OPEN AIMJ ORIGINAL ARTICLE

Neurology

Evaluation of Cerebral Microbleeds in Patients with Acute Ischemic Stroke

Ahmed Mohamed Ahmed Ghaly, [1] MBBCH, Sayed Elzayat, [1] MD, Ahmed Essmat Ali, [1] MD, Mahmoud Ibrahim Elshamy, [2] MD.

** Corresponding Author:*
Ahmed Mohamed Ahmed Ghaly
ahmedghaly928@gmail.com

Received *for publication June 5, 2022; Accepted November 18, 2022; Published online November 18, 2022.*

doi: 10.21608/aimj.2022.142376.1964.

Citation: Ahmed MAG, Sayed E, Ahmed EA and Mahmoud IE. Evaluation of Cerebral Microbleeds in Patients with Acute Ischemic Stroke. AIMJ. 2022; Vol.3-Issue11 .60-65.

[1]Neurology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

[2]Radiology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

ABSTRACT

Background: CMBs have long been regarded to be an early imaging indication of haemorrhage - recumbent vasculopathy - and consequently a predictor of symptomatic stroke, especially intracerebral haemorrhage, and dementia in old life.
Aim of the study: The primary goal of this study was to investigate the prevalence and risk factors for cerebral microbleeds (CMB) in acute ischemic stroke using T2* weighted imaging.
Patients and Methods: The 6-month Prospective Cohort Study was repeated with the same This study includes 150 cases from the inpatient and outpatient clinics of Al-Azhar University Hospitals' neurology departments. MRI brain T2* was utilised to determine the presence or absence of cerebral microbleeds after an acute ischemic stroke diagnosis was made based on clinical, radiographic, and laboratory data.
Results: Microbleeds in the brain were discovered to be prevalent in 21.3 percent of people. In terms of tobacco smoke, raised blood pressure, D.M, atrial fibrillation, ischemic heart disease, and hyperlipidemia, there were statistically non-significant differences between those with negative and positive CMB. Patients with a positive CMB had a statistically significant increase in antiplatelet medication use compared to those with a negative CMB, according to the current data.
Conclusion: Cerebral microbleeds were identified in 21.3 percent of patients over the age of 65 who had an ischemic stroke. One of the most significant risk factors connected to the development of CMBs has been identified as antiplatelet medications.

Keywords: *Acute ischemic stroke; microbleeds in the brain; MRI brain.*

Disclosure: *The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.*
Authorship: *All authors have a substantial contribution to the article.*

INTRODUCTION

A stroke occurs when the brain's cells die owing to a lack of blood flow. Ischemic and hemorrhagic strokes are the two types of stroke. A lack of blood flow causes an ischemic stroke, while a haemorrhage causes a hemorrhagic stroke. Both disorders impair the ability of some regions of the brain to function properly. [1].

According to the World Health Organization, "a clinical condition characterised by rapidly emerging clinical signs of localised (or occasionally worldwide) impairment of brain function lasting more than 24 hours or leading to death with no obvious cause other than vascular origin." [2.]

Cerebral microbleeds (CMBs) are minute, chronic brain haemorrhages caused by anatomical abnormalities in the small arteries of the brain. On T2*-weighted brain MRI imaging, they appear as circular anomalies with hypo-intensity. Because CMBs are usually asymptomatic, they are frequently discovered in the brain by chance. MRI scans for people who have had a stroke or who have dementia [3].

CMBs were recently discovered to be an early imaging marker of bleeding-prone vasculopathy, and hence a predictor of symptomatic stroke, particularly intracerebral haemorrhage, and dementia in the elderly. As a result, epidemiologic evidence supporting CMBs in older populations is regarded as critical for better understanding and avoiding stroke and dementia in the future. [4].

Hypertensive angiopathy CMBs are expected to be concentrated in deep or infratentorial brain regions, whereas amyloid angiopathy CMBs are thought to be concentrated in cerebral lobar regions. As a result, CMB risk factors are likely to vary depending on where you live. [5].

The primary purpose of this study was to explore the prevalence and risk factors related with cerebral microbleeds (CMB) in acute ischemic stroke using T2* weighted imaging.

PATIENTS AND METHODS

The research took place over the course of six months and was designed as a prospective cohort study. This study includes 150 cases from the inpatient and outpatient clinics of Al-Azhar University Hospitals' neurology departments.

Patients who have been diagnosed with acute ischemic stroke clinically, radiologically, and in the lab.

Acute intracerebral haemorrhage, SAH, subdural hematoma, extradural hematoma, and haematological abnormalities are not allowed to participate.

The patients had sustained severe head traumas and had developed an A-V malformation.

Tumors, aneurysms, arteriovenous malformations, cancer, severe cardiac disease (such as heart failure), liver disease (such as cirrhosis), as well as viral and inflammatory diseases MRI is not recommended for people with acute coronary syndrome, life-threatening arrhythmias, or cardiac illness.

The Faculty of Medicine at Al-Azhar University certified the procedure and its related documents for Ethical and Research approval.

Patients or their relatives signed a written informed consent form before enrolling and starting the trial.

All of the participants in the study were subjected to the following procedures:

must have a full medical and neurological history.

Previous antithrombotic treatment (antiplatelets or anticoagulants)

The National Institute of Health Stroke Scale, which determines how severe a stroke is (NIHSS).

Standard lab tests include the following:

Complete blood count, liver function tests, prothrombin time and concentration, and the international normalised ratio (INR), Renal function tests, fasting blood glucose, and glycosylated haemoglobin (HbA1C).

lipoprotein profile:

A T2* MRI of the brain to see if any microbleeds are present. A superconducting 1.5 T unit was used to perform brain MRIs (Achieva; Philips Medical Systems, Best, the Netherlands). All of the patients were scanned using a dedicated head coil and a typical stroke technique. Among the pulse sequences were the following:

Axial T1W pictures (rapid spin-echo sequence): TR = 597 ms, TE = 15 ms, NEX = 2, flip angle 90, matrix 137 208 with a field of view (FOV) of 230 (AP) 186 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm, matrix 137 208 with a field of view (FOV) of 230 (AP)

TR = 4845 ms, TE = 110 ms, NEX 2, flip angle 90, matrix 147 256, FOV 230 (AP) 183 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm, NEX 2, flip angle 90, matrix 147 256, FOV 230 (AP) 183 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm, TR = 4845 ms, TE = 110 ms, NEX 2, flip angle 90, matrix 147 256, FOV 230 (AP) 183 (RL) 131, NEX 2, flip angle 90, matrix 147 256, (FH)

FLAIR axial images (fluid-attenuated inversion recovery): NEX 2, flip angle 90, matrix 137 208, FOV 230 (AP) 184 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm, FLAIR axial images TI (inversion time) = 2800 ms, TR = 11000 ms, TE = 130 ms, TI (inversion time) = 2800 ms, TR = 11000 ms, TE = 130 ms, TI (inversion time) = 2800 ms, TR = 11000 ms, TE = 130 ms, TI (inversion NEX 2, matrix 137 208 with FOV 230 (AP)

Axial diffusion-weighted (DW) images: TR = 3724 ms, TE = 117 ms, b value = 0 and 1000 s/mm2, matrix 105 136 with FOV 232 (AP) 202 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm, matrix 105 136 with FOV 232 (AP) 202 (RL) 131 (FH) mm, slice thickness

TR = 691 ms, TE = 23 ms, matrix 133 208 with FOV 230 (AP) 184 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm MRA flight time of the Willis circle, matrix 133 208 with FOV 230 (AP) 184 (RL) 131 (FH) mm, slice thickness 5 mm, and gap 0 mm MRA flight time of the Willis circle

While being blinded to the clinical information, two trained observers tallied the amount of CMBs across the entire brain. The number of CMBs split the participants into two groups: those with 0-5 and those with >5.

Statistical Analysis:

To gather, categorise, review, and tabulate data, IBM Statistical Package for the Social Sciences version 20 was utilised (SPSS). Tokens comprised numbers and percentages for qualitative data; mean, standard deviations, and ranges for quantitative data with parametric distribution; and median and interquartile range for quantitative data with nonparametric distribution (IQR). The Chi-square test was used to compare qualitative data from two groups, and when the predicted count in any cell was less than 5, the Fisher exact test was used instead of the Chi-square test. The independent t-test was used to compare two groups with quantitative data and a parametric distribution, whereas the Mann-Whitney test was used to compare two groups with quantitative data and a non-parametric distribution. The acceptable

margin of error was set at 5%, while the confidence interval was set at 95%. As a result, the p-value below was deemed significant.

RESULTS

Table (1) This table showed that 55 patients (36.7%) were females and 95 patients (63.3%) were males, mean of age was 65.41 with range from 46 to 78.

		No	%
Sex	Female	55	36.7%
	Male	95	63.3%
Age	Mean± SD	65.41	5.56
	Range	46	78

Table 1: Demographic data among all patients.

Table (2) showed that 32 patients (21.3%) had AF, 17 patients (11.3%) had IHD, 92 patients (61.3%) had hyperlipidemia.

		No	%
HTN	Yes	95	63.3%
	No	55	36.7%
DM	No	105	70.0%
	Yes	45	30.0%
Smoker	No	111	74.0%
	Yes	39	26.0%
AF	No	118	78.7%
	Yes	32	21.3%
IHD	No	133	88.7%
	Yes	17	11.3%
hyperlipidaemia	No	58	38.7%
	Yes	92	61.3%

Table 2: History of associated diseases among all patients.

		No	%
Antiplatelet medication	No	48	32.0%
	Yes	102	68.0%
Type of stroke	Cardio embolism	30	20.0%
	Largr artery areteriosclerosis	59	39.3%
	Small vessels disease	47	31.3%
	Undetermined cause	14	9.3%
NIHSS (present)	Mean± SD	10.56	3.88
	Range	4	20

Table 3: Antiplatelet medication, Type of stroke and NIHSS (present) among all patients.

		No	%
Presence of CMB	No	118	78.7%
	Yes	32	21.3%
NO. of CMB	<5	28	18.7%
	>5	5	3.3%
	No	117	78.0%
Site of CMB	No	118	78.7%
	Cortical-subcortical and deep	10	6.7%
	Deep region	5	3.3%
	Infratentorial	8	5.3%
	Cortical-subcortical	9	6.0%

Table 4: Presence, NO and Site of CMB among all patients.

Table (4) showed that NO. of CMB was <5 in 28 patients (18.7%), was >5 in 5 patients (3.3%), Site of CMB was Cortical-subcortical in 9 patients (6%), was Cortical-subcortical and deep in 10 patients (6.7%), was Infratentorial in 8 patients (5.3%).

		Negative CMB (NO.117)		CMB (NO.33)		Chi square test	
		No	%	No	%	X2	P value
Sex	Female	46	39.3%	9	27.3%	1.608	0.205
	Male	71	60.7%	24	72.7%		
Age	Mean ±SD	64.85 ±6.10		67.36 ± 1.94		2.322	0.022

Table 5: Demographic data among CMB.

Table (5) showed that there was statistically significant increase old age in CMB

	Negative CMB (NO.117)		CMB (NO.33)		Chi square test	
	No	%	No	%	X2	P value
HTN	68	58.1%	27	81.8%	6.225	0.013
DM	35	29.9%	10	30.3%	0.284	0.868
Smoker	31	26.5%	8	24.2%	0.366	0.833
AF	25	21.4%	7	21.2%	0.000	0.985
Antiplatelet medication	72	61.5%	30	90.9%	10.204	0.001
IHD	13	11.1%	4	12.1%	0.026	0.872
Hyperlipidemia	72	61.5%	20	60.6%	0.009	0.923

Table 6: History among CMB.

Table (6) showed that there was statistically significant increase HTN and antiplatelet medication in CMB.

DISCUSSION

Cerebral microbleeds (CMBs) are minute chronic brain haemorrhages caused by structural anomalies in the cerebral small arteries. During brain MRI tests for stroke and dementia patients, CMBs are frequently detected by chance [3].

The main purpose of this study was to look at the prevalence and risk factors of cerebral microbleeds (CMB) in acute ischemic stroke using T2* weighted imaging.

A total of 150 patients with clinically, radiologically, and laboratory confirmed acute ischemic stroke were referred from Al-Azhar University neurology departments' inpatient and outpatient clinics for this prospective cohort study. They were chosen from the neurology departments of Al-Azhar University hospitals and screened for eligibility.

The demographic features of the investigated cases revealed a male majority (63.3 percent). The cases studied had an average age of 65.415.56 years. According to the available data on the clinical histories of the cases analysed, the majority of persons have hypertension (63.3 percent). Diabetes affects 30.0 percent of people, with smokers accounting for 26% of cases. According to the current findings, hyperlipidemia affects 61.3 percent of cases. Ischemic heart disease affects 11,3 percent of people, and atrial fibrillation affects 21,3 percent.

Furthermore, Chen et al.6 discovered that lowering serum LDL- cholesterol by 50% or more was linked with a lower risk of ischemic stroke recurrence, with an OR of 0.51 (95 percent CI: 0.36–0.72), demonstrating that statin medication is completely effective in preventing ischemic stroke.

According to our data, 39.3 percent of persons have stenosis in their main arteries, 31.3 percent have small vessel disease, and 20% have cardiac embolism. The mean NIHSS, according to our data, was 10.563.88, with a range of 4 to 20.

Similarly, Harris et al. [7] discovered that the most common ischemic subtype of stroke was atherosclerosis of the main arteries. Diabetes was found to be a risk factor for major artery atherosclerosis, although hypertension was found to be a risk factor for small vessel disease and subtypes of unknown origin. Atrial fibrillation has been associated to cardioembolism. Soliman et al. [8] also discovered that 61.7 percent of the ischemic stroke patients studied had a moderate NIHSS score of 5 to 15.

However, Higuchi et al. 9 reported that the majority of acute ischemic stroke patients (50%) had an embolic stroke of unknown origin, followed by major artery atherosclerosis (40%), cardioembolism (33%), transient ischaemic attack (17%), and brain microvascular disorders (17%). (14 percent).

A earlier investigation was undertaken by Kulesh et al.[10]. According to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, the pathogenetic subtypes of ischemic stroke in diseased persons under 45 years with ischemic stroke confirmed by magnetic resonance imaging (MRI) were large artery atherosclerosis (7.9%), cardioembolism (21.4%), and small vessel disease (11.9 percent).

According to our findings, CMB was detected in 21.3 percent of the cases studied. CMB were discovered in less than 5% of the population (18.7%) and more than 5% of the population (19.7%). (3.3 percent).

Our findings were lower than those of Yokoyama et al. [3], who detected CMBs in 36 percent (128/ 356) of patients in a case control study by Elkhatib et al.[11], despite the fact that CMBs were observed in 40.7 and 49.3 percent of patients with ischemic stroke with and without AF, respectively.

Tang et al.[12] found a 24 percent prevalence of CMBs in patients with ischemic stroke, while Ibrahim et al.[13] found a 29.4% prevalence of CMBs in elderly Egyptians with acute ischemic stroke. Our findings, on the other hand, surpass those of Wang et al.[14], who discovered an ischemic stroke prevalence of 5,7%.

In a systematic review and meta-analysis, Corica et al.[15] discovered that cerebral microbleeds are prevalent in atrial fibrillation patients, occurring in around one-fourth of them. In persons with atrial fibrillation, cerebral microbleeds have been associated to both hemorrhagic and thromboembolic consequences. In addition, the risk of ischemic heart disease rose in direct proportion to the amount of CMB consumed.

According to our findings, the site of CMB was cortical-subcortical and deep in 6.7 percent of patients, cortical-subcortical in 6% of cases, infratentorial in 5.3 percent of cases, and deep area in 3.3 percent of cases.

According to Ibrahim et al., CMBs are likewise more prevalent in the deep brain areas of hypertension patients [13] In a population-based observational investigation, Romero et al.[16] observed that increased blood pressure was connected to deep/infratentorial CMBs.

When it came to demographic data among CMB, our findings revealed no statistically significant gender or age differences between negative and positive CMB (P value > 0.05).

Similarly, Yokoyama et al.[3] investigated the prevalence and risk factors of silent cerebral microbleeds in people with coronary artery disease and found no link to sex, hypertension, dyslipidemia, or diabetes. According to the same study, CMBs were strongly associated with those in their senior years.

Ibrahim et al.[13] discovered that age has a substantial impact on the occurrence of CMBs.

In terms of being a smoker, hypertensive, diabetic, having atrial fibrillation, ischemic heart disease, or hyperlipidemia, there were statistically non-significant variations in medical histories between those with negative CMB and those with positive CMB (P value>0.05).

Patients with a positive CMB were far more likely to be prescribed antiplatelet medications than those with a negative CMB (P0.001).

According to Yokoyama et al. [3], CMBs were frequently identified in patients with coronary artery disease and were substantially related with long-term antiplatelet therapy, particularly long-term dual antiplatelet therapy. These findings are consistent with the prior ones.

There was also no statistically significant link between age and the presence or absence of cerebral microbleeds, according to Ibrahim et al. [13]. High blood cholesterol and antithrombotic medication treatment, on the other hand, were found to be the most major risk factors for CMB formation in the same study.

Elmaaty et al.[17] discovered that elevated blood pressure is an independent contribution to the formation of CMBs; however, IHD, the use of antiplatelet medications, a higher BMI, and dyslipidemia must all be considered. Corica et al.[15] also discovered that HbA1c is linked to CMBs in adults who haven't had a stroke or a transient ischemic attack, particularly diabetic patients.

When preventing CMB, the state of glycemic control should be considered. To lower the risk of CMBs, HbA1c levels should be constantly managed, especially in diabetic patients.

Age, high blood pressure, patients with D.M, prior stroke history, antiplatelets, anticoagulants, NIHSS, and white matter damage were all significant risk factors for CMB, according to Elkhatib et al.[11].

According to multivariate logistic regression, the only independent risk factors for CMBs were age, high blood pressure, anticoagulants, and white matter damage.

CONCLUSION

In the elderly group of patients with ischemic stroke, the incidence of cerebral microbleeds was 21,3 percent. The most significant linked risk factors for CMBs were discovered to be antiplatelet medications.

It is suggested that future studies incorporate a larger sample from a wider geographic region or expand to a multi-government examination.

Conflict of interest : none

REFERENCES

1. Kuriakose, D. and Xiao, Z. Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. International Journal of Molecular Sciences. 2020; 21(20): 7609.
2. Ibrahim Meneci, T., Hassan El-Sheshiny, A., et al. Ischemic stroke registry in Egypt: hospital based study. *Al-Azhar Medical Journal*. 2021; 50(1): 35-46.
3. Yokoyama, R., Kanzaki, Y., Watanabe, T., et al. Prevalence and Risk Factors of Silent Cerebral Microbleeds in Patients with Coronary Artery Disease. Journal of Stroke and Cerebrovascular Diseases. 2022; 31(1): 106211.
4. Puy, L., Pasi, M., Rodrigues, M., et al. Cerebral microbleeds: from depiction to interpretation. *Journal of Neurology, Neurosurgery & Psychiatry*. 2021; 92(6): 598-607.
5. Wu, X., Yan, J., Ye, H., et al. Pre-treatment cerebral microbleeds and intracranial hemorrhage in patients with ischemic stroke receiving endovascular therapy: a systematic review and meta-analysis. Journal of Neurology. 2020; 267(5): 1227-32.
6. Chen, K.-N., He, L., Zhong, L.-M., et al. Meta-analysis of dyslipidemia management for the prevention of ischemic stroke recurrence in China. *Frontiers in neurology*. 2020; 11: 483570.
7. Harris, S., Sungkar, S., Rasyid, A., et al. TOAST subtypes of ischemic stroke and its risk factors: a hospital-based study at Cipto Mangunkusumo Hospital, Indonesia. *Stroke research and treatment*. 2018;
8. Soliman, R.H., Oraby, M.I., Fathy, M., et al. Risk factors of acute ischemic stroke in patients presented to Beni-Suef University Hospital: prevalence and relation to stroke severity at presentation. *The Egyptian journal of neurology, psychiatry and neurosurgery. 2018; 54(1): 1-9.*
9. Higuchi, E., Toi, S., Shirai, Y., et al. Prevalence of microembolic signals in embolic stroke of undetermined source and other subtypes of ischemic stroke. Stroke.2020; 51(2): 655-658.
10. Kulesh, A., Nurieva, Y.A., and Syromyatnikova, L. Causes of ischemic stroke in patients younger than 45 years: analysis of data from the regional vascular center. *Neurology, Neuropsychiatry, Psychosomatics.* 2021;13(1): 24-30.
11. Elkhatib, T.H., Elsaid, A.F., Al-Molla, R.M., et al. Prevalence and Associated Risk Factors of Cerebral Microbleeds in Egyptian Patients with Acute Ischemic Stroke and Atrial Fibrillation. Journal of Stroke and Cerebrovascular Diseases. 2020; 29(5): 104703.

12. Tang, W., Chen, Y., Lu, J., et al. Cerebral microbleeds and quality of life in acute ischemic stroke. *Neurological Sciences.* 2011; 32(3):. 449-454.

13. Ibrahim, A.A., Ibrahim, Y.A., Darwish, E.A., et al. Prevalence of cerebral microbleeds and other cardiovascular risk factors in elderly patients with acute ischemic stroke. *Egyptian Journal of Radiology and Nuclear Medicine.* 2019; 50(1): 1-8.

14. Wang, C., Du, Z., Ye, N., et al. Hyperlipidemia and hypertension have synergistic interaction on ischemic stroke: insights from a general population survey in China. B*MC cardiovascular disorders*. 2022; 22(1): 1-8.

15. Corica, B., Romiti, G.F., Raparelli, V., et al. Epidemiology of cerebral microbleeds and risk of adverse outcomes in atrial fibrillation: a systematic review and meta-analysis. *EP Europace.* 2022.

16. Romero, J.R., Preis, S.R., Beiser, A., et al. Risk factors, stroke prevention treatments, and prevalence of cerebral microbleeds in the Framingham Heart Study. Stroke. 2014; 45(5): 1492-4.

17. Elmaaty, A., Ahmed, A., and Zarad, C.A. Role of magnetic susceptibility-weighted imaging in characterization of cerebral microbleeds in acute ischemic stroke Egyptian obese patients. T*he Egyptian Journal of Neurology, Psychiatry and Neurosurgery.* 2020; 56(1):1-9.