

Original article:

Correlation of dyslipidemia and other clinical factors with cognitive function in non-elderly diabetic type 1 patients

Dr Rashmi Gupta,¹ Dr Deepak Kumar², Dr VB Singh³, Dr.Abhishek Kawatra⁴ Saranshi Singh⁵

¹Associate Professor, PSM JLNMC,

²Assistant Professor, Medicine, PDU, MC Churu

³Sr Professor, Medicine, JLNMC

⁴Professor PSM, SP MC, Bikaner,

⁵Student, RUHS CMS, Jaipur

Corresponding Author: Dr Deepak Kumar, Assistant Professor, Medicine, PDU Medical College, Churu



CC BY 4.0

Abstract

Introduction: Type 1 diabetes is associated with altered brain function, a complication referred to as “Diabetic encephalopathy”. Insulin resistance is associated with a characteristic lipoprotein profile.

Aim : to assess the relation between their metabolic profile and cognitive functioning in Type 1 DM.

Material and Methods: The present study was conducted in the Department of Medicine, S.P. Medical College and PBM group of Hospitals, Bikaner during the study period from January 2015 to December 2015.

Observation: it was seen that duration of disease played a significant impact on the cognitive functioning of the patients. Hyperglycemia played a significant impact on cognitive functioning of as diabetics hypercholesterolemia was more in type 1 diabetics. Raised TC, TG, LDL and VLDL emerged as a risk factor for the development of MCI. HDL although a protective cholesterol didn't seem to have any impact on cognitive functioning and thus future studies are indicated to determine its impact on MCI.

On comparison of various affected domains of cognitive functioning, it was observed that type 1 diabetics had cognitive impairments. NC also emerged as a simple bedside indicator of cognitive impairments as most diabetics that had MCI also had higher NC values.

Keywords : type 1 diabetics, Hyperglycemia, cognitive functioning, metabolic profile

INTRODUCTION

The worldwide prevalence of diabetes has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013.¹ In India, about 50.9 million people suffer from diabetes, and this figure is likely to go up to 80 million by 2025, making it the “Diabetes Capital of the world”.² Insulin resistance is associated with a characteristic lipoprotein profile that includes a high very-low-density lipoprotein (VLDL), a low high-density lipoprotein (HDL), and small, dense LDL. Both low HDL and small, dense LDL are each independent

risk factors for macrovascular disease. Upper-body fat distribution has long been recognized as related to increased cardiovascular disease risk, and neck skinfold or neck circumference (NC)^{3,4} has been used as an index for such an adverse risk profile. Free fatty acid release from upper-body subcutaneous fat was reported to be larger than that from lower-body subcutaneous fat.⁵ Although obesity results in metabolic abnormalities, upper body obesity is more strongly associated with glucose intolerance, hyperinsulinemia, diabetes, hypertriglyceridemia, and gout than lower body obesity. Type 1 diabetes is associated with altered brain function, a complication referred to as “Diabetic encephalopathy”. Previous studies have shown that patients with either type of diabetes show mild to moderate impairments on a variety of neuropsychological tests. Furthermore, changes on brain MRI have been reported, including both cortical and subcortical atrophy and white-matter abnormalities. Diabetes is also associated with a higher prevalence of mood disorders.⁶

Much research has been done on cognitive dysfunction in patients with type 1 DM. In most patients, cognitive impairment consists of mental slowing. In patients with type 1 DM, deficits in speed of information processing, psychomotor efficiency, attention, mental flexibility, and visual perception seem to be present. Severe hypoglycemic episodes may contribute to cognitive dysfunction in the young; however, as patients age episodes seem to have less of an influence. Finally, improved diabetes control and decreased diabetic complications seem to be associated with less cognitive dysfunction, although this association is clearer in patients with type 2 diabetes than with type 1 diabetes. The evidence that risk factors that occur more frequently in people with diabetes are associated with cognitive impairment is limited, mainly because very few of these risk factors have been investigated in any depth. The evidence that is currently available points to a role for poor glycemic control, hypoglycemia, macro and microvascular disease, inflammation, and depression as potential risk factors for cognitive impairment in people with diabetes. However, the causality in these relationships is less clear. The roles of dyslipidemia, as putative risk factors are yet undetermined and require further investigation. In the present study, we sought to investigate the association of dyslipidemia and other clinical factors with cognitive function in non-elderly diabetic type 1 patients.

MATERIALS AND METHODS

This cross-sectional study was conducted from 1st January 2015 to 31st December 2015 in S.P. Medical College & Associated Group of P.B.M. Hospitals, Bikaner includes 98 non-elderly patients with diabetes attending medical outdoor and those admitted in the hospital. All patients are subjected to detailed clinical examination and relevant investigations. The study was carried out in accordance with the declaration of Helsinki (2000) of the World Medical Association and approved by the local medical ethics committee. Informed consent was obtained from all participants. The selected patients were briefed about the nature of the study and a written informed consent was obtained. Patients aged 15-60 years of age, Patients who are either known or recently diagnosed to have as diabetes. (according to ADA 2013 guidelines) were included. Patients who are seriously ill, who were on long- term corticosteroid therapy, Patients with a thyroid disorder. patients with cerebrovascular accidents, Patients who are known case of hypertension or recently diagnosed as hypertensive, Patients with spine deformities, Pregnant females/lactating Females., Patients on drugs like Benzodiazepines, opiates, tricyclic antidepressants, corticosteroids, and anticonvulsants in previous 6 months, with chronic diseases like chronic liver disease and chronic kidney

disease, History of auditory disorders and psychological disturbances, which might interfere with the MoCA test, History of alcohol or any drug abuse.

All the subjects included in the study were interviewed regarding age, gender, education level, duration and type of diabetes, history of smoking, history of alcohol abuse, sleep status (sleepless or not), history of hypertension, and dyslipidemia using a predesigned and pretested performance. Medication history regarding the use of lipid-lowering medications, antidiabetes medications, antihypertensive medications, antiplatelet medications or any drug causing cognitive impairment will be recorded through questionnaires and pill bottle reviews.

Data collection

Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma. A waist circumference of >102 cm in males and > 88 cm in females were considered abnormal. NC was measured midway of the neck between the mid-cervical spine and mid-anterior neck with subject standing. NC of ≥ 37 cm in males and ≥ 34 cm in females was considered abnormal. Fasting blood samples were drawn for investigations such as FBS and lipid profile (total cholesterol, triglycerides, HDL, LDL and VLDL). The fasting blood glucose and lipid profile, Thyroid function test (T_3 , T_4 , and TSH levels) are measured.

For assessment of cognitive functions; we used Montreal cognitive assessment score (MoCA version 7.1) which was designed as a rapid screening instrument for MCI. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation. It has been tested in 14 different languages, age ranging from as young as 49 in two reports to old (85+) with a variety of education levels. Time to administer the MoCA is approximately 10 minutes. The total possible score is 30 points; a score of 26 or above is considered normal. To better adjust the MoCA for lower educated individuals, 2 points should be added to the total MoCA score for those with 4-9 years of education and 1 point for 10-12 years of education (Johns et al., 2010). The MoCA detected MCI with 90%-96% range sensitivity and specificity of 87% with 95% confidence interval.⁷⁶ A thorough drug history is taken to rule out any drug-induced cognitive impairment.

Statistical Analysis:

The data obtained was tabulated on Microsoft Excel spreadsheet. Categorical data was expressed as rates, ratios, and percentages. Continuous data was expressed as mean \pm standard deviation (SD) Pearson's Correlation coefficient (r) was used to assess the correlation between NC and components of metabolic syndrome. SPSS 18 trial version software was used for analysis.

OBSERVATIONS

On analysis, it shows that demographic value of HbA_{1c}, TG, HDL, VLDL and NC were almost similar in both type 1 diabetics; duration of type 1 (14.4 \pm 28.19yrs.) diabetics Similarly, BMI was type 1 diabetics (21.37 \pm 3.11kg/m²). hypercholesteremia (295.25 \pm 61.29mg/dl)

out of total 98 diabetics, the mean age of diabetics with MCI (70 cases) was 29.00 \pm 8.84yrs and in diabetics without MCI (N=28) was 27.75 \pm 9.45 yrs. (p>0.05). In the study having 54 and 44 male and females respectively. Out of 54 males; 37 and 17 diabetics were with MCI (MoCA score <26) and without MCI (MoCA score \geq 26) respectively while out of total 44 females, 33 females had MCI (MoCA score <26) while 11 females had no MCI (MoCA

score \geq 26). $P=0.480$ NS. Out of total 57 rural area diabetics, 43 had MCI (MoCA score <26) while 14 diabetics did not have MCI (MoCA score ≥ 26), while out of 41 urban area diabetics, 27 and 14 diabetics had their MoCA score <26 and ≥ 26 respectively. ($p>0.05$).

The mean duration of diabetes in type 1 diabetics with MCI was significantly higher 14.42 ± 8.19 years and in diabetics without MCI, it was 10.33 ± 9.01 years. ($P=0.032$ S)

On analysis of general physical examination parameters, it was seen that mean systolic BP for the diabetics with and without MCI were 130.00 ± 9.44 mm Hg and 123.14 ± 9.49 mm Hg respectively and this difference was statistically insignificant ($p>0.05$). Similarly, other physical parameters such as height, weight, and diastolic BP were also having statistically non-significant correlations ($p>0.05$).

Mean BMI of type 1 diabetics with MCI was 21.37 ± 3.11 kg/m² whereas in diabetics without MCI, mean BMI was 20.64 ± 4.71 kg/m². On application of student 't' test, this difference was found statistically insignificant ($p>0.05$). Mean HbA_{1c} of type 1 diabetics with MCI was $8.67\pm 2.20\%$ and $7.07\pm 0.73\%$ in diabetics without MCI. On application of student 't' test, this difference was found to be highly statistically significant ($p<0.001$). Mean total cholesterol in type 1 diabetics with MCI was 295.25 ± 61.29 mg/dl while in diabetics without MCI, mean total cholesterol was 258.28 ± 62.20 mg/dl. On application of the student 't' test, this difference was found to be statistically significant ($p=0.009$ S) Mean triglyceride level in type 1 diabetics with MCI was 268.51 ± 59.37 mg/dl while in diabetics without MCI, mean triglyceride was 242.46 ± 55.65 mg/dl and this difference were found statistically significant ($p<0.05$). Mean HDL cholesterol level in type 1 diabetics with MCI was 38.30 ± 6.16 mg/dl while in diabetics without MCI, mean HDL cholesterol was 40.45 ± 5.59 mg/dl. On application of student 't' test this difference was found statistically insignificant ($p>0.05$). Mean LDL cholesterol in type 1 diabetics with MCI was 203.24 ± 61.51 mg/dl while in diabetics without MCI, mean total LDL cholesterol was 169.33 ± 62.83 mg/dl and on the application of the student 't' test, this difference was found statistically significant ($p<0.05$). Mean VLDL cholesterol in type 1 diabetics with MCI was 53.70 ± 11.87 mg/dl and in diabetics without MCI, mean VLDL cholesterol was 48.49 ± 11.13 mg/dl. On application of student t-test, this difference was found statistically significant ($p<0.05$). Mean NC in type 1 diabetics with MCI was 36.33 ± 3.49 cm while in diabetics without MCI, mean NC was 34.26 ± 5.15 cm. On application of student 't' test this difference was found statistically significant ($p<0.05$). On comparison of various component of MoCA test in type 1 diabetics with dyslipidemia; it was seen that most significant parameter that was affected was attention ($p<0.001$), followed by delayed recall /memory, naming and abstraction ($p<0.05$). Visuospatial functioning and orientation although affected however the impact were not statistically significant ($p>0.05$).

Table No 1 Mild cognitive impairment (MCI) with demographic profile

| | Mild cognitive impairment (MCI) | | | | P Value LS |
|------------------------------|---------------------------------|------|------------------------|------|---------------|
| | Present (MoCA score<26) | | Absent (MoCA score≥26) | | |
| | No. | % | No. | % | |
| Total | 70 | 100 | 28 | 100 | |
| Age | 29.00□8.84 | | 27.75□9.45 | | 0.537 |
| Female | 33 | 47.1 | 11 | 39.3 | 0.48 |
| Male | 37 | 52.9 | 17 | 60.7 | |
| Rural | 43 | 61.4 | 14 | 50 | 0.300NS |
| Urban | 27 | 38.6 | 14 | 50 | |
| Duration of Diabetes (years) | 14.42□8.19 | | 10.33□9.01 | | 0.032 |

Table No 2 Correlation of MCI in type 1 diabetics with general physical parameters

| General Physical Examination | Mild cognitive impairment (MCI) | | | | P Value LS | p |
|------------------------------|---------------------------------|-------|------------------------|------|---------------|--------|
| | Present (MoCA score<26) | | Absent (MoCA score≥26) | | | |
| | Mean | SD | Mean | SD | | |
| Height(cm) | 159.65 | 9.8 | 160.17 | 9.24 | 0.81 | 0.81 |
| Weight(kg) | 54.82 | 10.31 | 51.21 | 4.99 | 0.08 | 0.08 |
| Systolic BP | 130 | 9.44 | 123.14 | 9.49 | 0.002 | 0.002 |
| Diastolic BP | 78.31 | 5.45 | 77.78 | 5.47 | 0.666 | 0.666 |
| BMI (kg/m ²) | 21.37□3.11 | | 20.64□4.71 | | 0.372 | 0.372 |
| HbA _{1c} (%) | 8.67□2.20 | | 7.07□0.73 | | <0.001 | <0.001 |
| TG (mg/dl) | 268.51□59.37 | | 242.46□55.65 | | 0.049 | 0.049 |
| HDL Cholesterol (mg/dl) | 38.30□6.16 | | 40.45□5.59 | | 0.113 | 0.113 |
| LDL Cholesterol (mg/dl) | 203.24□61.51 | | 169.33□62.83 | | 0.016 | 0.016 |
| VLDL Cholesterol (mg/dl) | 53.70□11.87 | | 48.49□11.13 | | 0.049 | 0.049 |
| Neck Circumference | 36.33□3.49 | | 34.26□5.15 | | 0.023 | 0.023 |

Table No 3 Correlation coefficient of different components of MoCA test with components of lipid profile in relation to type 1 diabetics

| MoCA Test Components | | TC | TG | HDL | LDL | VLDL |
|-------------------------|---------------------|--------|--------|-------|--------|--------|
| Visuospatial/ Executive | Pearson Correlation | -0.061 | 0.090 | 0.137 | -0.081 | 0.090 |
| | Sig. (2-tailed) | 0.553 | 0.376 | 0.179 | 0.427 | 0.376 |
| Naming | Pearson Correlation | -0.265 | -0.201 | 0.066 | -0.206 | -0.201 |
| | Sig. (2-tailed) | 0.008 | 0.048 | 0.517 | 0.042 | 0.048 |
| Attention | Pearson Correlation | -0.417 | -0.059 | 0.120 | -0.391 | -0.059 |
| | Sig. (2-tailed) | <0.001 | 0.562 | 0.240 | <0.001 | 0.562 |
| Language | Pearson Correlation | -0.007 | 0.155 | 0.084 | -0.030 | 0.155 |
| | Sig. (2-tailed) | 0.948 | 0.127 | 0.409 | 0.770 | 0.127 |
| Abstraction | Pearson Correlation | -0.202 | 0.017 | 0.073 | -0.189 | 0.017 |
| | Sig. (2-tailed) | 0.047 | 0.868 | 0.473 | 0.063 | 0.868 |
| Delayed recall/ memory | Pearson Correlation | -0.262 | -0.097 | 0.139 | -0.245 | -0.097 |
| | Sig. (2-tailed) | 0.009 | 0.343 | 0.173 | 0.015 | 0.343 |
| Orientation | Pearson Correlation | -0.103 | -0.139 | 0.063 | -0.115 | 0.139 |
| | Sig. (2-tailed) | 0.314 | 0.173 | 0.541 | 0.261 | 0.173 |

Discussion

It was seen that out of 98 type 1 diabetics, 70 had mild cognitive dysfunction ,short duration of disease before cognitive impairments arise in them (14.42±8.19yrs.) This may be attributed to the fact that these patients often have a long standing hyperglycemia before they are diagnosed such that by the time of diagnosis or initiating treatment they often had developed MCI.

Numerous trial have been conducted till date assessing the cognitive functioning in DM; The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study, a long-term study that followed type 1 diabetics for approximately 18 years, found that a decline in cognitive function, such as motor speed and psychomotor efficiency, was associated with glycemic control level.^{7,8} Our findings are further supported by the fact quoted by Ruis, Carla, et al.⁹ Their study included 183 diabetic patients from a previously established study cohort and 69 control subjects. It was observed that relative to scores for the control group, mean z scores were between 0.01 and 0.2 lower in the diabetic group across all domains, but after adjustment for differences in IQ between patients and control subjects, only memory performance was significantly reduced (mean difference -0.15 [95% CI -0.28 to -0.03]). In our study,it was observed that cognitive impairments appeared in both type of diabetics irrespective of their age and type of DM. Numerous studies have shown appearance of MCI in type 1 diabetics as early as 2 yrs. of age group whereas some remain affected even at late stages of life.^{10,11}

However, Ryan et al showed that diabetic adults 34–65 years of age performed at least as well as their nondiabetic peers on all of our learning and memory measures after taking into account demographic factors that are known to affect cognitive test performance.¹⁰

Gender appeared to have a non-significant impact on the appearance of MCI in type 1 diabetics ($p>0.05$). Most human studies¹² have not distinguished between genders when describing results of neurocognitive testing; however few studies have shown gender to influence neurocognitive function in type 1 diabetics. Skenazy and Bigler¹³ found that type 1 diabetic men had reduced performance on oscillation, strength grip, and somatosensory testing compared with male controls, and the magnitude of this difference was greater than that measured between women with type 1 DM and their gender-matched controls. Similarly, Ryan et al¹⁰ also observed a gender-based difference in MCI as female were better at learning and showed little impairment in that field. However and, therefore, more controlled analysis should be done before any conclusions are drawn.

Residential area had an insignificant impact on MCI in DM diabetics and this is in line with the finding observed by Eze, C. O et al¹⁴ and Kataria, L., et al.¹⁵ Although education and general IQ ability may be better in the urban community however in our study we observed that both communities were equally affected and this confounding factor was reduced to a great extent by employing MoCA test in our study. However, more illustrative and large-scale population studies dedicated to the urban or rural area need to be done before drawing a specific conclusion.

In our study, we observed a statistically significant correlation of MCI with duration of diabetes The mean duration of diabetes in type diabetics with MCI was 14.42 ± 8.19 . This pattern of observation was consistent with the results from the Maastricht Aging Study where it appeared that disease-exposure time played an important role in the development of cognitive decline.¹²⁷ Similar results were obtained by Roberts RO et al¹⁶ and Ruis, Carla, et al.¹⁰ They suggested that long duration of diabetes may be associated with greater cerebral microvascular disease, clinical cerebral infarctions, and subclinical infarctions that may impair cognitive function.

The mean systolic BP of type 1 diabetics with MCI was 130.00 ± 9.44 mm Hg This finding is in line with the specifications suggested by recent studies on the potential benefit of cognitive functioning with intensive BP control.¹⁷ Although hypertension is a known risk factor for cognitive impairment as proved with numerous studies¹⁸ however in diabetics with concomitant hypertension; patient's risk for MCI is raised many-fold and they tend to develop MCI even at lower thresholds of BP. However, most of the type 1 diabetics included in our study were non-elderly hence cerebrovascular disease is very rare (and was often defined as an exclusion criterion), Therefore, in type 1 diabetics, we do not expect that either cerebrovascular disease or hypertension have a substantial contribution to the cognitive impairments.

In our study, Pearson's correlation showed a highly significant positive correlation ($p<0.001$) between HbA_{1c} and cognitive dysfunction in both type 1 diabetics which is consistent with results of different studies published earlier. Biessels et al.¹⁹ showed diabetes-related factors, such as insulin resistance and chronic hyperglycemia to be associated with impaired cognitive function. Complex effects on peptide neurotransmitters may be produced by uncontrolled diabetes.²⁰ Any one of these mechanisms alone may be insufficient, and several of these mechanisms could be additive.

In our study, we reported a high prevalence of dyslipidemia. Reports from the National Health and Nutrition Examination Survey (NHANES) 1999–2000 indicate that 55% of the U.S. general population and 51% of adults aged 20–59 years with diabetes have hypercholesterolemia.²¹ European data indicate a similar prevalence of 51% of type 1 diabetic adults with dyslipidemia in the EURODIAB study.²² Indian study by Sawant, A. M., et al done in 2008 also predicted similar results.²³

In our study we observed a statistically significant correlation of various components of lipid profile such as total cholesterol ($p < 0.05$); triglycerides ($p < 0.05$); LDL ($p < 0.05$) and VLDL ($p < 0.001$) in both type 1 HDL cholesterol failed to show any impact on cognitive impairment of diabetics ($p > 0.05$). Although numerous citations are available to state the impact of dyslipidemia on type 2 DM, our study is first of its type to study the impact on type 1 DM.

Similarly the DCCT/ EDIC study, which was carried out with type 1 diabetics, reported that motor speed and psychomotor efficiency were reduced more in patients with poor glycemic and metabolic control.^{7,8}

Very few studies are available that evaluated the impact of dyslipidemia on cognitive impairment in type 1 diabetics. This may be due the fact that type 1 diabetics tend to be a lesser degree of dyslipidemia. This fact has been established through various studies such as that of Saydah et al.²⁵ the reason that has been suggested for a lesser degree of dyslipidemia in type 1 diabetics being physiological decreased hepatic synthesis of cholesterol. Other possible reasons for less dyslipidemia in type 1 diabetes in this study may include younger age group and more conscious lifestyle changes in patients with type 1 diabetes

Some domains of cognitive functioning were spared ($p > 0.05$) in our study that may be due to heterogeneity of the population selected, limited sample size, and a lesser degree of dyslipidemia²⁶ that was observed in a study population of this area. Hence, a need of further longitudinal study for type 1 diabetics is necessary for better generalizations of results.

Although much insightful research has examined cognitive dysfunction in patients with diabetes, more needs to be understood about the mechanisms and natural history of this complication in order to develop strategies for prevention and treatment. The results of my study suggest that dyslipidemia chiefly raised total cholesterol and triglycerides are associated with poorer cognitive function and a higher risk of AD. Further studies are required to determine the significance and potential public health benefit of this association.

To conclude, this study indicated that even non-elderly diabetics suffer significant cognitive impairments that are associated with poorer metabolic control. Cognitive dysfunction should be listed as one of the many complications of diabetes, along with retinopathy, neuropathy, nephropathy, and cardiovascular disease in the future. Diabetic and dyslipidemic control from an early stage would be useful in preventing the onset of vascular events, as well as cognitive decline.

Bibliography :

1. Longo D.L. Fauci A.S. Harrison's principles of Internal Medicine. 19th edition. Mc Graw Hill; 2015: 2400.
2. <http://www.diabetesfoundationindia.org/about.htm>.

3. Chen G, Liang G, Ou J, et al: Central role for liver X receptor in insulin-mediated activation of Srebp-1c transcription and stimulation of fatty acid synthesis in the liver. *Proc Natl Acad Sci U S A* 2004; 101:11245-11250.
4. Sjöström CD, Hakangard AC, Lissner L, Sjöström L. Body compartment and subcutaneous adipose tissue distribution – risk factor patterns in obese subjects. *Obes Res* 1995;3:9–22.
5. Sjöström CD, Lissner L, Sjöström L. Relationship between changes in body composition and changes in cardiovascular risk factors: the SOS intervention study: Swedish obese subjects. *Obes Res* 1997;5:519–30.
6. Mehrabian S., Raycheva M., Gateva A., Todorova G., Angelova P., Traykova M., Stankova T., Kamenov Z., Traykov L. Cognitive dysfunction profile and arterial stiffness in type 2 diabetes. *J. Neurol. Sci.* 2012;322: 152–156.
7. The Diabetes Control and Complication Trial/Epidemiology of Diabetes Intervention and Complications (DCCT/EDIC) Study Research Group. Long-term effect of diabetes and its treatment on cognitive function. *N Engl J Med* 2007; 356:1842–1852.
8. Jacobson AM, Ryan CM, Cleary PA, et al. Biomedical risk factors for decreased cognitive functioning in type 1 diabetes: an 18-year follow-up of diabetes control and complications trial (DCCT) cohort. *Diabetologia* 2011; 54: 233–236.
9. Ruis, Carla, et al. "Cognition in the early stage of type 2 diabetes." *Diabetes Care* 32.7 (2009): 1261-1265R.
10. Ryan CM & Geckle MO. Circumscribed cognitive dysfunction in middle-aged adults with type 2 diabetes. *Diabetes Care* 2000 ;23, 1486–1493.
11. Northam EA, Anderson PJ, Werther GA, Warne GL, Adler RG, Andrewes D. Neuropsychological complications of IDDM in children 2 years after disease onset. *Diabetes Care* 1998 ;21:379–384.
12. Hung J, Menth L, Thompson MJ, Saner B, Rao KV, Barbosa J: The Minnesota Diabetes Complications Clinical Trial cognitive functions under long-term maximized and standard metabolic controls. *Diabetes Metab* 10:48 – 51, 1984.
13. Skenazy JA, Bigler ED .Neuropsychological findings in DM. *J Clin Psychol.* 1984 .40:246–258.
14. Eze, C. O., et al. The Prevalence of Cognitive Impairment amongst Type 2 DM Patients at Abakaliki South-East Nigeria. *J Diabetes Metab Syndr Disord.* 2015.
15. Kataria, L., et al. Prevalence and Pattern of Cognitive Dysfunction in Type 2 DM. *Int J Med and Appl Sci* .2013: 246-247.
16. Roberts RO, Geda YE, Knopman DS, et al. Association of Duration and Severity of DM With Mild Cognitive Impairment. *Arch Neurol.* 2008;65(8):1066-1073.
17. Godin, Ophélie, et al. Antihypertensive Treatment and Change in Blood Pressure Are Associated With the Progression of White Matter Lesion Volumes The Three-City (3C)–Dijon Magnetic Resonance Imaging Study. *Circulation.* 2011: 266-273.
18. Bruce DG, Davis WA, Casey GP, Starkstein SE, Clarnette RM, Foster JK et al. Predictors of cognitive impairment and dementia in older people with diabetes. *Diabetologia.* 2008; 51:2418.

19. Biessels, G.J., Staekenburg, S., Brunner, E., Brayne, C., & Scheltens P. Risk of dementia in DM: a systematic review. *Lancet Neurology*. 2006;5, 64–74.
20. Havel PJ, Hahn TM, Sindelar DK, Baskin DG, Dallman MF, Weigle DS, Schwartz MW: Effects of streptozotocin-induced diabetes and insulin treatment on the hypothalamic melanocortin system and muscle uncoupling protein 3 expressions in rats. *Diabetes* 49:244 –252, 2000.
21. Imperatore G, Cadwell BL, Geiss L, Saadine JB, Williams DE, Ford ES, Thompson TJ, Venkat Narayan KM, Gregg EW: Thirty-year trends in cardiovascular risk factor levels among US adults with diabetes: National Health and Nutrition Examination Surveys, 1971–2000. *Am J Epidemiol* 160:531–539, 2004.
22. Idzior-Walus B, Mattock MB, Solnica B, Stevens L, Fuller JH: Factors associated with plasma lipids and lipoproteins in type 1 DM: the EURODIAB IDDM Complications Study. *Diabet Med* 2001; 18:786 –796,.
23. Sawant, A. M., et al. Prevalence of dyslipidemia in young adult Indian population. *JAPI* 2008: 99-102.
24. Brands, Augustina MA, et al. The effects of type 1 diabetes on cognitive performance A meta-analysis. *Diabetes care* .2005;28.3 : 726-735.
25. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA* 291:335–342, 2004.
26. Miettinen TA, Gylling H, Tuominen J, Simonen P, Koivisto V. Low synthesis and high absorption of cholesterol characterize type 1 diabetes. *Diabetes Care* 27:53-58, 2004.

Author Declaration: Source of support: Nil, Conflict of interest: Nil

Ethics Committee Approval obtained for this study? YES

Was informed consent obtained from the subjects involved in the study? YES

For any images presented appropriate consent has been obtained from the subjects: YES

Plagiarism Checked: Urkund Software

Author work published under a Creative Commons Attribution 4.0 International License



DOI: 10.36848/IJBAMR/2020/26215.55632