



Original article

**Detection of cerebral microbleeds by Susceptibility-Weighted-MR-Imaging in elderly population in comparison with cognitive tests**

Sahar Mahmoud Abd elsalam<sup>1\*</sup>, Ahmad Hesham Mohamed Said<sup>1</sup>, Ahmed Ibrahim Harraz<sup>2</sup>, Mona Hussein Tawfik<sup>3</sup>, Ahmed Abdel Fatah Zidan<sup>1</sup>.

<sup>1</sup>Faculty of Medicine, Beni-Suef University, Egypt , Radiology department.

<sup>2</sup>Faculty of medicine , 6 October University, Radiology department.

<sup>3</sup>Faculty of medicine, Beni-Suef University, Egypt , Neurology department.

**Article Info**

**Article history:**

Received 26 January 2023

Accepted 4 February 2023

**Corresponding Author:**

Sahar Mahmoud Abd elsalam

[sahr.abdelsalam@med.bsu.](mailto:sahr.abdelsalam@med.bsu.edu.eg)

[edu.eg](mailto:sahr.abdelsalam@med.bsu.edu.eg)

**Keywords:**

Cerebral Microbleeds

Cognitive functions

Susceptibility Weighted

Imaging

MRI.

**Abstract**

**Background:** Neuroimaging results related to cerebral microbleeds are becoming more well known. Significant advancements have been made in recent years, notably in the creation of improved MRI detection technologies and their application to various diagnostic investigations of neuropsychological illnesses. The purpose of this research was to determine if susceptibility weighted imaging can identify cerebral microbleeds in older people and determine whether these microbleeds were associated with cognitive dysfunction.

**Results:** This study was an observational cross-sectional study performed on 58 elderly subjects above the age of 50. Cognitive functions for the included subjects were assessed using Paced Auditory Serial Addition Test (PASAT), Benton Visual Retention test (BVRT) and Paired Associate Learning

test (PALT). All included subjects underwent routine MRI and susceptibility weighted images. The mean values for PALT, BVRT, PASAT scores were  $10.2 \pm 3.2$ ,  $12.7 \pm 3.4$ , and  $27.9 \pm 10.9$  respectively. There were statistically significant negative correlations between the scores of PALT, BVRT, PASAT, and lobar (P-value  $< 0.001$  in all tests) and total number of microbleeds (P-value = 0.005, 0.016, 0.001 respectively). In addition, there was a statistically significant negative correlation between PASAT score and number of infratentorial microbleeds (P-value = 0.022). **Conclusions:** The occurrence of cerebral microbleeds detected by Susceptibility-Weighted-MR-Imaging had a significant impact on cognitive function. The Susceptibility-Weighted-MR-Imaging can be used as a screening for early detection of microbleeds in patients with impaired cognitive functions and so, we can avoid the consequences of CMBs specially in male subjects with associated comorbidities as diabetes and hypertension.

---

## 1. Introduction:

In general, MRI sequences; FLAIR, T1-weighted, and T2-weighted sequences do not show cerebral microbleeds (CMBs), which are defined as tiny (2–10 mm in diameter) patches of signal void seen at T2\* weighted MRI or other sequences. Additionally, cerebral small vessel disease exhibits CMBs (1).

Although cerebral microbleeds are often asymptomatic, they are thought to be a risk factor for future ischemic and hemorrhagic

strokes and are clinically associated with age, chronic hypertension, and white matter hyperintensities (WMH). The location of CMBs suggests distinct causes; those in the lobes are more likely to be linked to cerebral amyloid angiopathy, and new research has linked lobar CMBs to alterations in cognitive performance. CMBs in the deep white matter are linked to hypertensive arteriopathy. Numerous studies have shown that CMBs not only play a significant role in hemorrhagic transformation but are also thought to be a

risk factor for new ischemic stroke, transient ischemic attack, cognitive impairment, and stroke recurrence. Consequently, CMBs play a crucial role in the prevention and treatment of a variety of strokes <sup>( 2 )</sup> .

Neuroimaging results of cerebral microbleeds are becoming more widely acknowledged. Significant advancements have been made recently, especially in the creation of novel MRI CMB detection algorithms and their application to senior population-based samples <sup>( 3 )</sup> .

In most cases, magnetic resonance imaging (MRI) methods are used to find CMBs. Due to its exceptional sensitivity to the susceptibility effects brought on by blood products, susceptibility weighted imaging (SWI) is a commonly utilized MRI data post-processing approach for identifying CMBs. Susceptibility-weighting masks are created in SWI by multiplying magnitude pictures by susceptibility-weighting masks created from high-pass filtered phase images. On SWI photos, CMBs show as tiny, oval or spherical patches of low intensity. There are several kinds of CMB impersonators, too, including veins, iron buildup in the basal ganglia, calcifications, and signal voids brought on by subpar flow compensation or cusp artifacts. Therefore, manual CMB detection may be

time-consuming and susceptible to mistakes<sup>( 4 )</sup> .

The aim of this study was to investigate the correlation between cerebral microbleeds in elderly as detected by SWI and cognitive function.

## **2. Methods:**

This observational cross-sectional study was performed on patients referred to the diagnostic radiology department from the outpatient clinic of neurology department during the period from January 2020 to Mars 2022 on 58 elderly person over 50 years having the ability to read, write, and do simple calculations. **We excluded** from the study patients with major language disturbance, severe physical, auditory or visual impairment, patients with a history of drug intake or medical illness known to affect cognition or mentality, or patients with a previous history of neurological condition known to cause cognitive impairment e.g. Alzheimer's disease, Parkinson's disease or epilepsy, patients with MRI brain showing structural lesion like infarctions, intracerebral hemorrhage, subdural hematoma, tumors, hydrocephalus or cerebral venous thrombosis and patients with contraindications to MRI such as having cardiac pacemaker, an intracranial aneurysmal clip, any electrically

or magnetically activated implants (cochlear implants) and patients with severe claustrophobia.

Evaluation of the patients was done first by obtaining full history including demographics, history of systemic arterial hypertension, diabetes mellitus, and ischemic heart disease.

**Cognitive assessment:**

The PALT was used to evaluate cognitive function in the included patients using the technique published by Spaan et al. to evaluate auditory verbal memory (5). According to the methodology outlined by Manna et al., the Benton Visual Retention Test was used to evaluate visual perception, visual memory, visual motor, and visuo-constructive skills (6). The Nikraves et al. approach of using the Paced Auditory Serial Addition Test was utilized to evaluate

auditory working memory and attention (7).

**Neuro-radiological Examination Used in This Study:**

All MRI examinations were performed using SIEMENS-AERA MRI scanner 1.5 Tesla (Siemens Healthcare AG, Bern, Switzerland), In neutral supine posture, utilizing standard head coils. The patients were instructed to refrain from deep breathing while being examined.

First, routine conventional MRI scans were obtained, including coronal, axial, and sagittal fast spin echo (FSE) T1- and T2-weighted images, fluid attenuation inversion recovery (FLAIR), Diffusion weighted images, and apparent diffusion co-efficient. Susceptibility weighted images were then obtained. MRI sequences were performed using the criteria listed in the table (1 & 2).

**Table (1):** Conventional MRI Sequences.

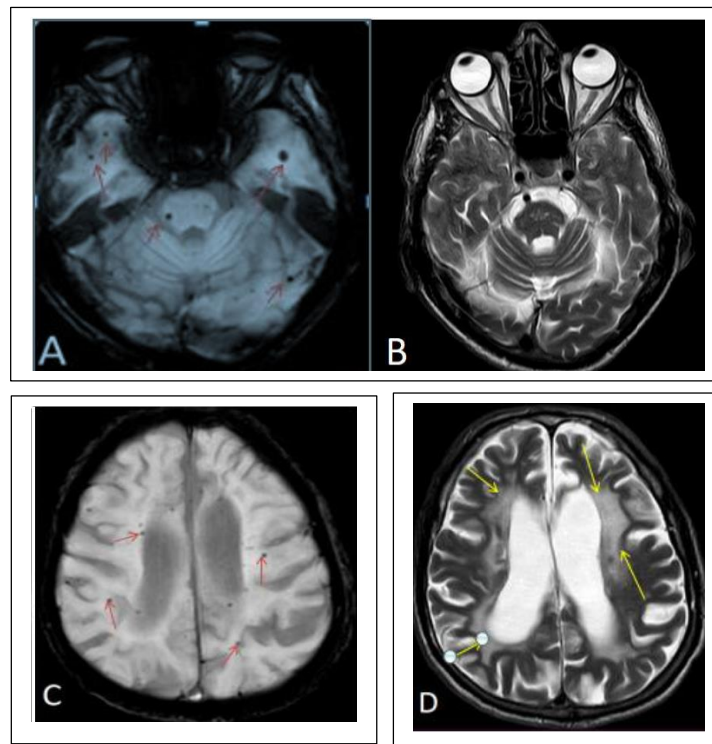
	T1	T2	FLAIR	DWI
<b>TR (ms)</b>	581	4000	11000	3614
<b>TE (ms)</b>	15	100	110	160
<b>TI (ms)</b>	-	-	2800	2800
<b>Planes</b>	axial, sagittal	axial	axial	axial
<b>Slice thickness</b>	5 mm			
<b>Gap</b>	1 mm			
<b>Flip angle</b>	69	90	90	90
<b>FOV</b>	230 mm			
<b>Matrix</b>	256			
<b>NEX</b>	1			

**Table (2):** Susceptibility weighted MRI examination (SWI) utilizing the following parameters.

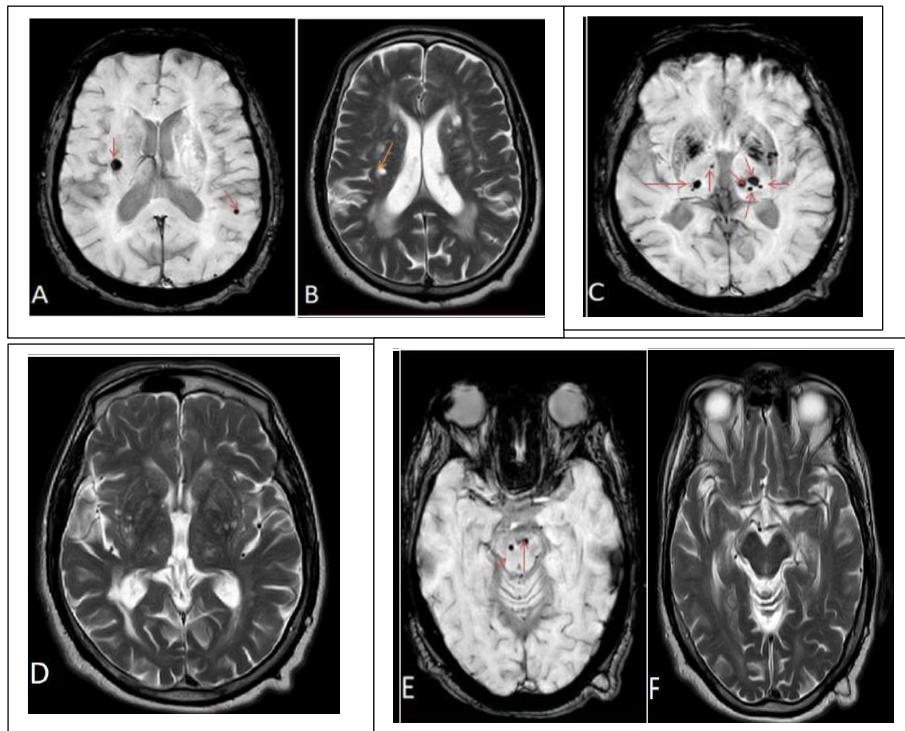
	SWI
TR (ms)	35
TE (ms)	20
TI (ms)	2800
Planes	axial
Slice thickness	5 mm
Gap	1 mm
Flip angle	20
FOV	230 mm
Matrix	512 × 256
Total Time	8 minutes
NEX	1

### Image Analysis

The provided images were first interpreted as standard brain MRI to look for any obvious disease, such as an infarction, tumor, infection, etc., and then a SWI sequence was used to carefully scrutinize the CMBs. The following criteria were used to evaluate CMBs: presence or absence, evaluation of the site and amount of detected microbleeds, comparison of the information gathered by SWI with data from other sequences, and correlation of the location of the detected microbleeds with the provided clinical information (figure 1, 2).



**Figure 1.** Male patient aged 56 years with hypertension and IHD. (A) Axial SWI at the level of brain stem revealed: multiple microbleeds at the right lateral aspect of the pons, both temporal and left cerebellar hemisphere (Red arrows) which could not be seen on T2WI (B). C: Axial SWI at the level of both fronto- parietal regions shows multiple microbleeds at both fronto-parietal regions (Red arrows). (D) Axial T2WI shows diffuse high SI in the periventricular and deep white matter regions (Yellow arrows) denoting chronic ischemic changes that that represent Fazekas scale Grade III.



**Figure 2.** 65 year-old male with long standing uncontrolled hypertension and history of multiple stroke episodes. A. Axial SWI showing two microbleeds at both parietal regions (Red Arrows), the largest seen at the right side that can be misdiagnosed with an old ischemic infarction seen at the same region on at T2 WI (Orange arrow) (B). (C) Axial SWI showing multiple microbleeds at both thalamic regions (Red

arrows) that couldn't be seen at T2 WI (D). (E) Axial SWI showing two microbleeds at the midbrain (Red arrows) that couldn't be seen at T2 images (F).

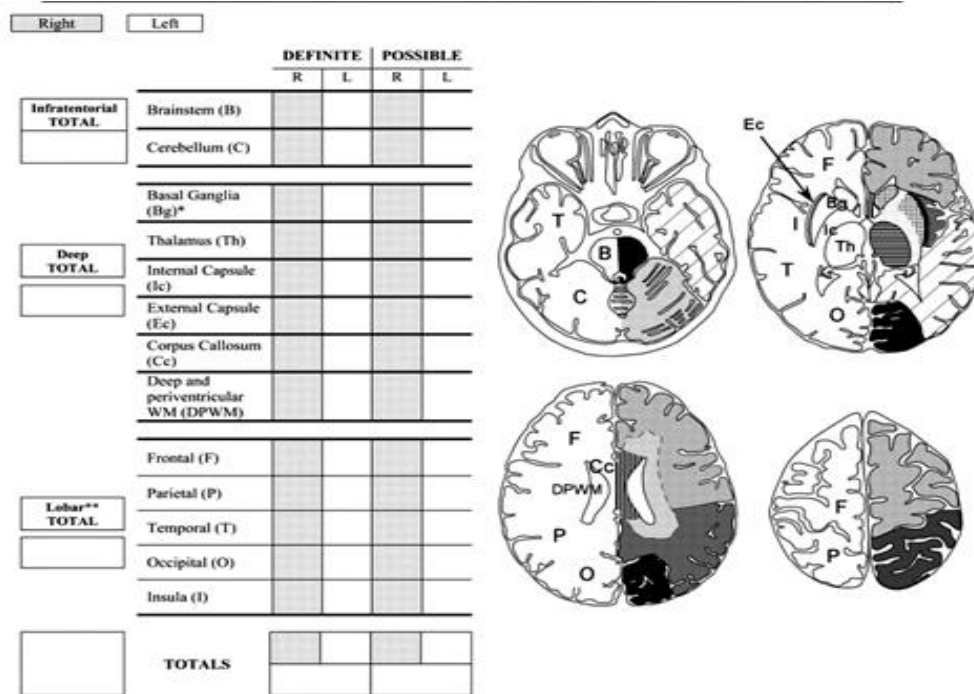
Using the Microbleeds Anatomical Rating Scale (MARS), the quantity and location of microbleeds were evaluated. It is a measuring instrument that accurately counts the number of cerebral microbleeds and their anatomical

distribution, and it has shown sufficient intrarater and interrater reliability <sup>( 8 )</sup> .

According to **fig. 3**, which showed that definite microbleeds were circular or oval hypointense foci of 2–10 mm in diameter that were clearly visible on SW images as opposed to other traditional sequences, such as T1WI and T2WI, microbleeds were identified and computed. The cerebellum and brain stem were included in the infratentorial section of the brain, along with the basal ganglia, thalami, internal capsule, external capsule, corpus callosum, and deep periventricular white matter. The frontal, parietal, temporal, and occipital lobes as well

as the insula were included in the lobar section.

Each hemisphere's microbleeds were computed separately, then all of them were added together for the whole brain. Exclusion criteria for microbleeds mimics included blood vessels seen in the subarachnoid, cortical, and juxta-cortical regions, air-bone interfaces around the frontal and temporal lobes, partial volume artifacts at the edges of the cerebellum, mineralization at the Globus pallidus that could be distinguished by bilaterally symmetrically distributed hypointense foci, and micro-hemorrhages related to frank intracerebral bleeding.



**Figure (3):** The Microbleed Anatomical Rating Scale <sup>( 9 )</sup>

**Fazekas scale:**

While it is obvious that not all white matter T2 hyper-intense lesions are caused by chronic small vessel ischemia, the Fazekas scale is used to simply measure the quantity of these lesions. The scale divides the white matter into periventricular and deep white matter, and each region is given a grade depending on the size and confluence of lesions as shown in table (3).

**Table (3):** Fazkas grading scale <sup>( 10 )</sup> .

<b>Fazekas Grading Scale</b>	
<b>Periventricular white matter (PVWM)</b>	0 = absent. 1 = “caps” or pencil-thin lining. 2 = smooth “halo”. 3 = irregular periventricular signal extending into the deep white matter.
<b>Deep white matter (DWM)</b>	0 = absent. 1 = punctate foci. 2 = beginning confluence. 3 = large confluent areas

**Statistical methods:**

SPSS v. 25 (Statistical Package for Social Science) for Windows was used to analyze the data. Variable descriptions were given. Mean and standard deviation were used to describe quantitative variables (SD). The qualitative factors were described using numbers (No.) and percentages (percent). To establish a link between normally distributed variables, Pearson correlation was utilized while Spearman Rho was used to correlate between normally distributed numeric variables. Mann-Whitney U test was used to compare non-parametric data between 2 independent groups The P-value used to

determine significance was used to categorize the findings as non-significant when it was less than 0.05 and significant when it was more than 0.05.

**3. Results:**

**The Baseline characters of the studied population:**

The mean age of the studied participants was 66.5±8.4 years. There were 63.8% males among the participants and 36.2% females. Only 37.9% of the included participants were diabetic, 78.9% were hypertensive, and 67.2% had ischemic heart disease.



**Cognitive assessment and Radiological characters of the included participants.**

Cognitive assessment revealed that the mean values for PALT, BVRT, PASAT scores were 10.2±3.2, 12.7±3.4, and 27.9±10.9 respectively. According to the radiological findings, only 3.4% of the included subjects had Fazekas grade 0, 27.6% had Fazekas

grade 1, 20.7% had Fazekas grade 2, and 48.3% had Fazekas grade 3. The mean value for the number of infratentorial microbleeds was 0.9<sup>v</sup>±0.3, deep microbleeds was 3.6±1.7, lobar microbleeds was 2.1±1.4 and total number of microbleeds was 6.6±1.5.

**Impact of sex on the occurrence of microbleeds (table 4)**

**Table (4):** Impact of sex on the occurrence of microbleeds.

Microbleeds	Males (n =37)	Females (n =21)	P-value (MW)
<b>Infra-tentorial [mean (SD)]</b> <b>Median (IQR)</b>	1.2±2.5 0(0, 1.5)	0.5±1.7 0(0,0)	0.032*
<b>Deep [mean (SD)]</b> <b>Median (IQR)</b>	4.1±4.3 2(1, 6.5)	2.6±5.3 1(0,3)	0.036*
<b>Lobar [mean (SD)]</b> <b>Median (IQR)</b>	2.4±6.1 0(0, 2.5)	1.4±4.2 0(0, 1)	0.520
<b>Total [mean (SD)]</b> <b>Median (IQR)</b>	7.7±11.6 3(2, 9)	4.5±11.1 2(1, 3.5)	0.005*

\*P-value is significant MW (Mann Whitney U non-parametric test)

Male subjects had a significantly higher number of microbleeds than females in infratentorial and lobar regions in addition to the total number of microbleeds (P-value= 0.032, 0.036, 0.005 respectively). **Impact of diabetes on the occurrence of microbleeds (table 5)**

**Table (5):** Impact of diabetes on the occurrence of microbleeds.

Microbleeds	Non-diabetic subjects (n =36)	Diabetic subjects (n =22)	P-value (MW)
<b>Infra-tentorial [mean (SD)]</b> <b>Median (IQR)</b>	0.8±1.8 0(0, 1)	1.3±2.9 0(0, 1.3)	0.1445
<b>Deep [mean (SD)]</b> <b>Median (IQR)</b>	3.3±5 1.5(1, 4.5)	3.9±4.1 3(1, 4)	0.109
<b>Lobar [mean (SD)]</b> <b>Median (IQR)</b>	1.7±3.7 0.5(0, 1)	2.5±7.6 0(0, 1)	0.746
<b>Total [mean (SD)]</b> <b>Median (IQR)</b>	5.8±9.8 2(1, 5.8)	7.7±13.8 3(2, 5.3)	0.197

MW (Mann Whitney U non-parametric test)

There were no statistically significant differences between subjects with and without diabetes regarding the number of microbleeds in all brain regions (P-value= 0.1445, 0.109, 0.746, 0.197 respectively). **Impact of hypertension on the occurrence of microbleeds (table 6).**

**Table (6):** Impact of hypertension on the occurrence of microbleeds.

Microbleeds	Non-hypertensive subjects (n =7)	Hypertensive subjects (n=51)	P-value (MW)
<b>Infra-tentorial [mean (SD)]</b>	1.6±2.8	0.9±2.2	0.290
<b>Median (IQR)</b>	1(0, 1)	0(0, 1)	
<b>Deep [mean (SD)]</b>	2.7±5.1	3.7±4.6	0.155
<b>Median (IQR)</b>	1(0, 2)	2(1, 4)	
<b>Lobar [mean (SD)]</b>	0.6±1.1	2.2±5.8	0.335
<b>Median (IQR)</b>	0(0, 1)	1(0, 1)	
<b>Total [mean (SD)]</b>	4.9±8.8	6.7±11.8	0.1
<b>Median (IQR)</b>	2(2, 2)	3(2, 6)	

MW (Mann Whitney U non-parametric test)

There were no statistically significant differences between subjects with and without hypertension regarding the number of microbleeds in all brain regions (P-value= 0.290, 0.155, 0.335, 0.1 respectively).

**The relationship between white matter hyper intensities (WMHs) and the occurrence of microbleeds (table 7).**

**Table (7):** The relationship between white matter hyper intensities (WMHs) and the occurrence of microbleeds.

Microbleeds	Subjects without WMHs (n =2)	Subjects with WMHs (n =56)	P-value (MW)
<b>Infra-tentorial [median (IQR)]</b>	0(0,0)	0(0,1)	0.484
<b>Deep [median (IQR)]</b>	0(0,0)	2(1,4)	0.024*
<b>Lobar [median (IQR)]</b>	1.5(1,2)	0(1,2)	0.209
<b>Total [median (IQR)]</b>	1.5(1,2)	3(2,5)	0.204

\*P-value is significant MW (Mann Whitney U non-parametric test)

Subjects with white matter hyper intensities had a significantly higher number of deep microbleeds than subjects without (P-value=0.024).

There was a significant linear positive correlation between FESAKAS score and infratentorial (r=0.331, P-value=0.011), deep (r=0.419, P-value=0.001), and total number of microbleeds (r=0.422, P-value=0.001). The correlation between the number of microbleeds and different neuropsychiatric tests are displayed in table (8).

**Table (8):** Correlation between the number of microbleeds and the neuropsychiatric tests scores

Microbleeds	PALT		BVRT		PASAT	
	(r) coef.	P-value	(r) coef.	P-value	(r) coef.	P-value
Infra-tentorial	-0.181	0.174	-0.184	0.166	-0.300	0.022*
Deep	-0.225	0.090	-0.124	0.353	-0.209	0.116
Lobar	-0.675	<0.001*	-0.806	<0.001*	-0.814	<0.001*
Total	-0.366	0.005*	-0.315	0.016*	-0.412	0.001*

\*P-value is significant

Multiple linear regression was run to predict the number of microbleeds from gender, age, DM, HTN, IHD and Fazekas grading. Only Fazekas grading had a statistically significant role in prediction of the number of microbleeds (P-value= 0.011) (Table 9).

**Table (9):** Predictors of the number of microbleeds.

Independent variables	B	P-value	95.0% Confidence Interval for B	
			Lower Bound	Upper Bound
(Constant)	13.941	0.297	-12.624	40.505
Gender (male)	.373	0.911	-6.322	7.068
Age (in years)	-.319	0.152	-.760	.121
Presence of DM	3.624	0.278	-3.005	10.253
Presence of HTN	-.836	0.882	-12.115	10.443
Presence of IHD	3.825	0.371	-4.682	12.331
Fazekas scale	4.732	0.011*	1.152	8.312

\*P-value is significant      DM: Diabetes mellitus, HTN: Hypertension, IHD: Ischemic heart disease.

#### **4. Discussion:**

A radiological construct, cerebral microbleeds show up as hypo-intense foci that can only be seen on MRI. Over the last two decades, interest in CMBs has risen. They may be seen in both healthy people and those who have cognitive problems or have had a stroke. Clinical practitioners often experience ambiguity when CMBs are present and numerous, particularly when antithrombotic therapies are taken into consideration <sup>( 11 )</sup> .

This study was conducted at Beni-Suef University Hospital to investigate the correlation between cerebral microbleeds in elderly as detected by SWI and cognitive function.

Our study showed that there were statistically significant negative correlations between the scores of PALT, BVRT, PASAT, and lobar microbleeds and total number of microbleeds. In addition, there was a statistically significant negative correlation between PASAT score and number of infra-tentorial microbleeds.

Similar to our findings, Li et al. demonstrated in their research that the existence and number of CMBs were linked with memory, executive function, and overall cognitive performance, which is consistent

with our results. Significantly negative correlations between executive function and overall cognitive function and CMB progression were observed <sup>( 12 )</sup> .

Jiménez-Balado et al. demonstrated in their study about impact of cerebral small vessel disease on cognitive function that the incidence of CMBs were related to a decline in attention; however, significant differences were not identified with other cognitive domains <sup>( 13 )</sup> . In contrary, in their investigation of the connection between cerebral microbleeds and cognition, Paradise et al. found no statistically significant differences in whole brain CMB and global cognitive performance, attention and processing speed, language, or memory <sup>( 14 )</sup> .

Numerous studies have shown correlations between CMB location and cognitive task performance. For instance, deep CMBs in the brain's thalamus, infra-tentorial region, and basal ganglia were linked to worse performance on cognitive tasks <sup>( 15 )</sup> . In the Poels et al. Rotterdam investigation, lobar CMBs had the most significant effects on cognition <sup>( 16 )</sup> . According to different research, having several CMBs or mixed microbleeds (both in deep and lobar regions) was linked to a higher risk of dementia <sup>( 17 )</sup> , whereas some

claimed that lobar CMBs were linked to a faster rate of cognitive aging <sup>( 18 )</sup> .

The cognitive consequences of CMBs are a debatable matter <sup>( 19 )</sup> . According to the two most popular theories, CMBs either influence brain activity by strategically disrupting connections between brain areas <sup>( 20 )</sup> , or that the (sub)clinical deficiencies are brought on by the underlying brain illness that CMBs represent <sup>( 16 )</sup> .

The exact ways that CMBs affect cognitive function are yet unknown. The significant correlation between CMBs and cognition that was discovered, which was not mediated by other neuroimaging indicators, suggests that CMBs may not only serve as a marker for the severity of small artery disease but also have a causative effect on cognitive performance <sup>( 21 )</sup> . White matter tracts may be directly damaged by CMBs, which might lead to the disconnecting of functionally crucial cortical-subcortical connections <sup>( 22 )</sup> .

The fact that CMBs cause structural and functional changes in the surrounding brain environment is another potential pathophysiological mechanism by which they might affect cognition. Microbleeds may impair the function of adjacent astrocytes and neurons while promoting an

inflammatory response via the migration and proliferation of microglia <sup>( 23 )</sup> .

Diffuse cerebrovascular endothelial failure is the main mechanism behind brain damage brought on by CMBs. Dysfunction of the blood brain barrier is caused by endothelial injury. Extravasation of blood components may result in widespread brain tissue injury, local vascular alterations, and brain inflammation <sup>( 24 )</sup> . As an alternative, CMBs may affect cognition indirectly by causing micro-ischemic damage and cerebral hypoperfusion as a result of arteriolar constriction. A larger number of CMBs in this context may thus signify more widespread and severe subclinical microvascular damage <sup>( 25 )</sup> .

Regarding the radiological findings of patients in our study, there were statistically significant positive correlations between Fazekas grades and the number of infratentorial and deep microbleeds in addition to the total number of microbleeds. Multiple linear regression was run to predict the number of microbleeds from gender, age, DM, HTN, IHD and Fazekas grading. Only Fazekas grading had a statistically significant role in prediction of the number of microbleeds. Subjects with white matter hyper-intensities had a significantly higher

number of deep microbleeds than subjects without white matter hyper-intensities.

In agreement with our results, that reported by Sakuta et al. who revealed in their study that the number of CMBs was positively linearly correlated with the Fazekas scale <sup>( 26 )</sup>. Similarly, Kesav et al. showed in their study about the distribution of cerebral microbleeds and its association with vascular risk factors that 54% exhibiting moderate to severe grades on FAZEKAS scale. Also, they showed a significant positive correlation between the number of CMBs and Fazekas grade scale. In patients with four or more CMB, FAZEKAS grade 3 periventricular and deep WMHI were seen in 33.3%, whereas only 7.2% with one to three CMB had similar changes <sup>( 27 )</sup>. Also, Diker et al. demonstrated that the proportion of patients with Fazekas scores reflecting moderate to severe WMH (Fazekas grades 2-3) was higher in patients with CMB compared to patients without CMB in their study about the association between cerebral microbleeds and inflammatory biomarkers in patients with ischemic stroke. 36 percent of individuals with microbleeds had CMBs that were exclusively lobar in nature. Only 17.0 percent and 6.4 percent, respectively, of places were strictly deep or infratentorial <sup>( 27 )</sup>.

The mean age of the studied participants was 66.5±8.4 years. There were 63.8% males among the participants and 36.2% females. There were no statistically significant correlations between age and number of microbleeds in either infratentorial, deep, lobar regions or the total number of microbleeds. Male subjects had a significantly higher number of microbleeds than females in infratentorial and lobar regions in addition to the total number of microbleeds.

In agreement with the results were reported by Graff-Radford et al. who revealed in their study that the mean age of the patients was 69.8 years and the prevalence increased with age. Also, they showed that males (72%) were commonly affected than females (28).

Elmståhl et al. showed in their study that the prevalence of CMB strongly increased with age. The prevalence of CMB increased from 18% among subjects in their 70s to 30% among those over 80 years old. Also, they revealed that the presence of CMB was associated with male sex <sup>( 29 )</sup>.

As regards the vascular risk factors in our study, only 37.9% of the included participants were diabetic, 78.9% were hypertensive, and 67.2% had ischemic heart disease. There were no statistically

significant differences between subjects with and without diabetes regarding the number of microbleeds in all brain regions. However, the occurrence of microbleeds is still higher in diabetic patients than non-diabetic patients. In addition, there were no statistically significant differences between subjects with and without hypertension regarding the number of microbleeds in all brain regions. However, the occurrence of microbleeds is still higher in hypertensive patients than non-hypertensive patients in all brain regions except the infra-tentorial region.

Similarly, Yu et al. revealed in their study about the association between HbA1c and CMBs an increase in CMBs risk with an increase in HbA1c level <sup>( 30 )</sup> . Also, the systematic review of Cordonnier et al. revealed that DM was associated with presence CMBs in neurologically healthy adults <sup>( 31 )</sup> . However, in a population-based study by Qiu et al. regarding diabetes, brain pathology indicators, and cognitive performance, they discovered that DM was strongly related with CMBs <sup>( 32 )</sup> .

Regarding hypertension as a risk factor for CMBs, Xu et al. agreed with our study and revealed that age and hypertension were associated with the presence of CMBs. The presence of CMBs was higher in patients

with hypertension than without hypertension with no statistical significance <sup>( 33 )</sup> . Also, Nagaraja et al. showed in their study that patients with CMB were more likely to have a history of hypertension, greater systolic blood pressure, and diastolic blood pressure as risk factors for cerebral microbleeds <sup>( 34 )</sup> .

## **5. Conclusions and Limitations:**

The occurrence of cerebral microbleeds detected by Susceptibility-Weighted-MR-Imaging had a significant impact on cognitive function. The Susceptibility-Weighted-MR-Imaging can be used as a screening for early detection of microbleeds in patients with impaired cognitive functions and so, we can avoid the consequences of CMBs specially in male subjects with associated comorbidities as diabetes and hypertension.

The main limitations of our study were the small sample size and the cross-sectional design. We also did not do lipid profile or carotid and vertebro-basilar duplex for the included patients, which might be correlated with the occurrence cerebral microbleeds.

### **List of Abbreviations:**

BVRT: Benton Visual Retention test.

CMBs: Cerebral microbleeds.

FLAIR: Fluid attenuation inversion recovery.

MARS: Microbleeds Anatomical Rating Scale.

PALT: Paired Associate Learning test.

PASAT: Paced Auditory Serial Addition Test.

SWI: Susceptibility weighted imaging.

WMH: White matter hyperintensities.

## 6. References:

1. Wang M, Hu HY, Wang ZT, Ou YN, Qu Y, Ma YH, Dong Q, Tan L and Yu JT (2021). Association of cerebral microbleeds with risks of cognitive impairment and dementia: a systematic review and meta-analysis of prospective studies. *Brain Disorders*, 2: 100010.
2. Abou Elmaaty AA and Zarad CA (2020). Role of magnetic susceptibility-weighted imaging in characterization of cerebral microbleeds in acute ischemic stroke Egyptian obese patients. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, 56: 1-9.
3. Caunca MR, De Leon-Benedetti A, Latour L, Leigh R and Wright CB (2019). Neuroimaging of cerebral small vessel disease and age-related cognitive changes. *Frontiers in aging neuroscience*, 11: 145.
4. Liu S, Utriainen D, Chai C, Chen Y, Wang, L, Sethi SK, Xia S and Haacke EM (2019). Cerebral microbleed detection using susceptibility weighted imaging and deep learning. *Neuroimage*, 198: 271-282.
5. Spaan PE, Raaijmakers JG and Jonker C (2005). Early assessment of dementia: the contribution of different memory components. *Neuropsychology*, 19(5): 629.
6. Manna CBG, Filangieri CM, Borod JC, Alterescu K and Bender HA (2011). Benton visual retention test. *Encyclopedia of clinical neuropsychology*. New York: Springer, 392-4.
7. Nikraves M, Jafari Z, Mehrpour M, Kazemi R, Shavaki YA, Hossienifar S and Azizi MP (2017). The paced auditory serial addition test for working memory assessment: Psychometric properties. *Medical journal of the Islamic Republic of Iran*, 31: 61.
8. Cordonnier C, Potter GM, Jackson CA, Doubal F, Keir S, Sudlow CL, Wardlaw JM and Salman RAS (2009). Improving interrater agreement about brain microbleeds: development of the Brain Observer MicroBleed Scale (BOMBS). *Stroke*, 40(1): 94-99.
9. Gregoire SM, Chaudhary UJ, Brown MM, Yousry TA, Kallis C, Jäger HR and Werring DJ (2009). The Microbleed Anatomical Rating Scale (MARS): reliability of a tool to map brain



- microbleeds. *Neurology*, 73(21): 1759-1766.
10. Kim KW, MacFall JR and Payne ME (2008). Classification of white matter lesions on magnetic resonance imaging in elderly persons. *Biological psychiatry*, 64(4): 273-280.
11. Puy L, Pasi M, Rodrigues M, Van Veluw SJ, Tsivgoulis G, Shoamanesh A and Cordonnier C (2021). Cerebral microbleeds: from depiction to interpretation. *Journal of Neurology, Neurosurgery & Psychiatry*, 92(6): 598-607.
12. Li L, Wu DH, Li HQ, Tan L, Xu W, Dong Q, Tan L, Yu JT and Alzheimer's Disease Neuroimaging Initiative (2020). Association of cerebral microbleeds with cognitive decline: a longitudinal study. *Journal of Alzheimer's Disease*, 75(2): 571-579.
13. Jiménez-Balado J, Riba-Llena I, Abril O, Garde E, Penalba A, Ostos E, Maisterra O, Montaner J, Noviembre M, Mundet X and Ventura O (2019). Cognitive impact of cerebral small vessel disease changes in patients with hypertension. *Hypertension*, 73(2): 342-349.
14. Paradise M, Seruga A, Crawford JD, Chaganti J, Thalamuthu A, Kochan NA, Brodaty H, Wen W and Sachdev PS (2019). The relationship of cerebral microbleeds to cognition and incident dementia in non-demented older individuals. *Brain Imaging and Behavior*, 13(3): 750-761.
15. Qiu C, Cotch MF, Sigurdsson S, Jonsson PV, Jonsdottir MK, Sveinbjrnsdottir S, Eiriksdottir G, Klein R, Harris TB, Van Buchem MA and Gudnason V (2010). Cerebral microbleeds, retinopathy, and dementia: the AGES-Reykjavik Study. *Neurology*, 75(24): 2221-2228.
16. Poels MM, Ikram MA, van der Lugt A, Hofman A, Niessen WJ, Krestin GP, Breteler MM and Vernooij MW (2012). Cerebral microbleeds are associated with worse cognitive function: the Rotterdam Scan Study. *Neurology*, 78(5): 326-333.
17. Miwa K, Tanaka M, Okazaki S, Yagita Y, Sakaguchi M, Mochizuki H and Kitagawa K (2014). Multiple or mixed cerebral microbleeds and dementia in patients with vascular risk factors. *Neurology*, 83(7): 646-653.
18. Chiang GC, Hernandez JC, Kantarci K, Jack CR, Weiner MW and Alzheimer's Disease Neuroimaging Initiative (2015). Cerebral microbleeds, CSF p-tau, and cognitive decline: significance of anatomic distribution. *American Journal of Neuroradiology*, 36(9): 1635-1641.

19. Haller S, Bartsch A, Nguyen D, Rodriguez C, Emch J, Gold G, Lovblad KO and Giannakopoulos P (2010). Cerebral microhemorrhage and iron deposition in mild cognitive impairment: susceptibility-weighted MR imaging assessment. *Radiology*, 257(3): 764-773.
20. Fagerholm ED, Hellyer PJ, Scott G, Leech R and Sharp DJ (2015). Disconnection of network hubs and cognitive impairment after traumatic brain injury. *Brain*, 138(6): 1696-1709.
21. Nannoni S, Ohlmeier L, Brown RB, Morris RG, MacKinnon AD, Markus HS and DNA Lacunar 2 investigators (2022). Cognitive impact of cerebral microbleeds in patients with symptomatic small vessel disease. *International Journal of Stroke*, 17(4): 415-424.
22. van Norden AG, van den Berg HA, de Laat KF, Gons RA, van Dijk EJ and de Leeuw FE (2011). Frontal and temporal microbleeds are related to cognitive function: the Radboud University Nijmegen Diffusion Tensor and Magnetic Resonance Cohort (RUN DMC) Study. *Stroke*, 42(12): 3382-3386.
23. Ahn SJ, Anrather J, Nishimura N and Schaffer CB (2018). Diverse inflammatory response after cerebral microbleeds includes coordinated microglial migration and proliferation. *Stroke*, 49(7): 1719-1726.
24. Wardlaw JM, Smith C and Dichgans M (2013). Mechanisms of sporadic cerebral small vessel disease: insights from neuroimaging. *The Lancet Neurology*, 12(5): 483-497.
25. Charidimou A, Imaizumi T, Moulin S, Biffi A, Samarasekera N, Yakushiji Y, Peeters A, Vandermeeren Y, Laloux P, Baron JC and Hernandez-Guillamon M (2017). Brain hemorrhage recurrence, small vessel disease type, and cerebral microbleeds: a meta-analysis. *Neurology*, 89(8): 820-829.
26. Sakuta K, Yaguchi H, Sato T, Komatsu T, Sakai K, Mitsumura H, Matsushima S and Iguchi Y (2020). The impact of cerebral microbleeds presence on outcome following minor stroke treated with antiplatelet therapy. *Frontiers in neurology*, 11: 522.
27. Diker S, Gelener P, Eker A, Kaymakamzade B, Mut S, Erem A and Balyemez U (2022). Association between cerebral microbleeds and inflammatory biomarkers in patients with ischemic stroke. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, 58(1): 1-9.
28. Graff-Radford J, Botha H, Rabinstein AA, Gunter JL, Przybelski SA, Lesnick

- T, Huston J, Flemming KD, Preboske GM, Senjem ML and Brown RD (2019). Cerebral microbleeds: prevalence and relationship to amyloid burden. *Neurology*, 92(3): 253-262.
29. Elmståhl S, Ellström K, Siennicki- Lantz A and Abul- Kasim K (2019). Association between cerebral microbleeds and hypertension in the Swedish general population “Good Aging in Skåne” study. *The Journal of Clinical Hypertension*, 21(8): 1099-1107.
30. Yu M, Jia Y, Yang D, Zhang R, Jiang Y, Zhang G, Qiao H, Han H, Shen R, Ning Z and Zhao X (2022). Association between Hemoglobin A1c and Cerebral Microbleeds in Community- based Stroke- free Individuals: A cross- sectional study. *Diabetes/Metabolism Research and Reviews*, 38: 3557.
31. Cordonnier C, Al-Shahi Salman R and Wardlaw J (2007). Spontaneous brain microbleeds: systematic review, subgroup analyses and standards for study design and reporting. *Brain*, 130(8): 1988-2003.
32. Qiu C, Sigurdsson S, Zhang Q, Jonsdottir MK, Kjartansson O, Eiriksdottir G, Garcia ME, Harris TB, van Buchem MA, Gudnason V and Launer LJ (2014). Diabetes, markers of brain pathology and cognitive function: the Age, Gene/Environment Susceptibility– Reykjavik Study. *Annals of neurology*, 75(1): 138-146.
33. Xu CX, Xu H, Yi T, Yi XY and Ma JP (2021). Cerebral Microbleed Burden in Ischemic Stroke Patients on Aspirin: Prospective Cohort of Intracranial Hemorrhage. *Frontiers in Neurology*, 12.
34. Nagaraja N, Farooqui A, Zahid AB and Kaur S (2021). Factors associated with the presence of cerebral microbleeds and its influence on outcomes of stroke not treated with alteplase. *Clinical Neurology and Neurosurgery*, 207: 106798.