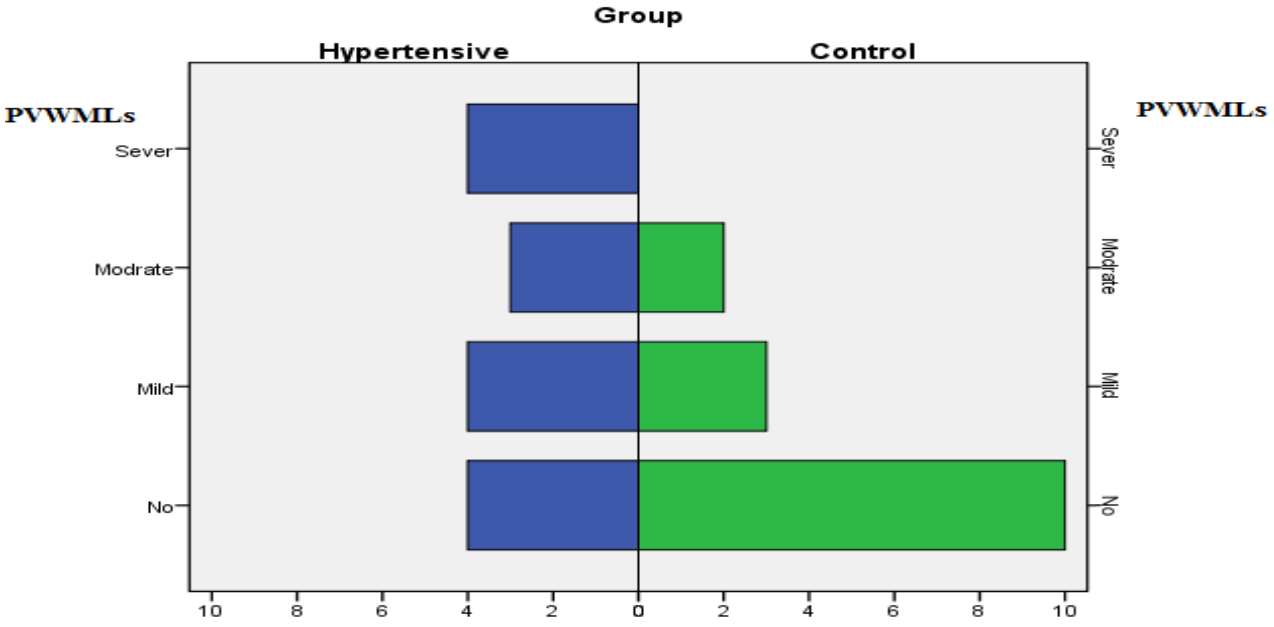

Figure (4.1) shows a bar graph for the difference between control group and hypertensive group in periventricular white matter lesions.

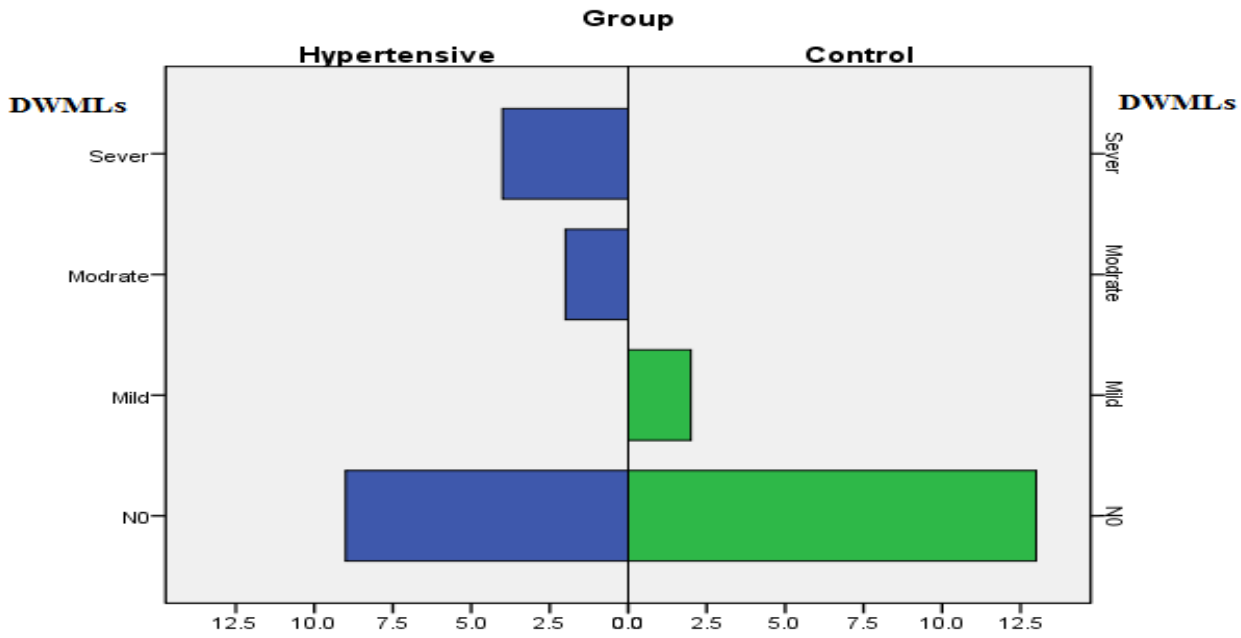

Figure (4.2) shows a bar graph for the difference between control group and hypertensive group in deep white matter lesions.

Table (4.1) demonstrates the distribution of WMLs (PVWMLs and DWMLs) for both control and hypertensive group.

Group		N	Mean rank	Sum of ranks
PVWMLs				
	Hypertensive	15	19.20	288.00
	Control	15	11.80	177.00
	Total	30		
DWMLs				
	Hypertensive	15	17.90	268.50
	Control	15	13.10	196.50
	Total	30		

Table (4.2) demonstrates the Mann-Whitney test for mean ranks for both control and hypertensive group.

	PVWMLs	DWMLs
Mann-Whitney U	57.000	76.500
Wilcoxon W	177.000	196.500
Z	-2.454	-1.922
Asymp. Sig. (2-tailed)	0.014	0.055
Exact Sig. [2*(1-tailed Sig.)]	0.021	0.137

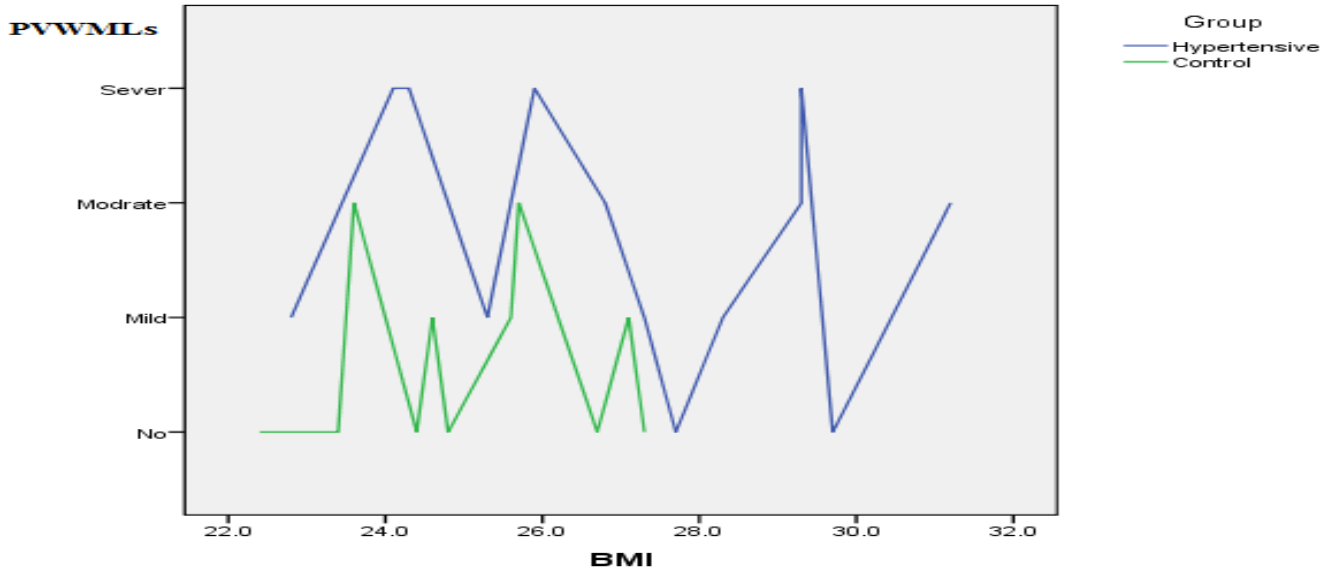

Figure (4.3) shows a line graph for the association between body mass index and periventricular white matter lesions for control and hypertensive group.

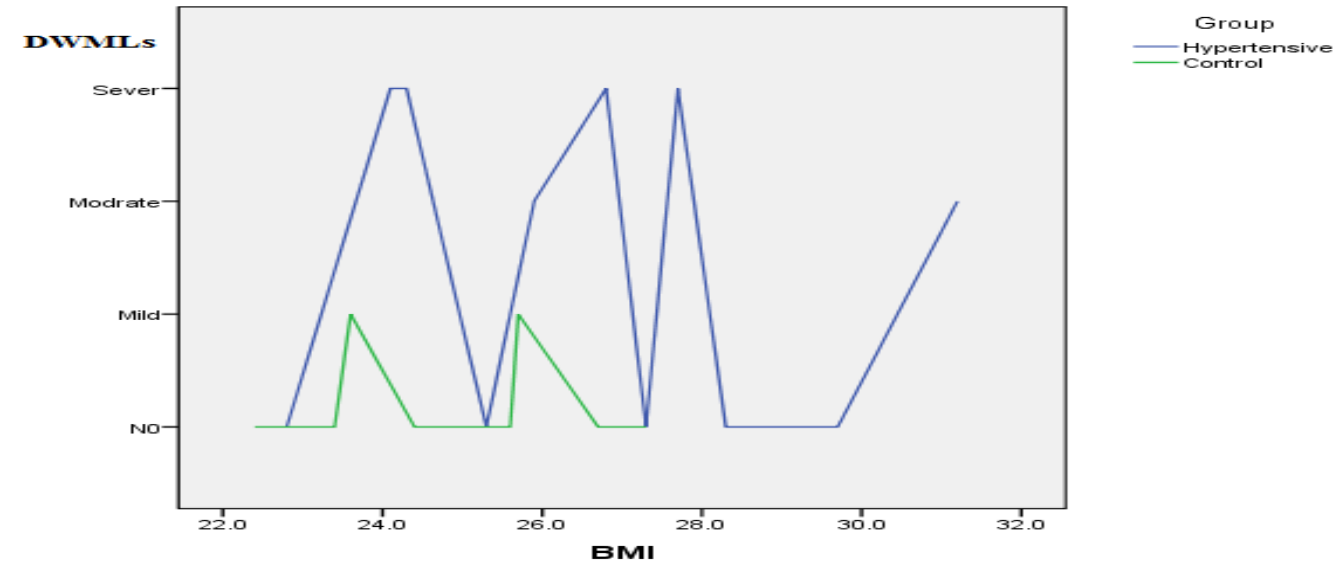

Figure (4.4) shows a line graph for the association between body mass index and deep white matter lesions for control and hypertensive group.

Table (4.3) shows the correlation Coefficients between BMI and WMLs (PWMLs and DWMLs) on the two groups, as well as the corresponding significance values of Spearman's Correlation Coefficients.

			Hypertensive	Control
			BMI	BMI
Spearman's rho	BMI	Correlation Coefficient	1.000	1.000
		N	15	15
	PVWMLs			
		Correlation Coefficient	0.394	-0.423
		Sig. (2-tailed)	0.146	0.116
		N	15	15
	DWMLs			
		Correlation Coefficient	0.136	-0.363
		Sig. (2-tailed)	0.628	0.184
		N	15	15

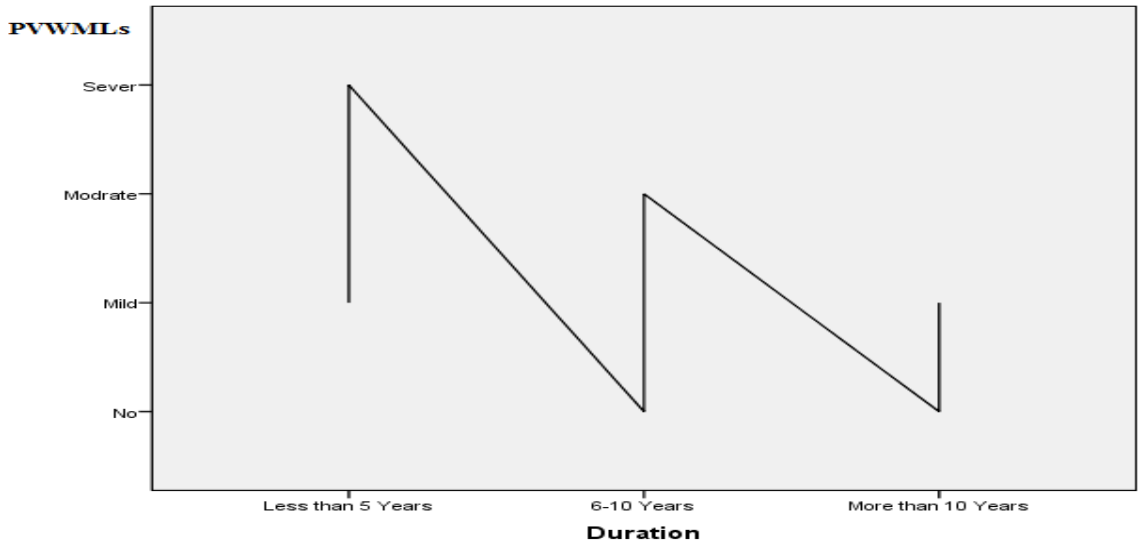

Figure (4.5) shows a line graph for the association between the duration of hypertension and periventricular white matter lesions.

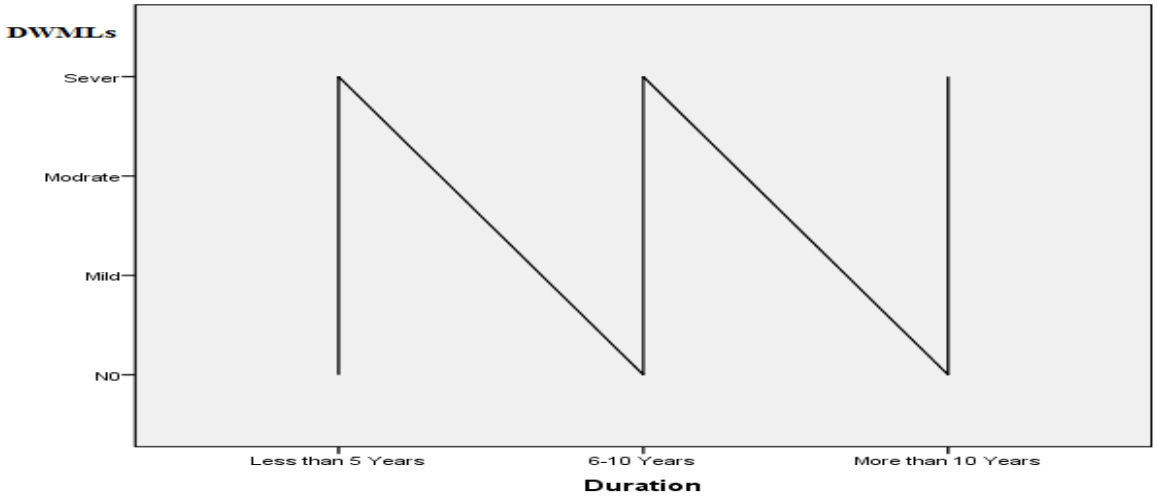

Figure (4.6) shows a line graph for the association between the duration of hypertension and deep white matter lesions.

Table (4.4) demonstrates the correlation Coefficients between the duration of HTN and WMLs (PVWMLs and DWMLs), as well as the corresponding significance values of Spearman's Correlation Coefficients.

			Duration	PVWMLs	DWMLs
Spearman's rho	Duration	Correlation Coefficient	1.000	-0.743	-0.230
		Sig. (2-tailed)	.	0.001	0.409
		N	15	15	15

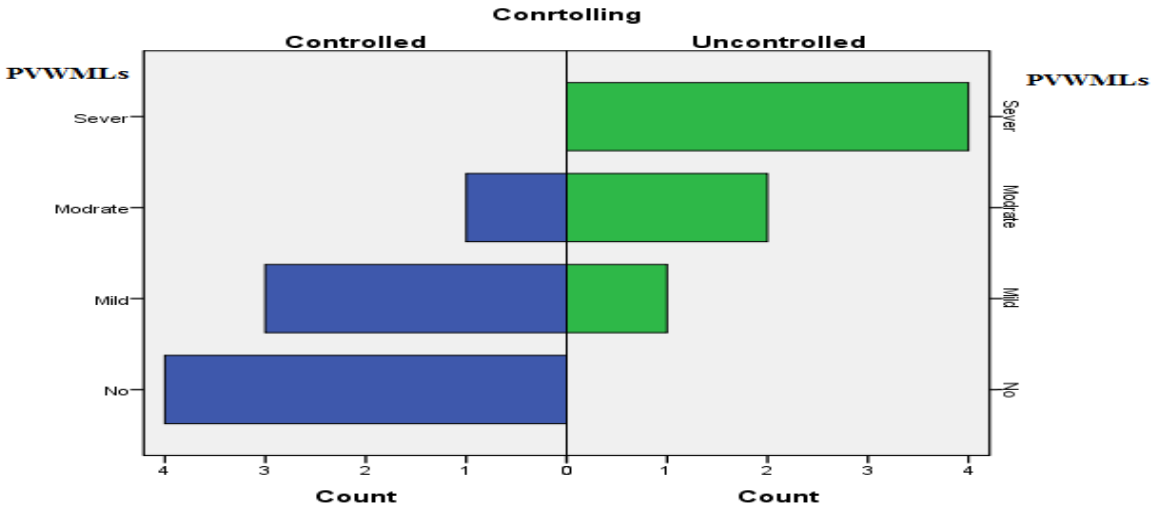

Figure (4.7) a bar graph for the differences between controlled and uncontrolled hypertensive patients in periventricular white matter lesions.

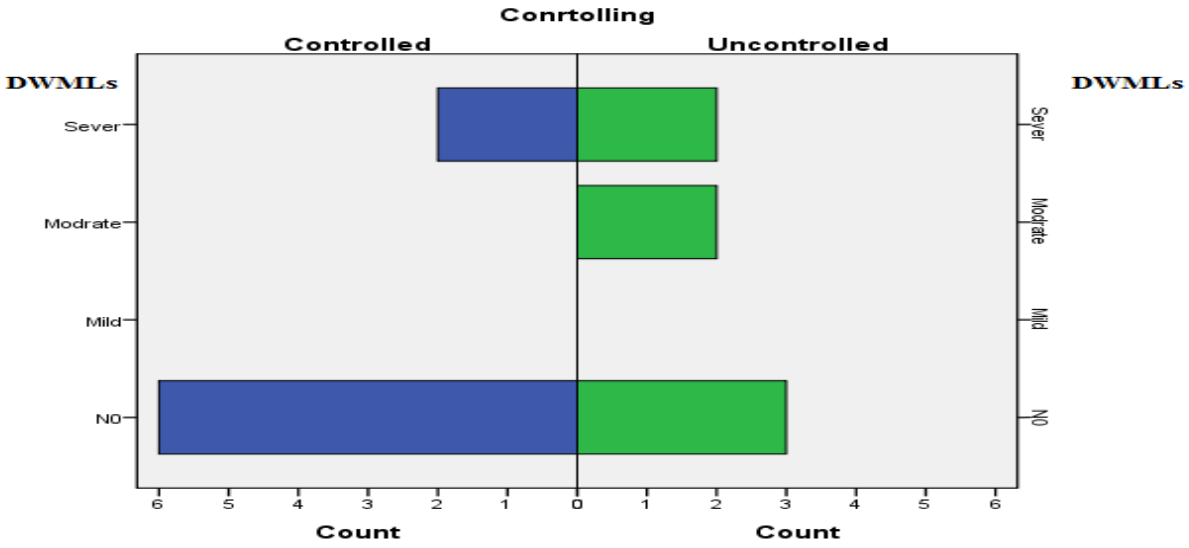

Figure (4.8) shows a bar graph for the differences between controlled and uncontrolled hypertensive patients in deep white matter lesions.

Table (4.5) shows the distributions of PWMLs and DWMLs according to the control status of HTN.

	HTN controlling	N	Mean rank	Sum of ranks
PVWMLs				
	Controlled	8	4.94	39.50
	Uncontrolled	7	11.50	80.50
	Total	15		
DWMLs				
	Controlled	8	7.12	57.00
	Uncontrolled	7	9.00	63.00
	Total	15		

Table (4.6) demonstrates the Mann-Whitney test for mean ranks of controlled and uncontrolled hypertensive patients.

	PVWMLs	DWMLs
Mann-Whitney U	3.500	21.000
Wilcoxon W	39.500	57.000
Z	-2.926	-0.926
Asymp. Sig. (2-tailed)	0.003	0.355
Exact Sig. [2*(1-tailed Sig.)]	0.002	0.463

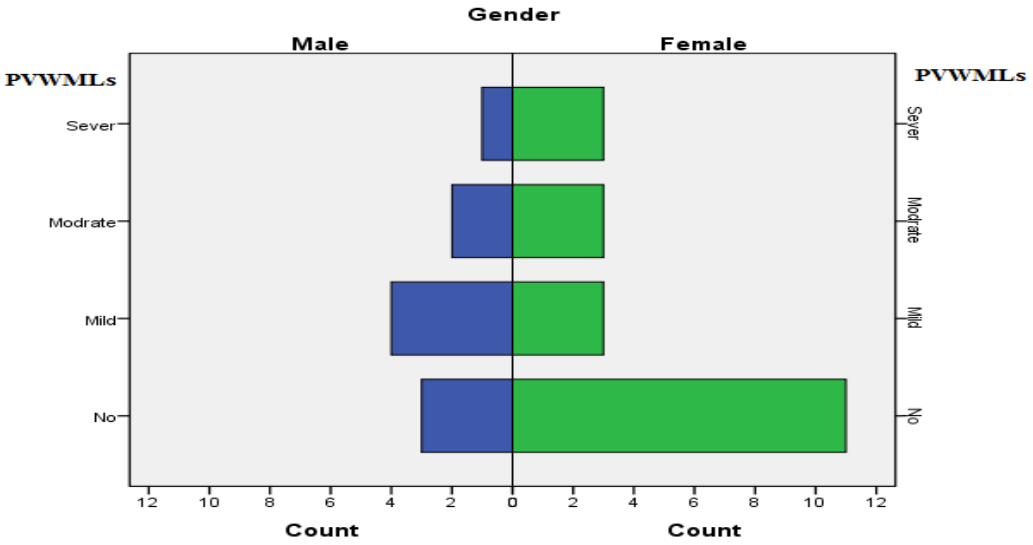

Figure (4.9) shows a bar graph for the differences between male and female in periventricular white matter lesions.

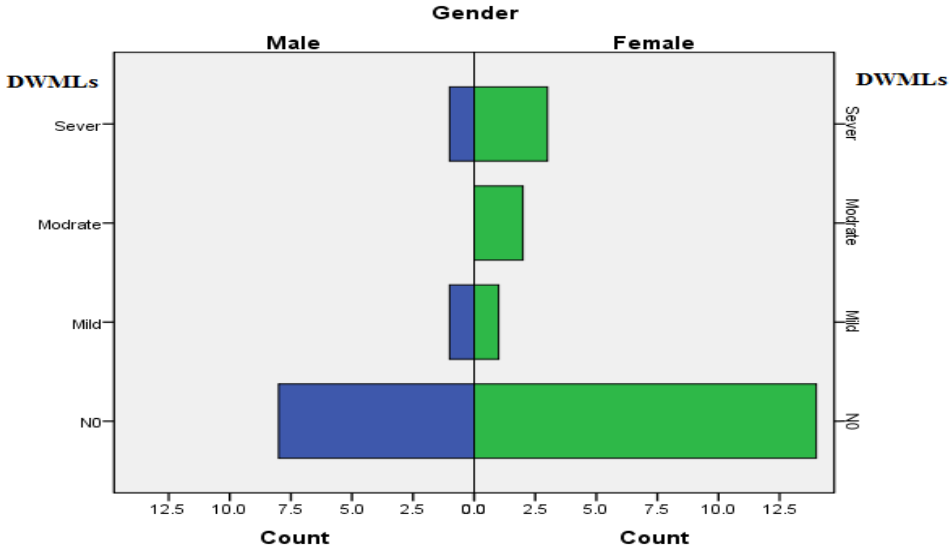

Figure (4.10) shows a bar graph for the differences between male and female in deep white matter lesions.

Table (4.7) shows the distributions of (PWMLs and DWMLs) according to gender.

	Gender	N	Mean rank	Sum of ranks
PVWMLs				
	Male	4	9.12	36.50
	Female	11	7.59	83.50
	Total	15		
DWMLs				
	Male	4	7.12	28.50
	Female	11	8.32	91.50
	Total	15		

Table (4.8) demonstrates the Mann-Whitney test of mean ranks for both genders.

	PVWMLs	DWMLs
Mann-Whitney U	17.500	18.500
Wilcoxon W	83.500	28.500
Z	-0.606	-0.522
Asymp. Sig. (2-tailed)	0.544	0.602
Exact Sig. [2*(1-tailed Sig.)]	0.571	0.661

Figure (4.11) shows a line graph for the association between the age and periventricular white matter lesions for hypertensive group.

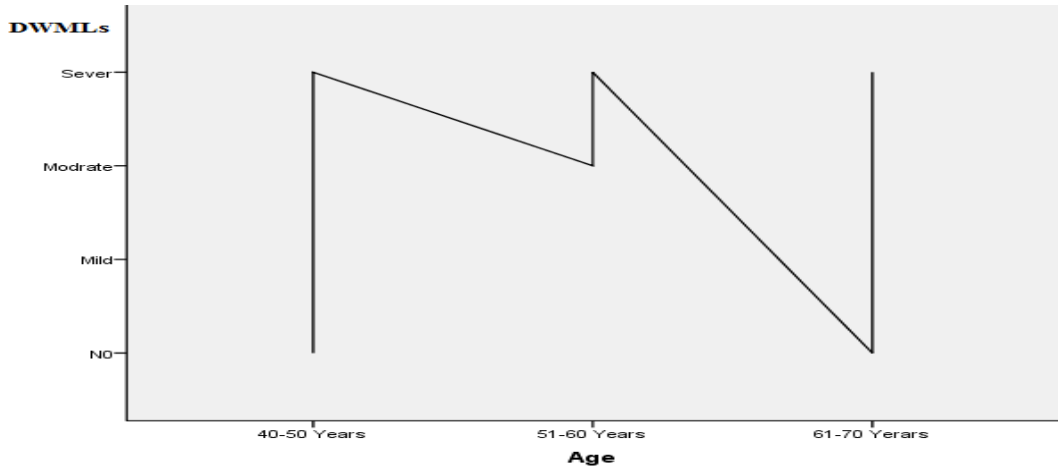

Figure (4.12) shows a line graph for the association between the age and deep white matter lesions for hypertensive group.

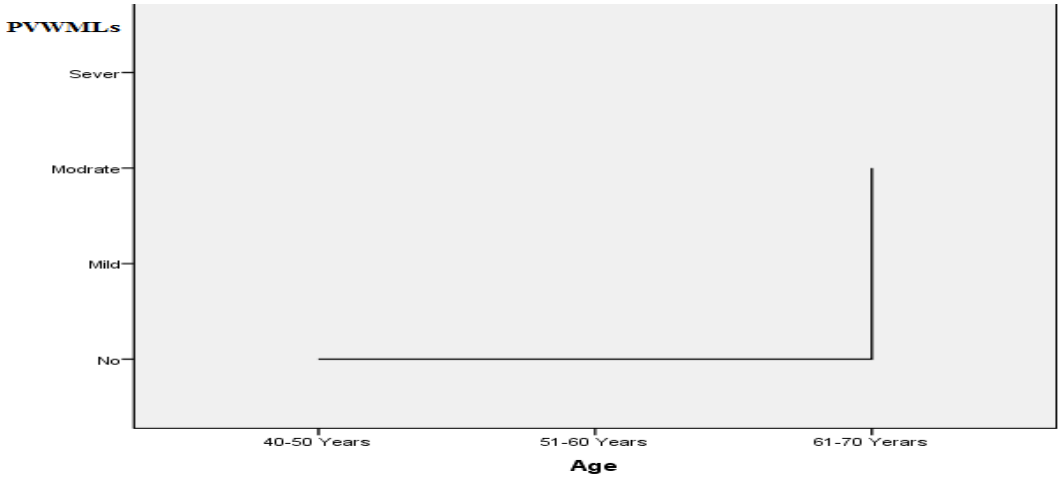

Figure (4.13) shows a line graph for the association between the age and periventricular white matter lesions for control group.

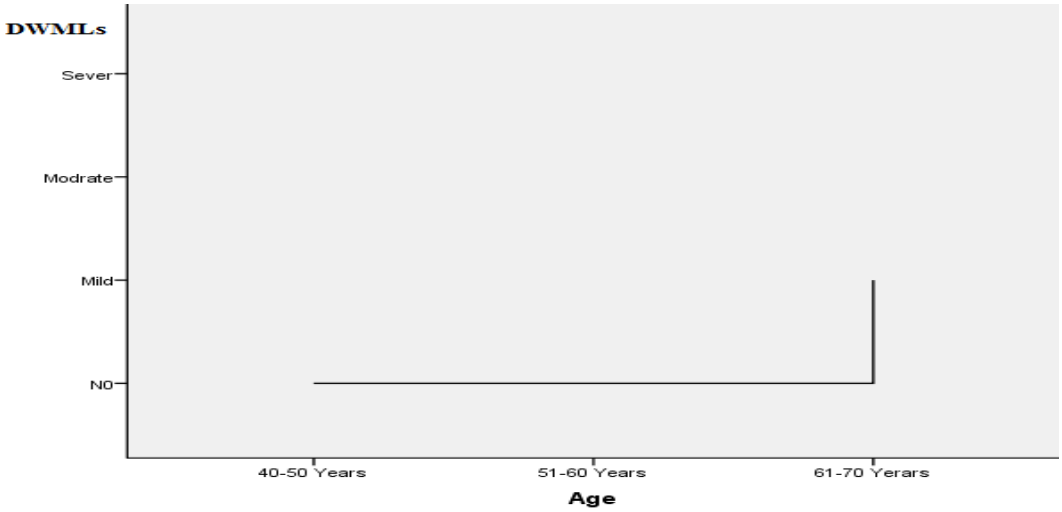

Figure (4.14) shows a line graph for the association between the age and deep white matter lesions for control group.

Table (4.9) demonstrates the correlation Coefficients between age and WMLs (PVWMLs and DWMLs) in HTN group, with the corresponding significance values of Spearman's Correlation Coefficients.

			Age	PVWMLs	DWMLs
Spearman's rho	Age	Correlation Coefficient	1.000	-0.223	-0.258
		Sig. (2-tailed)	.	0.425	0.354
		N	15	15	15

Table (4.10) demonstrates the correlation Coefficients between age and WMLs (PVWMLs and DWMLs) in control group, as well as the corresponding significance values of Spearman's Correlation Coefficients.

		Age	PVWMLs	DWMLs
Spearman's rho Age	Correlation Coefficient	1.000	0.693	0.392
	Sig. (2-tailed)	.	0.004	0.148
	N	15	15	15

Chapter five

Discussion, conclusion and recommendations

Chapter five

Discussion, conclusion, and recommendations

5.1 Discussion:

The study used a comparative analytical method by SPSS statistical programme based on descriptive statistics, comparative, and relationship tests (0.05 sig. level) to demonstrate the differences in WMLs (PVWMLs and DWMLs) for hypertensive patients group comparing to control group, according to gender, age, BMI, as well as the duration and control status of the disease. The tests which used were Mann-Whitney U test and Sperman's rho.

The mean ranks of PVWMLs and DWMLs were (19.20, 11.80) and (17.90, 13.10) respectively, for Hypertensive group and control group, with corresponding significance values of Mann-Whitney tests (0.014, 0.055) which implies; there were statistically significant differences between two groups for PVWMLs, while no significant differences for DWMLs were present. The values were shown on tables (4.1) and (4.2). In general hypertensives had more severe WMLs than control group as shown on figures (4.1) and (4.2); this was compatible with Liao et al., in (1996), but inconsistent with Vlek et al., in (2009).

The correlation coefficients of body mass index with PVWMLs and DWMLs were (0.394, ¯0.423) and (0.136, ¯0.363) respectively for hypertensive and control group, and the corresponding significance values of Spearman's Correlation Coefficients were (0.146, 0.116) and (0.628, 0.184), as demonstrated on table (4.3). This implies that; there were no statistically significant correlation between BMI and WMLs as shown on figures (4.3) and (4.4).

The Correlation coefficients between the duration of HTN and (PVWMLs and DWMLs) were (-0.743, -0.230) with corresponding significance values of Spearman's Correlation Coefficients (0.001, 0.409) respectively, table (4.4). This means the duration of HTN had a statistically significant high negative correlation with PVWMLs, and insignificant, weak, negative correlation with DWML. This was incongruous with the study of Leeuw et al. in (2002) which found a direct association. The inconsistency may be due to that; the relationship was influenced strongly by control status of HTN and/or due to small sample size. The relation was explained on figures (4.5) and (4.6).

The mean ranks of PVWMLs and DWMLs were (4.94, 11.50) and (7.12, 9.00) respectively, for controlled and uncontrolled hypertensive patients, with corresponding significance values of Mann-Whitney tests (0.003, 0.355), this was demonstrated on tables (4.5) and (4.6). It implies that; there were statistically significant differences between two groups in PVWMLs, while no significant differences were found in case of DWMLs. Having WMLs for uncontrolled patients with more severity than the controlled was shown on figures (4.7) and (4.8), it was consistent with the studies of Liao et al., in (1996) and Dijk et al., in (2004).

The mean ranks of PVWMLs and DWMLs were, (9.12, 7.59) and (7.12, 8.32) respectively, for male and female, with corresponding significance values of Mann-Whitney tests (0.544, 0.602), this was presented on table (4.7) and (4.8). It means that; there were no statistically significant differences between two groups in WMLs. Generally men tend to have more PVWMLs than women; while women tend to have more DWMLs than men; the former was inconsistent, whereas the latter was consistent with the study of Leeuw et al., in 2001. The differences were

explained on figures (4.9) and (4.10).

The correlation coefficients for age with PVWMLs and DWMLs were (-0.223, 0.693) and (-0.258, 0.392) respectively -for both hypertensive and control group- with corresponding significance values of Spearman's Correlation Coefficients were (0.425, 0.004) and (0.354, 0.148), tables (4.9 - 4.10). That implies; there were no statistically significant correlation between WMLs and age in hypertensive, but there was a statistically significant high Positive correlation (0.693), between PVWMLs and age in control group. The latter result was agreeable with leeuw et al., in 2001. This was shown on figures (4.11 through 4.14), they also showed that hypertensive group tend to have WMLs earlier and with more severity than control group.

5.2 Conclusion:

The cerebrum as a whole has many critically important functions including thought, judgment, memory, and discrimination. It consists of gray matter-neuron cell bodies- and white matter which contains the myelinated axons. Cerebral white matter can develop lesions that are a common finding on brain magnetic resonance imaging of elderly people; these lesions are an important prognostic factor for stroke, cognitive impairment, dementia, and death. The goal of this study was to evaluate the changes of cerebral white matter in relation to hypertension, as well as its duration and control.

The association between white matter lesions and high blood pressure had been studied previously, some of those studies found a relationship between them but others stated that there was no significant association. The scholars said; hypertensives had more WMLs than normotensives, and uncontrolled one had more WMLs than the controlled, in addition they found a direct relation between WMLs and the duration of HTN. They also said; the prevalenc and degree of WMLs increase with age, and female tend to have more WMLs than male.

The study was an analytical, combined a control group and another group of hypertensive patients. Both groups underwent magnetic resonance scanning - an axial T_1, T_2, and fluid attenuated inversion recovery- for the brain. White matter lesions were considered to be present if there were bright signals on both the fluid attenuated inversion recovery and T_2 weighted images without a prominent hypointensity on T_1 weighted image. The lesions were assessed by a visual rating scale (Fazekas) to evaluate their location, size, and shape.

The study found that; hypertensives had more WMLs than normotensive subjects; also the patients with poorly controlled hypertensives tend to have more severe WMLs than those with controlled HTN. The duration of hypertension had an inverse proportion with the severity of WMLs; this may be due to small sample size and/or the strong effect of control status for HTN. A little period of extreme and uncontrolled HTN can cause severe changes on cerebral white matter more than a long period of controlled hypertension.

The age was the most common cause of WMLs, and had a direct relationship with it in normal individuals, in hypertensive group there were no significant association with age. Hypertensive patients developed WMLs on relatively young age; this may indicate that HTN can accelerate the aging process of the brain. Regarding the gender; male had more PVWMLs than female, while the female had more DWMLs than male. Body mass index had no significant association with WMLs.

5.3 Recommendations:

Automated techniques or semi-automated segmentation methods are more accurate and gives a quantitative data; it can be used instead of visual rating scales when high quality magnetic resonance images are available.

The limitation of conventional MRI can potentially be overcome with the use of Diffusion Tensor Imaging (DTI) which allows the assessment of microstructural integrity of the whole white matter. A study can be done with DTI for further assessment of controlled hypertensive patients who had normal appearing white matter on the conventional MRI.

Future studies can be conducted to evaluate the association between WMLs and hypertension with a larger sample size, and more variables such as the blood pressure parameters (systolic, diastolic, and pulse pressure).

The presence of ARWMCs on the HTN group in a relatively young age may indicate that; HTN can accelerate brain aging; so further theses should be conducted on other structures of the brain such as gray matter and CSF spaces to approve this theory.

Normotensive subjects should check their blood pressure every two years after the age of eighteen. Adequate control of HTN can lead to lesser grades of WMLs; so hypertensive patients should keep their blood pressure controlled as much as possible.

References

References:

American heart association. (2014). Understanding blood pressure readings Available at: www.heart.org (Accessed: 21 Octoper 2015).

Antranik. 2011. CNS: Intro to Brain and Ventricles, Medulla oblongata, Pons, Midbrain, and Cerebellum. Available at: http://antranik.org/ (Downloaded: 7 December 2015).

Babiker, F.A., Elkhalifa, A.L. and Moukhyer, M.E. 2013. Awareness of hypertension and factors associated with uncontrolled hypertensionin Sudanese adults. Cardiovascular journal of Africa, 24(6): 208-212.

Barkhof, F., Smithuis, R. and Hazewinkel, M. 2013. Role of MRI in the diagnosis of multiple sclerosis.Radiology assistant. Available at: www.radiologyassistant.nl/en/p483910a4b6f14/html (Accessed: 12 November 2015).

Calif, I. 2005. Intelligence in men and women is a gray and white matter. University of California. Available at: www.Sciencedaily.com/releases/2005/01/050121100142.htm (Accessed: 10 August 2015).

Casanova, M. 2013. Key Players in Autism: IV. The Brain stem. Available at: https://coticalchauvinism.com (Downloaded: 7 December 2015).

Cheng, P.W. 2011. MRI Study of brain and incidental finding of white matter hypertensities and microbleeds. The hong kong diary, 16(2): 25-27.

Circle of Willis- Isolated (Labeled). 2010. Health Education Assets Library. Available at: https://meducation.net/resources/21390 (Downloaded: 7 December 2015).

Corpus callosum. 2011. Medical dictionary. Available at: http://medicine.academic.ru/80069 (Downloaded: 7 December 2015).

Dean, M.R.E. and West, T.E.T. 1987. Basic anatomy and physiology for radiographers, 3rd edition, Blackwell scientific publications, London, 414-446.

Debette, S. and Markus, H.S. 2010. The clinical importance of white matter hyperintensities on brain magnetic resonance imaging. British medical journal, 341. doi: 10.1136/bmj.c3666

Dijk, e.j., Bretele, M.M., Schmidt, R., Berger, K., Nilsson, G., Oudkerk, M., Pajak, A., Sans, S., Ridder, M., Dufouil, C., Fuhrer, R., Giampaoli, S., Launer, L.J. and Hofman, A. 2004. The Association Between Blood Pressure, Hypertension, and Cerebral White Matter Lesions, cardiovascular Determinants of Dementia Study. Hypertension, 44: 625-630.

Douglas, F.R. 2008. White matter matters. Scientific American, 298 (3): 54-61.

Downes, S. 2014. Basics of brain and blood supply, cranial nerves. Available at: http://myroadtomedicalschool.blogspot.com/html (Downloaded: 7 December 2015).

Federal ministry of health in Sudan. 2016. National health survey for chronic diseases. Available at: www.fmoh.gov.sd/newsDetails.php?newsID=659 (Accessed: 13 January 2016).

Gaillard, F. 2008. Fazekas scale for white matter lesions. Available at: www.radiopaedia.org (Accessed: 6 September 2015).

Gill, M. 2015.Hypertension;causes, symptoms, treatments. Medical news today. 1-3. Available at: www.medicalnewstoday.com/articles/150109.php (Accessed: 25 August 2015).

Giovannoni, G. 2015. Education. Whats an MRI. Barts MS Blog. Available at: http://multiple-sclerosis-research.blogpost.com/html (Downloaded: 7 December 2015).

Keenan, N.L. 2011. Prevalence of hypertension and controlled hypertension. Centers for disease control and prevention (mortality and morbidity weekly report). 60(01): 94-97.

Kelley, L.L., and Petersen, C.M. 1997. Sectional anatomy for imaging professionals, 1st edition, Mosby Inc, United States of America, 37-81.

Kim, K.W., Fall, J.R. and Payne, M.E. 2008. Classification of white matter lesions on magnetic resonance imaging in elderly persons. Journal of biological psychiatry, 64(4): 273-280.

Klein, S.B. and Thorne, B.M. 2007. Biological psychology, Worth publishers Inc, New York.

Launer, L.J., Berger, K. and Breteler, M.M. 2005. Regional variability in the prevalence of cerebral white matter lesions. Neuroepidemiology, 26(1): 23-29.

Leeuw, F.E., Groot, J.C., Achtenb, E., Oudkerk, M., Ramosc, L.M.P., Heijboer, R., Hofman, A., Jollese, J., Gijnd, J., and Breteler, M.M.B. 2001. Prevalence of

cerebral white matter lesions in elderly people, J neurol Neurosurge Psychiatry, Rotterdam 70(1): 9-14, doi: 10.1136/Jnnp.70.1.9

Leeuw, F.E., Groot, J.C., Oudkerk, M., Witteman, J.C., Hofman, A., Gijn, J. and Breteler, M.M. 2002. Hypertension and cerebral white matter lesions in a prospective cohort study. Brain, 125(4): 765-772.

Liao, D., Cooper, L., Cai, J., Toole, J. F., Bryan, N.R., Hutchinson, R.G. and Tyroler, H. A. 1996. Presence and severity of cerebral white matter lesions and hypertension, its treatment, and its control. The ARIC Study. Stroke, 27(12): 2262-2270.

Liney, G. 2006. MRI in Clinical Practice, springer science, Singapore. 63-76.

Maniega, S.M., Hernandez, M.C., Clayden, J.D., Royle, N.A., Murray, C., Morris, Z., Aribisala, B.S., Gow, A.J., Starr, J.M., Bastin, M.E., Deary, I.J. and Wardlaw, J.M. 2015. White matter hyperintensities and normal appearing white matter integrity in the aging brain. Journal of neurobiology of aging, 36(2): 909-918.

Marner, L., Nyengaard, J.R., Tang, Y. and Pakkenberg, B. 2003. Marked loss of myelinated nerve fibers in the human brain with age. Journal of comparative neurology, 462 (2): 52-144.

Micheau, A. 2008. Fazekas in ARWMC sale on MRI. Available at: www.imaios.com/en/e-Cases/Channels/Radiology (Downloaded: 5 September 2015).

Moeller, T.B. and Reif, E. 2003. MRI Parameters and Positioning, Thieme, New York. 1-32.

Pantoni, L. 2010. Cerebral small vessel disease from pathogenesis and clinical characteristics to therapeutic challenges. The lancet neurology, 9(7): 689-701.

Pietrangelo, A. 2014. The effects of high blood pressure on the body. Healthline networks Inc. New York. Available at: www.healthline.com/health/ (Accessed: 18 October 2015).

Runge, V.M., Smoker, W.R.K. and Valavanis, A. 2015. Neuroradiology; the essentials with MR and CT, Thieme medical publishers Inc, China, 1-89.

Ryan, S., Nicholas, M. and Eustace, S. 2004. Anatomy for diagnostic imaging, 2nd edition, Elsevier, China, 49-84.

Saladin, K. 2012. Anatomy and physiology, the unity of form and function, 6th edition, Springer publishing, New York, 531.

Sowell, E.R., Peterson, B.S., Thompson, P.M., Welcome, S.E., Henkenius, A.L. and Toga, A.W. 2003. Mapping cortical change across the human life span, Journal of nature neuroscience, 6 (3): 15-309.

Vlek, A.L., Visseren, F.L., Kappelle, L.J., Witkamp, T.D., Vincken, K.L., Mali, W.P., and Graaf, Y. 2009. Blood pressure and white matter lesions in patients with vascular disease. The SMART-MR study. Journal of current neurovascular research, 6(3): 155-162.

Westbrook, C. 2008. Handbook of MRI technique, 3rd edition, Blackwell, United kingdom, 61-137.

Wong, T.Y., Klein, R., Sharrett, A.R. and Couper, D.J. 2002. Cerebral white

matter lesions, retinopathy and incidence of clinical stroke. Journal of American medical association, 288(1):67-74.

World health organization. 2012. Raised blood pressure situation and trends. Global health observatory data. Available at: www.who.int/gho/ncd/risk-factors/blood-pressure-prevalence-text/en/ (Accessed: 1 August 2015).

Xiong, Y.Y. and Mok, V. 2011. Age related white matter changes. Journal of aging research. doi: 10.4061/2011/617927x.

Appendices

Appendices

Appendix (A) data sheet:

Table (A.1) shows the master table which used for data collection.

No.	BMI	Age	Gender	Duration	Control	PVWMLs	DWMLs
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
…							
15							

Gender:

1 = Male 2 = Female

Duration:

1 = < 5 years 2 = (5-10) years 3 = > 10 years

Control:

1 = Controlled hypertension 2 = Uncontrolled hypertension

PVWMLs and DWMLs:

0 = No lesions 1 = Mild 2 = Moderate 3 = Severe

Appendix (B) images:

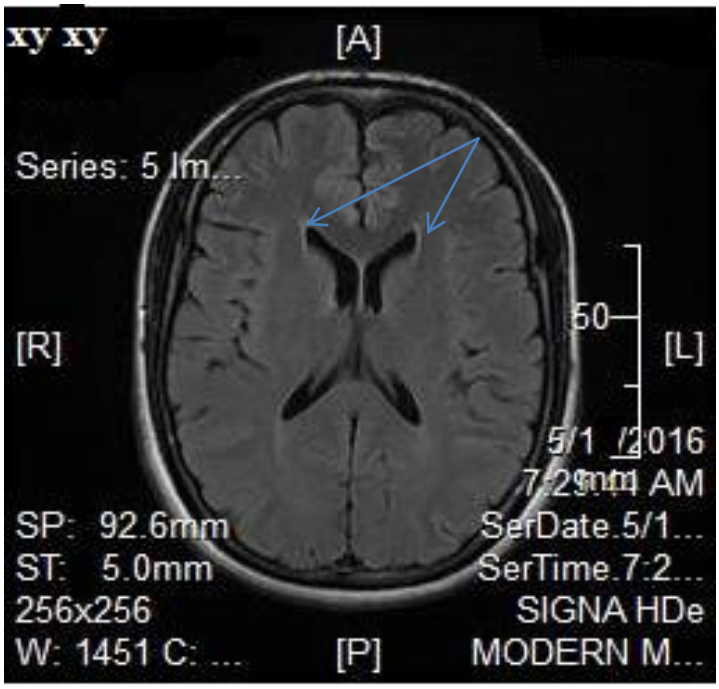

Figure: (B.1) shows an axial, FLAIR MR image of forty nine years old male, with a controlled HTN and duration between five to ten years; he had grade one periventricular WMLs (arrows heads) and grade zero deep WMLs.

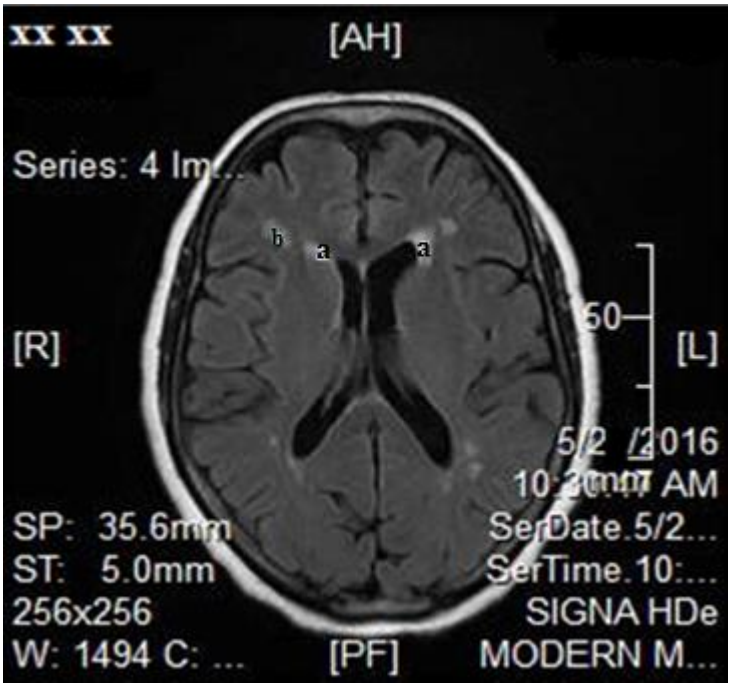

Figure: (B.2) shows an axial, FLAIR MR image for fifty years old uncontrolled hypertensive female, with duration less than five years; she had grade two periventricular (a) and grade two deep (b) WMLs.

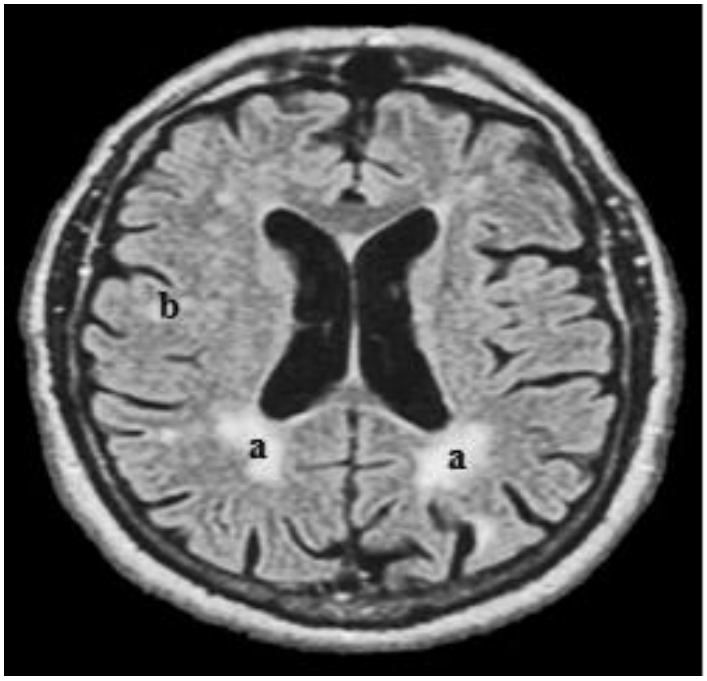

Figure: (B.3) shows an axial, FLAIR MR image, for a subject grade three periventricular (a) and grade two deep (b) WMLs.