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Research Paper

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

Medical science

KEYWORDS:

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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 (T_1, T2 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.

1. Introduction: 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.

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2. Materials and Methods

2.1 Materials:

2.1.1 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.

2.1.2 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.

2.2 Methods:

2.2.1 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.

2.2.2 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.

2.2.3 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

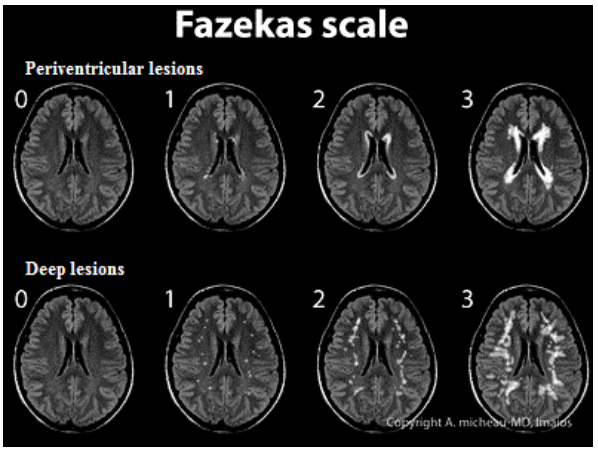


Figure (1) shows Fazekas scale for white matter lesion; periventricular (upper row) and deep (lower row) (Micheau, 2008).

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.

2.2.4 Data analysis: The data were analyzed by (SPSS), and the tests which used were Mann-Whitney U test and Sperman's rho.

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

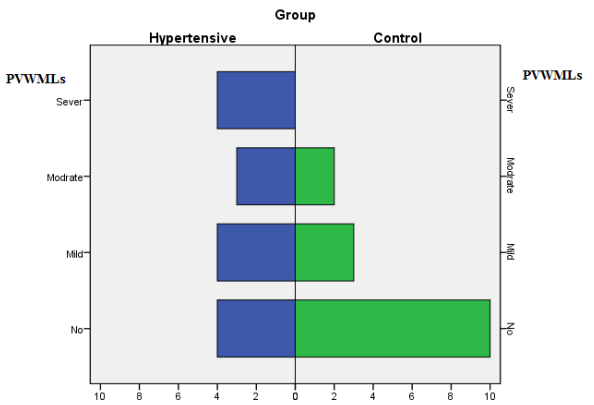


Figure (2) shows a bar graph for the difference between control group and hypertensive group in periventricular white matter lesions.

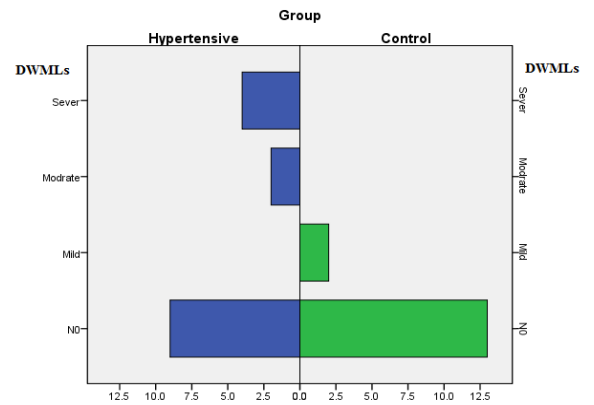


Figure (3) shows a bar graph for the difference between control group and hypertensive group in deep white matter lesions.

Table (1) demonstrates the distribution of WMLs (PVWMLs and DWMLs)forbothcontrolan-dh-yp-ertensivegroup.

	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(2)demonstratestheMann-Whitneytestformeanranksforboth controlandhypertensivegroup.

	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

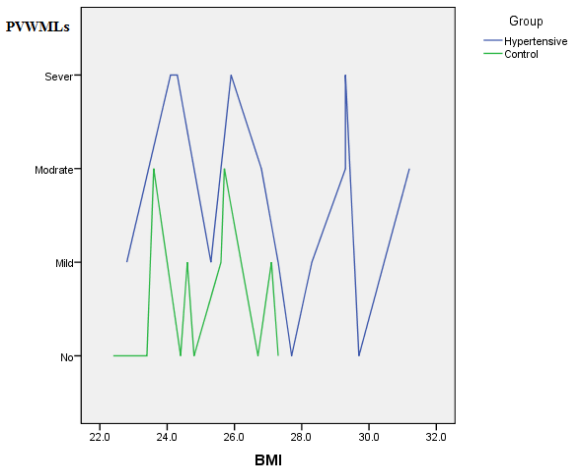


Figure (4) shows a line graph for the association between body mass index and periventricular white matter lesions for control and hypertensivegroup

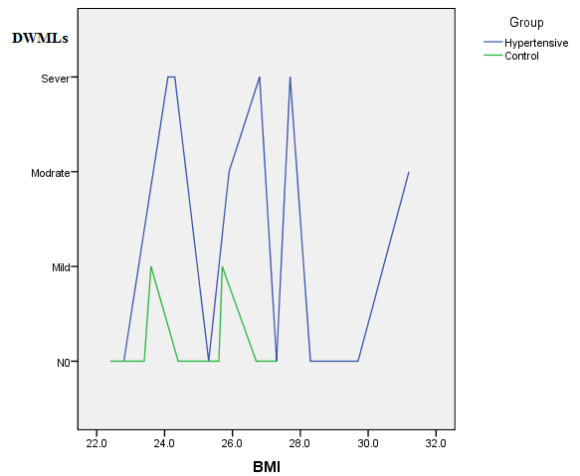
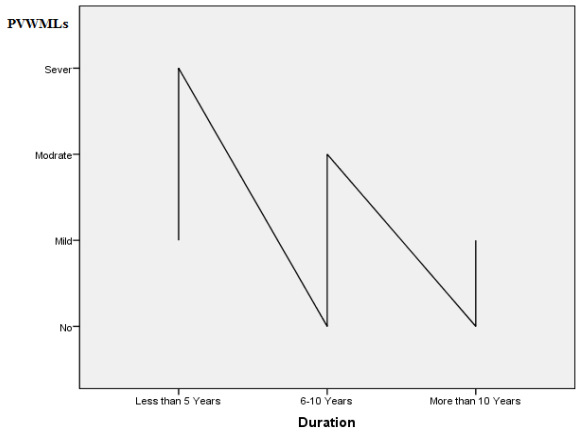


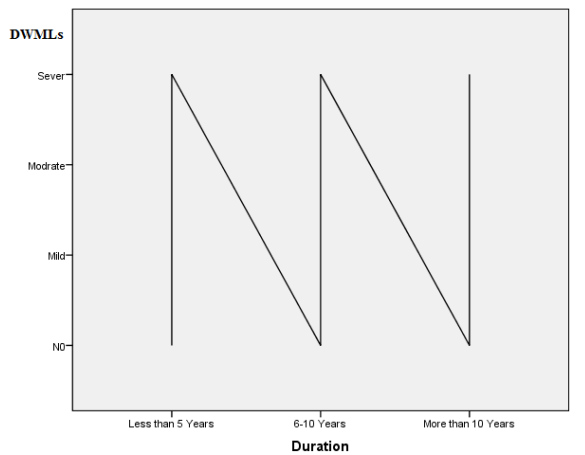
Figure (5) shows a line graph for the association between body mass indexanddeepwhitematterlesionsforcontrolandhypertensivegroup.

Table (3) shows the correlation Coefficients between BMI and WMLs (PWMLs and DWMLs) on the two groups, as well as the corresponding significancevaluesofSpearman'sCorrelationCoefficients.

		Control	
		BMI Hypertensive	BMI
Spearman's rho	BMI	1.000	1.000
		15	15
	PVWMLs	0.394	-0.423
		0.146	0.116
		15	15
	DWMLs	0.136	-0.363
		0.628	0.184
		15	15



Figure(6)showsalinegraphfortheassociationbetweenthedurationof hypertensionandperiventricularwhitematterlesions.



Figure(7)showsalinegraphfortheassociationbetweenthedurationof hypertensionanddeepwhitematterlesions.

Table (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' Durations rho	Correlation Coefficient	1.000	-0.743	-0.230
	Sig. (2-tailed)	.	0.001	0.409
	N	15	15	15

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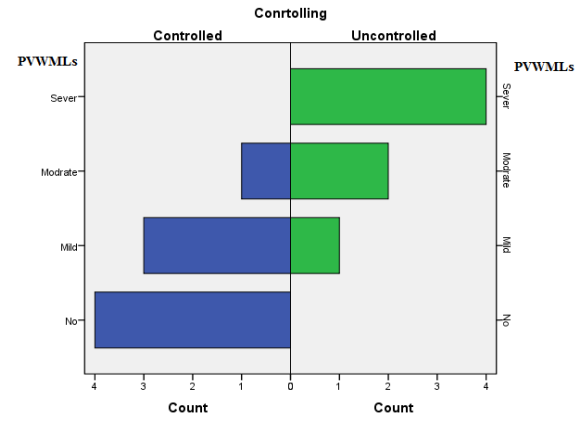


Figure (8) a bar graph for the differences between controlled and uncontrolled hypertensive patients in periventricular white matter lesions.

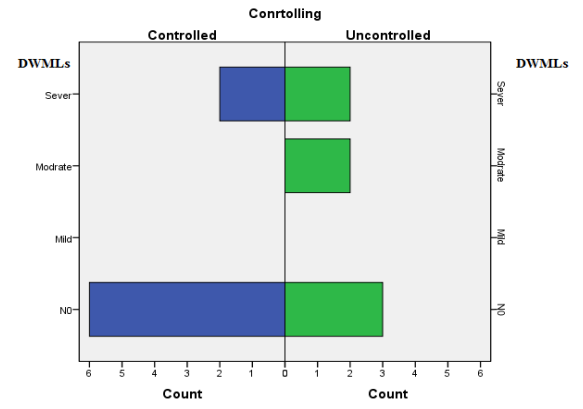


Figure (9) shows a bar graph for the differences between controlled and uncontrolled hypertensive patients in deep white matter lesions.

Table(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 (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

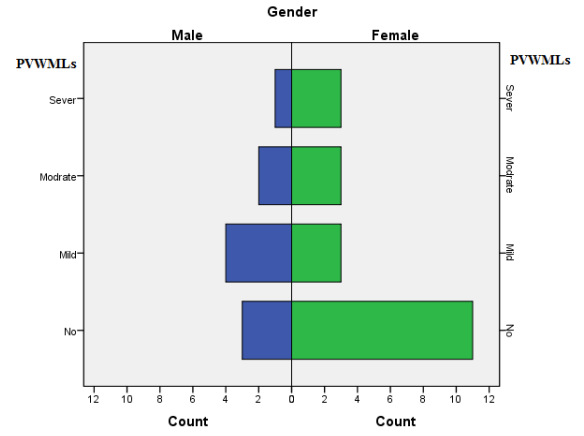


Figure (10) shows a bar graph for the differences between male and female in periventricular white matter lesions.

Figure (11) shows a bar graph for the differences between male and female in deep white matter lesions.

Table(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(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

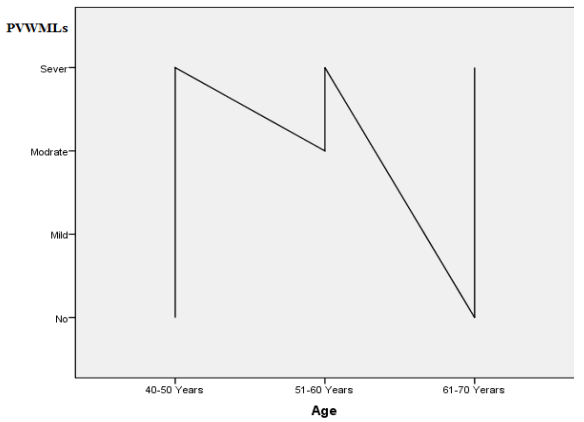
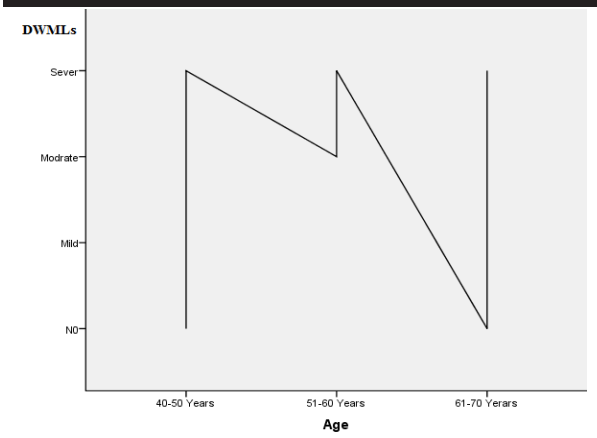
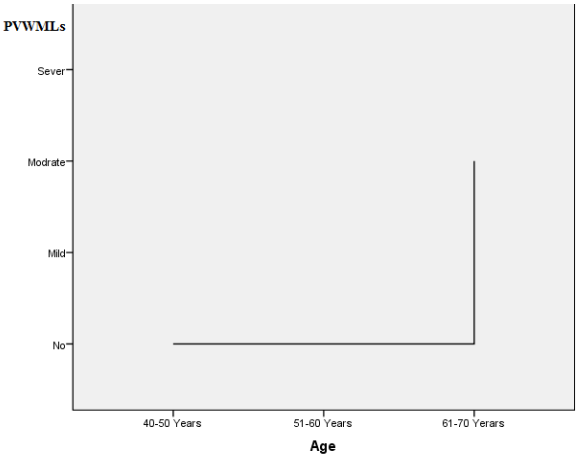


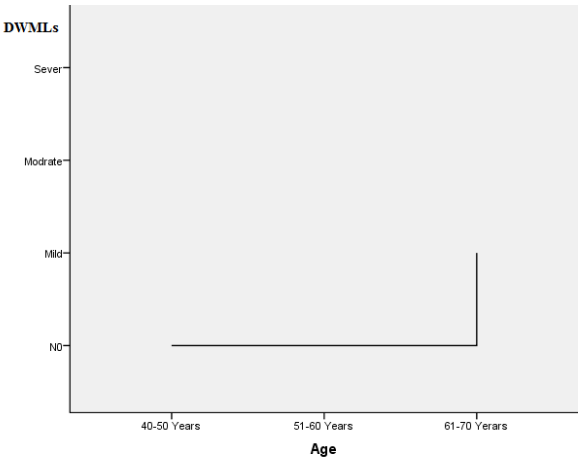
Figure (12) shows a line graph for the association between the age and periventricular white matter lesions for hypertensive group.



Figure(13) showsalinegraphfor the association between theage and deep white matter lesions for hypertensivegroup



Figure(14) shows a line graph for the association between the age and periventricular white matter lesions forcontrol group.



Figure(15) shows a line graph for the association between the age and deepwhitematterlesionsforcontrolgroup.

Table (9) demonstrates the correlation Coefficients between age and WMLs (PVWMLs and DWMLs) in HTN group, with the corresponding significancevaluesofSpearman'sCorrelationCoefficients.

		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(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

4.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.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.

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