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Research Article

The spectrum of mild cognitive impairment in dyslipidemic non-elderly type 1 diabetics

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ABSTRACT

Background: Diabetics often have reduced performance in numerous domains of cognitive function, a process termed as Diabetic encephalopathy. The exact pathophysiology of cognitive dysfunction in diabetes is not completely understood, but it is likely that hyperglycaemia, vascular disease, hypoglycemia, and insulin resistance play significant roles. Although cognitive dysfunction is quite common in elderly, however, its occurrence in non-elderly diabetics is not much investigated. Aim of the study was to identify the correlation among various components of lipid profile with mild cognitive impairment in non-elderly type 1 diabetics.
Methods: 98 type 1 diabetics were enrolled justifying relevant inclusion &exclusion criteria. Anthropometric indices, biochemical and clinical parameters were measured. MoCA test was employed for the assessment of cognitive dysfunction. Receiver operating characteristic, partial correlation, and logistic regression analyzes were employed for evaluation.
Results: 71.42% of enrolled diabetics had some degree of cognitive dysfunction. Duration of the disease had a significant impact on cognitive functioning ($p=0.032$).Gender, residential area as well as the age of onset of diabetes appeared to have an insignificant impact on cognitive functioning ($p>0.05$). Diabetics with poor glycemic control were more prone to develop MCI ($p<0.001$).On comparison of various component of MoCA test; it was seen that most significant parameter that was affected was attention ($p<0.001$), followed by delayed recall /memory, naming and abstraction ($p<0.05$).
Conclusions: The results of our study suggest that dyslipidemia chiefly raised total cholesterol, triglycerides and LDL is quite common in non-elderly type 1 diabetics and are associated with poorer cognitive function. Cognitive dysfunction should be listed as one of the many complications of diabetes, along with retinopathy, neuropathy, nephropathy, and cardiovascular disease in the future.

Keywords: Mild cognitive impairments, Dementia, Type 1 diabetes, Non elderly diabetics

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. Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035.[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]

Mild cognitive impairment (MCI, also known as incipient dementia, or isolated memory impairment) is a brain function syndrome involving the onset and evolution of cognitive impairments beyond those expected based on

the age and education of the individual, but which are not significant enough to interfere with their daily activities[3]. It is often found to be a transitional stage between normal aging and dementia.

The deleterious effects of diabetes mellitus (DM) on the retinal, renal, cardiovascular, and peripheral nervous systems are widely acknowledged. Less attention has been given to the effect of diabetes on cognitive function. Both type 1 and type 2 DM have been associated with reduced performance on numerous domains of cognitive function, a process often termed as "Diabetic encephalopathy".

The exact pathophysiology of cognitive dysfunction in diabetes is not completely understood, but it is likely that hyperglycemia, vascular disease, hypoglycemia, and insulin resistance play significant roles.

The magnitude of these cognitive deficits is mild to moderate, but it is important to stress the clinical relevance of even mild forms of cognitive dysfunction that might hamper day to day activities since they can be expected to present problems in more demanding situations. A growing group of evidence suggests that diabetes is associated with lower levels of cognitive function and may be a risk factor for the development of MCI and dementia.[4,5] It is reported that a diagnosis of diabetes increased the odds of cognitive decline 1.2 fold and future dementia 1.6 fold.[6]

With cognitive aging as a continuum, people with diabetes have been found to experience accelerated cognitive decline within a dementia-free range of between 20 % and 50 % and recent reports have suggested a role of midlife (rather than late life) diabetes in particular in promoting this cognitive dysfunction.[9,10]

Diabetics are characteristically associated with a 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. The role of dyslipidemia, as putative risk factors is quite undetermined. Past work in other samples of the population has shown inconsistent effects of lipid levels on neurological outcomes.

For example, a recent study by Ruis C et al found no relationship between hyperlipidemia and cognitive function in a cohort of patients with diabetes.[7] A recent examination of the Baltimore Longitudinal Study of Aging data showed a nonlinear relationship between total cholesterol and cognitive functioning. Such findings suggest that the association between lipid levels and neurocognitive outcomes may be more complicated than typically conceptualized.

The current study will examine associations between dyslipidemia and assessments of general health, physical and cognitive function of non-elderly diabetics. Such findings highlight the need for this study to determine the impact of dyslipidemia on cognitive function in diabetics. In the present study, we sought to investigate the association of dyslipidemia and other clinical factors with cognitive function in non-elderly type 1 diabetics.

METHODS

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, anti-diabetes medications, antihypertensive medications, antiplatelet medications or any drug causing cognitive impairment will be recorded through questionnaires and pill bottle reviews.

Patient's aged 15-60 years of age, who are either known or recently diagnosed to have as type 1 diabetes (According to ADA 2013 guidelines) and were willing to participate were included in the study.

Patients who were seriously ill, on long- term corticosteroid therapy, with a thyroid disorder, had suffered cerebrovascular accidents, known case of hypertension or recently diagnosed as hypertensive, having spine deformities, pregnant females/lactating females, on drugs like Benzodiazepines, opiates, tricyclic antidepressants, corticosteroids, and anticonvulsants in previous 6 months, suffering with chronic diseases like chronic liver disease and chronic kidney disease or having history of auditory disorders and psychological disturbances, which might interfere with the MoCA test etc. were excluded from the study.

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, visuoconstructional 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.

Ethical clearance

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.

Statistical analysis

The data obtained was tabulated on Microsoft Excel spread sheet. Categorical data was expressed as rates, ratios, and percentages. Continuous data was expressed as mean±standard deviation (SD) Pearson's Correlation coefficient (r) was used to assess the correlation between lipid profile and various domains of cognitive impairment. SPSS 10 trial version software was used for analysis.

RESULTS

Ninety-eight type 1 diabetics were included in the study and various components of lipid profile and cognitive function were evaluated.

Table 1: Demographic details of type 1 diabetics with and without MCI

Characteristics	Mild cognitive impairment	
	Present (MoCA score<26)	Absent (MoCA score≥26)
Total diabetics (n=98)	70(71.42%)	28(28.57%)
Gender (Male; Female)	37;33	17;11
Residence (Urban; Rural)	27;43	14;14
Mean age (years)	29.00±8.84	27.75±9.45
Duration of disease (years)	14.42±8.19	10.33±9.01
Height (cm)	159.65±9.80	160.17±9.24
Weight (Kg)	54.82±10.31	51.21±4.99
BMI (Kg/m^2)	21.37±3.11	20.64±4.71
Systolic BP (mm Hg)	127.42±10.74	123.14±9.49
Diastolic BP (mm Hg)	78.31±5.45	77.78±5.47
HbA_1C (%)	8.67±2.20	7.07±0.73

Table 2: Spectrum of dyslipidemia in type 1 diabetics with and without MCI.

Characteristics*	Mild cognitive impairment		p value
	Present (MoCA score<26)	Absent (MoCA score≥26)	
TC(mg/dl)	295.25±61.29	258.28±62.20	0.009
TG(mg/dl)	268.51±59.37	242.46±55.65	<0.001
LDL(mg/dl)	203.24±61.51	169.33±62.83	0.016
VLDL(mg/dl)	53.70±11.87	48.49±11.13	0.049
HDL l(mg/dl)	38.30±6.16	40.45±5.59	0.113

*TC: total cholesterol; TG: triglycerides; LDL: low density lipoprotein; VLDL: very low density lipoprotein; HDL: high density lipoprotein.

Out of 98 diabetics included in the study 70 (71.42%) had some degree of cognitive impairments. Among these 70 diabetics 37(52.9%) were male and 33(47.1%) were females.

The mean duration of diabetes in cognitively impaired diabetics was found to be 14.42±8.19 years. Mean HbA_1C of diabetics with MCI was 8.67±2.20% in contrast to 7.07±0.73% of those without MCI. Other demographic details are mentioned in Table 1.

Table 2 highlights the spectrum of dyslipidemia in diabetics. It was seen that although dyslipidemia was present in all diabetics included in the study, however, those having MCI tend to have greater metabolic derangements.

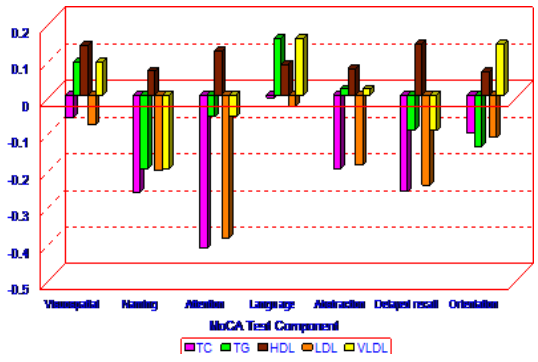

Figure 1: Correlation coefficient of different components of MoCA score with components of lipid profile in relation to DM type-1.

Table 3 (and graph 1) describes correlation coefficient of different components of MoCA test with various components of the lipid profile of diabetics included in the study.it was seen that most significant parameter that was affected was attention followed by delayed recall/memory, naming and abstraction.

Table 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

Given the prevalence of dyslipidemia in diabetes, it appears likely that components of lipid profile may also contribute to the cognitive decline observed in diabetics. Specifically, recent work suggests that lipid levels may be especially important contributors to cognitive function in persons with diabetes, but not many studies have studied the impact of dyslipidemia in non-elderly adults.[8,9]

Hence, this study was undertaken at Department of medicine, S P medical college Bikaner from January 2015 to December 2015 and included 98 type 1 diabetics attending medical outdoor and those admitted to hospital.

Our study showed that 71.4% (70 out of 98) of the type 1 diabetics had MCI. This high prevalence of MCI may be attributed to numerous factors such as early onset of disease, more incidences of glycemic fluctuations due to the employment of insulin therapy and underestimated dyslipidemia prevalent in these patients. Gender, residential area and age of onset of diabetes had a non-significant impact on the appearance of MCI in our study. Although, most human studies have not distinguished between genders when describing results of neurocognitive testing; however few studies (Skenazy JA et al) have shown gender to influence neurocognitive function in type 1 diabetic.[10] Although education appeared to have an impact on cognitive functioning but this confounding factor was reduced to a great extent by employing MoCA test in our study.

In our study, we reported a high prevalence of dyslipidemia among the subjects included in the study. This is in line with the results of recent studies (NHANES and EURODIAB) that indicated high incidences of dyslipidemia in young and non-elderly adults An Indian study by Sawant AM et al also predicted similar results.[11-14] Thus, although dyslipidemia tends to occur more commonly in type 2 diabetes, type 1 diabetics are not spared from these metabolic derangements and hence more stringent control are indicated irrespective of the age and type of diabetes.

On analysis of various components of cognitive functioning, it was seen that most significant parameters that were affected was attention ($p<0.001$). Delayed recall /memory, naming and abstraction were also affected although not to the same extent as that of naming ($p<0.05$).Visuospatial functioning and orientation were also affected however their impact was not statistically significant ($p>0.05$).

Brands, Augustina MA, et al conducted a meta-analysis of a total of 33 studies and concluded that type 1 diabetics tend to have a slowing of mental speed and a diminished mental flexibility, whereas learning and memory are spared.[15] 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.[16,17] 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 SH et al The reason that has been suggested for a lesser degree of dyslipidemia in type 1 diabetics being physiological decreased hepatic synthesis of cholesterol.[18,19] 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 dyslipidemia 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.[18]

There are few limitations in our study. Firstly, it was conducted on small sample size, which may not be a true representative of the whole population. As we know, because of small sample size the entire spectrum of dyslipidemia as well as cognitive impairments may not be detected. Secondly, all the participants were from the same health examination center and a selection bias could not be excluded.

CONCLUSION

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. These findings provide insight into the pathophysiology of different types of cognitive impairment and possible therapeutic avenues. Diabetic and dyslipidemia management from an early stage would be useful in preventing the onset of vascular events, as well as cognitive decline.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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