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Magnetic Resonance Spectroscopic Imaging in Leukoaraiosis patients with associated risk factor of Type II diabetes mellitus

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Abstract

Purpose:

We aim to investigate the association of Type II diabetes with Leukoaraiosis, measure metabolite changes in the brain using Magnetic resonance spectroscopy (^{1}H-MRS), and determine neurocognitive impairment in this study.

Materials and Methods:

We recruited 64 patients with LA and 64 healthy controls all patients, regardless of gender, were enrolled in the study, with an age range of (50 to 90 years). It was a prospective study conducted in the period of (2022-2023).^{1}H-MRS was performed with the selected region of interest in the periventricular white matter. Three main ratios are considered NAA/Cho, NAA/Cr and Cho/Cr and are obtained.

Results:

We found the metabolite ratios of NAA/Cho, NAA/Cr in the white matter lesions is lower in the T2 DM group than the healthy control group (1.56 ± 0.45 vs 1.93 ± 0.24 and 1.42 ± 0.58 vs 1.98 ± 0.35, $p<0.001$) respectively. Whereas when comparing Cho/Cr with HbA1c values it shows that there is no significance between Cho/Cr and T2 DM (1.22 ± 0.31 vs 1.09 ± 0.15 and 8.49 ± 1.90 vs 5.55 ± 0.38, $p> 0.05$ respectively).There was a positive correlation between NAA/Cho with ACEIII ($r=0.495$, $p=0.0001$) and NAA/Cr with ACEIII ($r=0.434$, $p=0.0001$) and when Correlating Cho/Cr with ACEIII it shows a negative correlation ($r=-0.206$, $p=0.020$). The p-value and regression coefficient of HbA1c with NAA/Cho, which showed a positive significance ($r=0.446$, $p=0.0001$ and $r=0.425$, $p=0.0001$). The regression coefficient of HbA1cwith Cho/Cr ratio did not show any significance.

Conclusion:

In light of our findings, we conclude that the results estimate that Type II diabetes mellitus has a strong association with the increased risk of leukoaraiosis, and Magnetic Resonance Spectroscopy (^{1}H-MRS) is a potential biochemical marker compared to structural MRI for monitoring cognitive impairment in patients with leukoaraiosis.

Keywords: N-acetylaspartate; Choline; Creatinine; T2 Diabetes Mellitus; Magnetic Resonance spectroscopy; Addenbrookes cognitive examination.

Introduction

Leukoaraiosis, also known as white matter lesion, is a term originated by Hachinski et al and colleagues in 1987[(1)]. It implies to the abnormal appearance of white matter, which appears as patchy or diffuse areas of reduced attenuation in CT scans, and as areas of increased intensity in MRI T2 flair or T2 weighted sequences, but is not visible in T1 weighted sequences. Furthermore, Leukoaraiosis falls under the classification of cerebral small vessel disorders[(2)]**.**The pathological characteristics of LA include myelination and axonal degeneration, sporadic demyelination, and erosion of ependymal cells in lesions of the white matter.Evidently, these types of white matter lesions can also manifest in elderly control patients who are both healthy and cognitively unimpaired. Within the population of patients with LA, another notable contributing factor is the heightened occurrence of well-known risk factors for cerebrovascular disorders, including hypertension, diabetes mellitus, and cardiovascular issues [(3)],[(4)].Numerous significant and well-known risk factors cause leukoaraiosis. One of the factors that might cause leukoaraiosis is the Type 2 Diabetes mellitus. Diabetes mellitus has emerged as an apparent global health issue, with a sustained rise in its prevalence worldwide [(5)]. In the context of Type 2 diabetes mellitus, various changes occur in the brain tissues, such as vascular changes and endothelial

dysfunction. The vascular changes result in alterations in the small blood vessels in the brain as well as throughout the body. This compromised blood flow can affect the integrity of the blood vessels in the brain, potentially contributing to the development of leukoaraiosis. Additionally, the association between diabetes and endothelial dysfunction leads to impaired function of the inner lining of blood vessels, known as the endothelium. This dysfunction can cause reduced vasodilation, increased inflammation, and altered regulation of blood flow.The primary concern in numerous cerebrovascular diseases is a decline in cognitive function, particularly in senior adults. The concurrent existence of Type 2 diabetes and leukoaraiosis may lead to cognitive impairment, potentially because to disruptions in neuronal networks and the integrity of white matter. Utilizing brain imaging techniques may aid in emphasizing the mechanisms that contribute to cognitive deterioration in individuals with Type 2 Diabetes mellitus[6].

LA can be categorized into two categories, periventricular and subcortical, according to the reported imaging features. It is noted that The Fazekas approach was mostly employed to assess LA lesions in the periventricular and deep subcortical white matter using MRI[7](Fig 1).Scoring of periventricular lesions (PVM)is as follow:

0: No lesions
1: Caps or pencil like thinning
2: Smooth "halo"
3: irregular periventricular signal extending into the deep white matter.

The Scoring of deep white matter as follow:
0: absent
1: Punctate Foci
2: beginning Confluence

Magnetic Resonance Spectroscopy (MRS), a sophisticated MRI imaging technology, non-invasively delivers precise information on the concentration of metabolites in specific regions. As a result, this method has the potential to be applied widely to examine the alterations and progression in leukoaraiosis. Magnetic resonance spectroscopy (MRS) can quantify many metabolites, including N-acetyl aspartate (NAA), choline (Cho), creatine (Cr), myo-inositol (MI), lactate, lipid, glutamine/glutamate, and alanine. The frequently employed metabolites in MRS spectra include NAA (N-acetyl aspartate), Cho (Choline), and Cr (Creatine). Studies have demonstrated that MRS is effective as a surrogate marker for assessing cognitive impairments[8],[9],[10],[11].NAA is a marker of neuronal dysfunction or preservation; choline (Cho) signifies the process of sheath formation as well as breakdown; and creatine (Cr) depicts energy metabolism, which is relatively constant between individuals[12]. The other two metabolites were measured using creatine (Cr) as a reference. MRS is sensitive for detecting hypoxic damage due to vascular or other diseases. We anticipated to assess the effectiveness of white matter lesions on cognitive function through the correlation of metabolite spectra using Magnetic Resonance Spectroscopy with a clinical psychological battery. Our hypothesis was that LA is significantly associated with T2DM 2. As the lesion burden increases, there is a noticeable decline in cognitive function. 3. There is an abnormal alteration in metabolic parameters in the brain compared to that of healthy control patients. 4 In order to assess the importance of magnetic resonance spectroscopy (MRS)in the early identification of cognitive impairment associated with type 2 diabetes mellitus (T2 DM) in white matter lesions.

Materials and methods:

LA Subjects:

We consecutively recruited sixty-four patients with LA for this study from the Department of Radiology, SRM Medical College Hospital, and Research Centre. All patients, regardless of gender, were enrolled in the study, with an age range of (50 to 90 years). It was a prospective study conducted in the period of (2022-2023). The inclusion criteria for the LA group are as follows. 1) Changes in the periventricular region on MRI of any degree. 2) Patients with Periventricular changes and with T2 DM. 3) No disability assessed by instrumental activities of daily living scale[13],[14].The presence of a Hemoglobin A1C (HbA1c) value (≥ 6.0) validates the diagnosis of T2 DM. Exclusion Criteria are as follows. 1) Patients with other comorbidities like SHTN, cardiac diseases, Hepatic or renal failure, and Malignancies. 2) Any other neurological diseases like Intracranial tumors, lacunar infarct, Stroke, Recent Head injury, other space-occupying lesions, Multiple sclerosis, or Parkinsonism.3) Patient exhibiting psychiatric problems and associated mental conditions.4) Patient expressing unwillingness to undergo MRI. 5) An accepted contraindication for undergoing MRI scanning.

Control Group:

This study includes sixty-four healthy elderly patients selected based on MRI image findings who underwent routine MRI without any findings. The inclusion criteria for healthy elderly patients are 1) Age and gender as

the same selected for the LA group and 2) No history of seizure, stroke or added disabilities. 3) No history of visual ailments or hearing disabilities 4) No cognitive disorders. 5) No previous history of head injury.

Initially all the one hundred and twenty-eight patients were assessed for demographic characteristics (e.g., age, sex) and educational details between the control and LA groups, as it should be within the inclusion criteria. Patients were then checked for vascular risk factors, especially for type 2 diabetes mellitus. HbA1c reports within a period of 6months were considered. Only patients who met all criteria underwent MR Spectroscopy, followed by neuropsychological assessment.

Neuropsychological assessment:

Our study administered standardized measures to assess cognitive decline in all patients. In our study, we followed Addenbrooke's Cognitive Examination III in the Tamil version to screen for patients who underwent MR spectroscopy. Informed consent was obtained from all the patients, and a trained clinical psychologist conducted the ACE III test. ACE III is a sensitive tool that is widely used for diagnostic screening in our centre to assess patients with mild cognitive impairment and dementia. The test encompasses assessments measuring Attention, Memory, Fluency, Language, and Visuospatial abilities. Scores upto100 can be obtained, with a higher score implyingenhanced cognitive performance and is weighted in such a way as attention (18), memory (26), fluency (14), language (26), and visuospatial (16). A cutoff value of ≥ 86 was considered normal. Thus, this test takes approximately 15-20 minutes to be performed. .The assessment of attention comprised seeking information about the patient's awareness of the date, seasons, and their current whereabouts and having them repeat three uncomplicated words and engage in a sequential subtraction task. Memory tests encompass activities such as retrieving three words that have previously been mentioned, committing to memory, repeating an anonymous identity and location, while recollecting generally recognized historical events.To evaluate the patient's fluency, they had to provide a list of as many animal names as possible within a minute and to produce as many words beginning with a specific letter within the same time. Language was examined by instructing the patient to perform a sequence of physical tasks with a pencil. To complete the task, one must do the following: 1. Write two grammatically correct sentences using the given sentence "Stack the paper and pencil together."2. Complex words comprised of several syllables and two brief proverbs were repeated.4. Identify and label the objects depicted in the 12-line drawings. 5. Answers to contextual questioning regarding certain objects. 6. Test words that exhibit irregular phoneticcorrespondences. To test the patient's visual abilities, Participants are instructed to replicate two schematics, depict a clock face with the hands positioned at a specific time, estimate the number of dots, and identify four fragmented letters[(15)].

MRI Image Acquisition:

MRI brain images were obtained using the MRI Siemens Magnetom_a Tim+Dot system 1.5 Tesla scanner. The 16-channel TIM head/neck coil was used for both standard MRI imaging and MR spectroscopy, which eliminates the necessity of repositioning the patient to be imaged separately. Routine brain MRI consists of a series of sequences, including axial T2 flair, axial T1, and axial T2 images. T2 weighted and T2 FLAIR sequences were employed in this study to detect LA. 1) T1-weighted axial images are taken along these parameters: TR: 500ms, TE=8.9 ms, Slice thickness= 5.0mm, distance factor: 30% No. of Slices: 23; Voxel Size: 0.7x0.7x5.0mm; Flip Angle: 90°; FOV: 2) T2 weighted axial image is a spin echo sequence with the TR=4290, TE=101ms, slice thickness=5.0mm, distance factor=30%, number of slices=23, voxel size=0.5x0.5x5.0mm, flip angle=150°, FOV=230x T2 Flair Axial is a Turbo Inversion Recovery Sequence with TR = 9000ms, TE = 92ms, slice thickness = 5.0mm, distance factor = 30%, number of slices = 23, voxel size = 0.4x0.4x5.0mm, flip angle = 150°, and FOV = 230x220mm.

WMH Volume Measurements:

In this brain imaging study, we grade visually the hyperintense signal changes identified as leukoaraiosis. Volume measurements of the graded areas are used for additional validation using a semi-automated software package known as ITK Snap. ITK Snap was developed by the National Institutes of Health and funded by the Chen-Zuckerberg Initiative. In the active contour step, the low threshold mode must be set so the hyperintense area can be segmented and separated automatically. This segmentation has not accounted for all hyperintensities. Only the specific region of interest inside the ^{1}H-MRS area is considered.

Multi-Voxel Magnetic Resonance Spectroscopy:

^{1}H-MRS is employed to precisely determine the concentration of metabolites in the specific area of interest within the brain.The image-acquired localizer obtained the spin echo T1 sagittal, T2 coronal, and T2 flair images. In addition, these images serve as references for our approach, which helps find the voxel of interest and acquires MRS data. We conducted an H-MRS using a point-resolved spectroscopy sequence derived from

chemical shift imaging. The subsequent technical parameters were employed. TR=1690 ms, TE= 135ms, average= 2, FOV R>>L=154mm, FOV A>>P= 50mm, Slice thickness= 15mm, Spectral bandwidth= 1000Hz, Voxel size=8.6x9.6x15.0 mm. To avoid the sinus, the scanning baseline was parallel to the anterior commissure–posterior commissure (AC–PC). We placed a region of interest above the posterior and anterior horns of the lateral ventricle. Using the T2 flair axial image,(fig 2) we identified the specific areas, primarily composed of white matter voxels. VOI was adjusted to encompass the hyperintense areas with a Vol R>>L=75mm, Vol A>>P=60 mm. Volume of interest (VOI) was precisely positioned within the periventricular region to avoid partial volume effects from the skull, ventricle, or gray matter. So as to prevent the presence of lipids and fats from the anterior, posterior, and lateral of the scalp, we positioned four saturation bands around the volume of interest (VOI). Shimming ensures an even signal by adjusting coils according to manufacturers' specifications. Upon acquiring the spectra, we carry out water suppression to achieve optimal viewing of the peaks for this sequence with an acquisition time of 5.45 seconds.

Post-Processing Technique of MRS:

At the Siemens MRI workstation, we transfer the acquired MRS data for further MR spectroscopy evaluation. The peaks are heavily filtered using a Hamming filter with a width of 300ms. An interpolation resolution of 32 is kept for R>>L and 32 for A>>p. The automated post-processing procedure includes water reference processing, zero-filling, Fourier transformation, frequency shift correction, baseline correction, phase correction, and curve fitting. To prevent voxel misplacement and to make sure that the VOI includes both the hyperintense areas and the normal white matter, the same investigator scans and supervises all of the patients. Signals outside the VOI are excluded by using the Shimming technique, as this area produces a large amount of chemical shift artifacts and can interfere with the obtained signal peaks. To evaluate metabolites such as NAA, Cr, and Cho, a spectrum comprising distinct peaks was obtained. These metabolic peaks are then semi-quantitatively interpreted by contriving their metabolic ratios: NAA/Cho, NAA/Cr, and Cho/Cr.

Statistical analysis:

Means and standard deviations of demographic characteristics were calculated. Statistical analysis was performed using SPSS Software version 29.0. Pearson Correlation coefficient is used to evaluate the linear association and strength between the metabolic ratios, HbA1c and WMHV. Linear Regression analyses is used to assess the relationship between the variables in both the groups and a P-value of $p < 0.001$***, $p < 0.01$** and $p < 0.05$*was considered as statistically significant.

Results:

A total of 128 subjects were selected and categorized into two groups: the control group and T2 DM group. Of these, 64 were included in the control group, including male (n=39) and female (n=25). In the T2 DM group, 64 patients were male (n=38) and female (n=26). The demographic characteristics of all subjects are described in Table 1. Table 2 shows the comparison between the neuropsychological examination ACEIII over all scores between the control subjects and T2 DM subjects with LA: the ACEIII overall score was 62.30 ± 11.38, which is lower than that of the controlled group 86.17 ± 3.47). The correlation of HbA1c with ACE III between the groups showed that there was a positive correlation; when the HbA1c value increased, there was a change in the ACEIII Cognitive score (r=-0.720, p=0.001), indicating that there is an association between HbA1c and mild cognitive changes in patients with leukoaraiosis and almost we couldn't find any association between lesion volume and the neuropsychological score Table 4 illustrates that the metabolite ratios of NAA/Cho, NAA/Cr in the white matter lesions is lower in the T2 DM group than the healthy control group (1.56 ± 0.45 vs 1.93 ± 0.24 and 1.42 ± 0.58 vs 1.98 ± 0.35, p<0.001 respectively). Whereas when comparing Cho/Cr with HbA1c values it shows that there is no significance between Cho/Cr and T2 DM (1.22 ± 0.31 vs 1.09 ± 0.15 and 8.49 ± 1.90 vs 5.55 ± 0.38, p> 0.05 respectively). There was a decisive correlation between NAA/Cho with ACEIII (r=0.495, p=0.0001) and NAA/Cr with ACEIII (r=0.434, p=0.0001) and when Correlating Cho/Cr with ACEIII it shows a negative correlation (r=-0.206, p=0.020). Table 5 shows the p-value and regression coefficient of HbA1c with NAA/Cho, which showed a positive significance (r=0.446, p=0.0001 and r=0.425, p=0.0001). The regression coefficient of HbA1c with Cho/Crratio did not show any significance.

Table 1: The Demographic Characteristics of Control and Case group

Parameters	Control (n=64)	T2DM (n=64)
Male n (%)	39 (60.9%)	38 (59.3%)

Female n (%)	25 (39.06%)	26 (40.6%)
Age	66.4 ±8.97	58.75 ± 7.79
Systolic blood pressure (mmHg)	114.50 ± 15.79	118.30 ± 10.85
Diastolic blood pressure (mmHg)	78.53 ± 9.98	79.45 ± 9.64
Education (Years)	7.41 ± 2.91	8.73 ± 3.06
HbA1c (%)	5.55 ± 0.38	8.49 ± 1.90
NAA/Cr (ratio)	1.93 ± 0.24	1.56 ± 0.45
NAA/Cho (ratio)	1.98 ± 0.35	1.42 ± 0.58
Cho/Cr (ratio)	1.09 ± 0.15	1.22 ± 0.31

Table 2: Neuropsychological test (ACE-III) in T2 DM and in Healthy controls

Parameters	Control (n=64)	T2DM (n=64)
ACEIII overall Score	86.17 ± 3.47	62.30 ± 11.38
Attention	17.88 ± 9.83	13.25 ± 2.56
Memory	17.41 ± 2.76	12.34 ± 3.65
Fluency	11.97 ± 1.66	8.48 ± 2.11
Language	23.69 ± 2.25	18.09 ± 3.34
Visuospatial	14.34 ± 1.95	9.90 ± 2.27

Table 3: The Correlation HbA1c with ACE III

Parameters	ACE III	
HbA1c	r value	-0.720
	P value	0.001**

Table 4: The Correlation of NAA/Cho, NAA/Cr and Cho/Cr with HbA1c, ACEIII AND WMHV

Parameters	HbA1c		ACEIII	WMHV
NAA/Cr	r value	-0.44	0.434	-0.072
	P value	0.001**	0.001**	0.599
NAA/Cho	r value	-0.46	0.495	-0.086
	P value	0.001**	0.001	0.527
Cho/Cr	r value	0.126	-0.206*	0.259
	P value	0.157	0.020	0.054

Table 5: Regression Analysis of HbA1c Vs NAA/Cho, NAA/Cr and Cho/Cr

Parameters	NAA/Cho			NAA/Cr			Cho/Cr		
	P value	β	r	P value	β	r	P value	β	r
HbA1c	0.001	-.446	0.446	0.001	-0.425	0.425	0.222	0.109	0.109

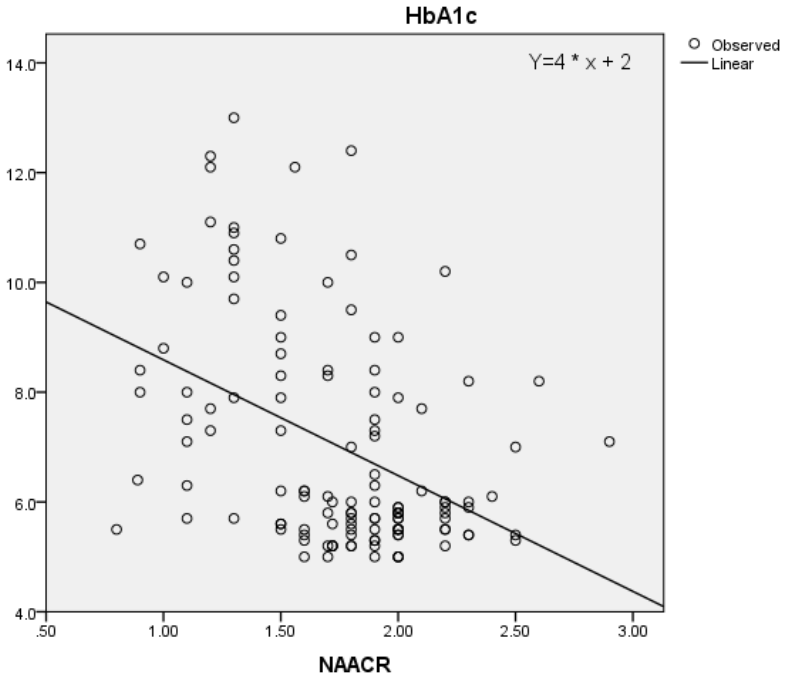

Figure 1: There was a positive interrelation between HbA1c and NAA/Cr in the T2 DM patients with Leukoariosis.

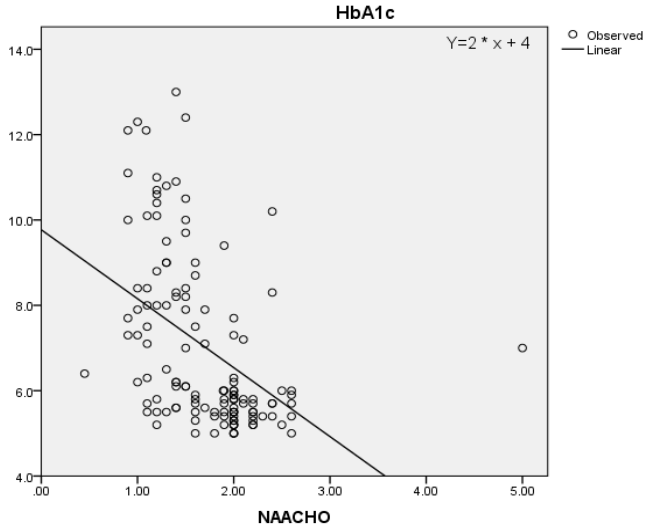

Figure 2: There was a positive interrelation between HbA1c and NAA/Cho in the T2 DM patients with Leukoariosis.

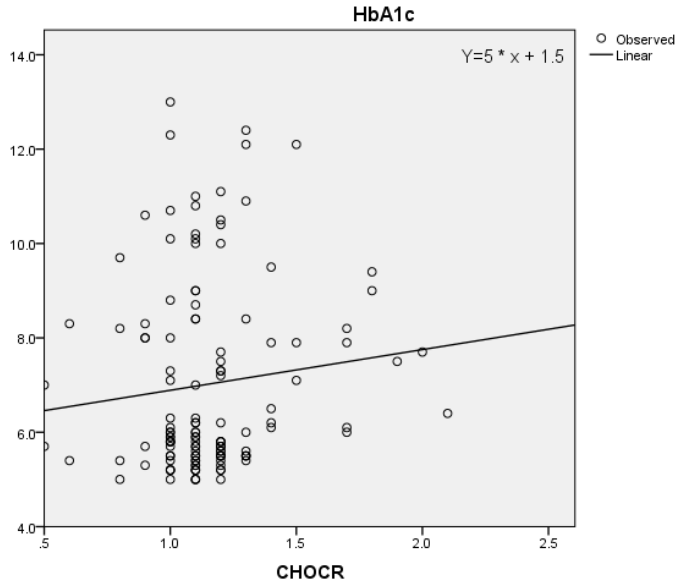

Figure 3: There was a negative interrelation between HbA1c and Cho/Cr in the T2 DM patients with leukoaraiosis.

Discussion:

The primary objective of this study was to demonstrate the link between T2DM as a risk factor and leukoaraiosis. Recent years have seen limited research on the correlation between MRS metabolites, cognition, and type II diabetes mellitus; no study has examined this relationship as of now. We evaluated the changes that occurred in brain metabolites using MR spectroscopy. ^{1}H-MRS was acquired using the multi-voxel technique with an intermittent TE 135ms and as a representative region, we considered the periventricular region for all patients. This area is selected as white matter lesions in the peri ventricle disrupts longer connections to cortical regions that are spatially distant this can impact multiple regions of cognitive domains[(16)].When analyzing the demographic data, we found that most patients aged > 55 years tended to have an increased incidence of T2 DM associated with white matter lesions. As with previous data, we know that age is also a primary risk factor for leukoaraiosis. In our study, we first correlated HbA1c with the neuropsychological test ACEIII, which showed a significant reduction in ACEIII over all scores compared with normal patients. In contrast, there was no significant increase in lesion load, and no association was found between cognitive decline and lesion volume. Second, we found a positive association between MRS metabolite ratios and HbA1c; there was a significant reduction in NAA/Cho and NAA/Cr ratios between the groups. NAA is a neuronal marker that indicates the loss of integrity and axonal damage. It is believed that the Cho peak signifies cellular density[(17)].Moreover, the evaluation of the Cho/Cr ratio did not relate to HbA1c; there was an increase in the Cho/Cr ratio when compared to that of the normal control groups, as the creatine peak remains relatively constant across individuals in the majority of regions. Therefore, it serves as an internal reference. In addition, to prove the association between ACE III and MRS metabolite ratio, we compared the ACE III neuropsychological examination with NAA/Cho and NAA/Cr. There was a correlation between the NAA/Cho, NAA/Cr, and ACE III overall score, where there is a significant reduction in the ACE III score as the NAA/Cho and NAA/Cr ratio decreases. It provides sufficient information that there is a cognitive decline as the metabolite ratios decreases. In contrast, to strengthen the hypothesis, we correlated the metabolite ratios NAA/Cho, NAA/Cr, and Cho/Cr with white matter hyperintensity volume to prove whether there are any changes occurring as the lesion load increases. We found that there was a negative relationship between the lesion volume and the metabolite ratios. Lan-mei Chen et al[(6)], in their Study, made a comparison between MRS and Diffusion tensor imaging in Type II diabetes patients, and their results show the mean of NAA/Cr, and NAA/Cho were notably reduced in diabetes patients when compared to that of the normative group. They also found that the association between DTI parameters in diabetic patients has an association with the metabolic changes and it is consistent with Axonal loss or dysfunction which leads to cognitive dysfunction. This suggests that there may be a direct link between cognitive dysfunction and metabolic changes in diabetes patients. Similarly, this was also evident in this study, that there is an interrelation between cognition and metabolic changes in Type II diabetes patients. Another study by Shauangkun Wang[(11)], where he did a neurochemical correlation of cognitive deterioration in patients

with leukoaraiosis using MR spectroscopy, stated that LA patients show shortfall in broad and peculiar domains, and the results align with the hypothesis that neuronal loss and dysfunction are the prevailing phenomena observed in individuals diagnosed with LA. However, in his study, he didn't find any association between vascular risk factors with the exception of the risk of hypertension. Whereas, in our study, we found that Patients with diabetes has a decrease in NAA/Cho and NAA/Cr ratios and found to have an association with neuropsychological test. Margret Hund-Georgiadis et al.,[18]in their study, showed that single-voxel spectroscopy can be used as an independent diagnostic tool to estimate the severity of cerebral small vessel disease. They observed a decrease in the NAA/Cr and NAA/Cho ratios; however, Cho/Cr did not yield any significance between the groups. In particular, they found a relation between NAA and attention deficits in the case group, and they also did not find any association between the MR score and the extent of white matter lesions or ACEIII. This study clearly shows no significance between Cho/Cr and neuropsychological examination, as well as with LA, as accurately reflected in the findings. In our study, we correlated the lesion volume instead of MR visual scores with the metabolite ratios, and the neuropsychological test did not show any significance. The results of this study give a better insight into T2DM and its association with cognitive decline in leukoaraiosis patients. When the HbA1c value increases, the metabolite ratios decline, clearly stating that this MRS provides additional information. It also proves that type 2 diabetes plays a crucial role in the incidence of white matter hyperintensities, as it can lead to the dysfunction of the microvascular endothelial cells, and an increase in HbA1c levels will also increase the level of oxidative stress and further impair the endothelial[19].Our study has some limitations. Firstly, we failed to compare specific domains in the neuropsychological test; further studies are essential to find the association between the definitive domains and analyze which domains are categorically involved in cognitive decline. Secondly, we placed the region of interest in the periventricular region, as it is impossible to avoid signals from the CSF and some gray matter. It could possibly affect the metabolite ratios. Thirdly, we measured the relative ratios of the spectra instead of absolute quantification. This absolute quantification of the peaks provides further sensitivity to the population and gives much more information about the individual metabolite peak. Finally, we used an intermittent TE of 135ms, and due to that, we couldn't find any involvement of other metabolites in T2 DM patients and their impact on leukoaraiosis. Further study is needed to gain a deeper understanding of whether any other metabolic ratios contribute to changes in the white matter hyperintense region.

Conclusions:

In conclusion, it appears that Type II diabetes mellitus has a strong association with the increased risk of leukoaraiosis, which also affects the cognitive function of the individual. Proper monitoring of the blood glucose level and taking this factor earnestly are essential for controlling the disease progression. In addition, this study also found that magnetic resonance spectroscopy is a potential biochemical marker compared to structural MRI for monitoring cognitive impairment in patients with leukoaraiosis.

Declaration:

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Conflicts of Interest: No potential conflict of interest relevant to this article was reported
Ethical approval: Ethical approval obtained from Institutional Ethical Committee

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