Original research article

Correlation among various components of lipid profile with mild cognitive impairment in non-elderly adults with type 2DM

Dr V.B Singh[1], Dr Rashmi Gupta[2] , Dr Deepak kumar[3] ,Dr Abhishek Kawatra[4], Saranshi[5]

[1]SR Professor, Department of Medicine; [2]Associate Professor, Department of community medicine, JLN MC Ajmer, Rajasthan , [3]Assistant Professor, Medicine PDU MC Churu, [4] Professor Department of community Medicine SP MC Bikaner5. MBBS Student RUHS MC Jaipur

Corresponding Author: Dr Rashmi Gupta, Associate Professor , Department of Community Medicine , JLN Medical College, Ajmer

Abstract:

Background: The prevalence of DM is rapidly increasing and it has become a major health problem in recent years in the world. 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. In the present study, we sought to investigate the association of dyslipidemia and other clinical factors with cognitive function in non-elderly diabetic patients**.**

Methods: The present study is a cross-sectional study and includes 214 non-elderly patients with type 2 diabetes attending medical outdoor and those admitted in the hospital. Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma. A thorough clinical examination was conducted and the findings were also recorded. 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.

Results: Out of 214 type 2 diabetics, 178 had MCI. Type 2 diabetics were more prone to develop cognitive impairments. Hyperglycemia played a significant impact on cognitive functioning of as diabetics with poor glycemic control were more prone to develop MCI. 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. Conclusion: This study indicated that even non-elderly diabetics suffer significant cognitive impairments that are associated with poorer metabolic control.

Key words: Non-elderly type 2 diabetics, lipid profile, cognitive impairment

INTRODUCTION

The worldwide prevalence of diabetes has risen dramatically over the past two decades. In India, about 50.9 million people suffer from diabetes, and this figure is likely to go up to 80 million by 2025, making India the "Diabetes Capital of the world".[1] Insulin resistance is associated with a characteristic lipoprotein profile .Both low HDL and small, dense LDL are each independent risk factors for macrovascular disease. This profile arises as a direct result of increased net free fatty acid (FFA) release by insulin-resistant adipocytes. Increased FFA flux into hepatocytes stimulates VLDL secretion. In the presence of cholesterol ester transfer protein, excess VLDL transfers significant amounts of triglyceride to both HDL and LDL while depleting HDL and LDL of cholesterol ester.

Type 2 diabetics are 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. The pathogenesis of diabetic encephalopathy is likely to be a multifactorial process that involves vascular disturbances. 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.[2,3] It is reported that a diagnosis of diabetes increased the odds of cognitive decline 1.2 fold and future dementia 1.6fold.[4]

In most patients, cognitive impairment consists of mental slowing. This is similar to the reduction of mental efforts that occurs during normal aging, except that in patients with DM, the onset of cognitive downfall is seen at a younger age. 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.

 In patients with type 2 DM, an increase in memory deficits, a reduction in psychomotor speed, and reduced frontal lobe/executive function have been identified. 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 clear in patients with type 2 diabetes . However, in view of the greater risk of cognitive impairment affecting diabetic people and the potential differences in underlying mechanisms between people with diabetes and the general population, more information that is specific to diabetic populations is required, particularly in non-elderly adults. 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 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 type 2 diabetic patients.

Methods:

This cross-sectional study was conducted from 1st January 2015 to 31st December 2015 at S.P. Medical College & Associated Group of P.B.M. Hospitals, Bikaner that included 312 non-elderly patients with diabetes attending medical outdoor and those admitted in the hospital. All patients were 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 hospital+ medical ethics committee. Informed consent was obtained from all participants. 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 were seriously ill, were on long- term corticosteroid therapy, with thyroid disorder, patients with cerebrovascular accidents, Patients who are known case of hypertension or recently diagnosed as hypertensive, patients with spine deformities, pregnant /lactating Females, patients on drugs like Benzodiazepines, opiates, tricyclic antidepressants, corticosteroids, and anticonvulsants in previous 6 months, patients 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, patients who are not co-operative were excluded.

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 were recorded through questionnaires and pill bottle reviews.

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. 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.[5]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 ± 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.

Results:

Out of total 214 type 2 diabetics, 178 patients had some degree of mild cognitive impairment. Among these 178 patients, 94 were male whereas 84 were females. The mean age of diabetics with MCI was 52.21±5.90yrs and in diabetics without MCI, it was 51.75±4.81yrs (p>0.05).Out of total 74 rural area diabetics, 63 had their MoCA score <26 while 11 diabetics had their MoCA score ≥26, while out of 140 urban area diabetics, 115 and 25 diabetics had their MoCA score <26 and ≥26 respectively. (p>0.05). The mean duration of diabetes in diabetics with MCI was significantly higher 8.42±5.56years and in diabetics without MCI, it was 6.32±3.85years.other demographic details are mentioned in table 1.

Table 2 highlights the general variability of mild cognitive impairment with vital parameters of the patients. It was noted that mean systolic BP for diabetics with and without MCI were 130.59±9.90mm Hg and 125.83±10.45mm Hg respectively and this difference was statistically significant (p<0.05). Similarly, mean weight of the diabetics with and without MCI were 71.02±15.08 and 59.28±10.29 kg respectively and this was highly statistically significant (p<0.001). Other physical parameters were having non-significant correlations. Mean HbA$_1$C in diabetics with MCI was 8.46±1.34% and in diabetics without MCI mean HbA$_1$C was 7.49±0.71%. (p<0.001) and the difference was also statistically significant.

Table 3 highlight the variability of lipid profile with mild cognitive impairments. It was seen that mild cognitive impairments were present in most of diabetics, however more dyslipidemic tend to have greter degree of cognitive impairments.

Table 4 demonstrates the impact of dyslipidemia on various components of MoCA test. It was seen that in type 2 diabetics significant impairments were seen in all domains of cognitive functioning. The most significant parameter that were affected was naming, attention and language (P<0.001) whereas abstraction, delayed recall, orientation and visuospatial functioning were impaired in a statistically significant manner (p<0.05).

Table No 1

Mild cognitive impairment (MCI) with Demographic Profile

		Mild cognitive impairment (MCI)				Total		P Value LS
		Present (MoCA score<26)		Absent (MoCA score≥26)				
		No.	%	No.	%	No.	%	
	Total	178	100	36	100	214	100	
Age groups	≤20	0	-	0	-	0	-	
	21-40	7	3.9	0	-	7	3.3	
	>40	171	96.1	36	100	207	96.7	
	Mean□SD	52.21□5.90		51.75□4.81				0.659
Gender	Female	84	47.2	19	52.8	103	48.1	0.334
	Male	94	52.8	17	47.2	111	51.9	
Residential Area	Rural	63	35.4	11	30.6	74	34.6	
	Urban	115	64.6	25	69.4	140	65.4	0.578
Duration of Diabetes (years)	≤5	55	30.9	14	38.9	69	32.2	
	10-Jun	70	39.3	17	47.2	87	40.7	
	15-Nov	31	17.4	4	11.1	35	16.4	
	>15	22	12.4	1	2.8	23	10.7	
	Mean□SD	8.42□5.56		6.32□3.85				0.032

Table No2

Mild cognitive impairment (MCI) with vital Parameters

	General Physical Examination	Mild cognitive impairment (MCI)				P value LS
		Present (MoCA score<26)		Absent (MoCA score≥26)		
		Mean	SD	Mean	SD	
Anthropometry	Height(cm)	159.97	6.77	160.55	7.53	0.648
	Weight(kg)	71.02	15.08	59.28	10.29	<0.001
Blood presssure	Systolic BP	130.59	9.9	125.83	10.45	0.01
	Diastolic BP	79.41	6.91	78.66	6.28	0.548
BMI (kg/m^2)	<18.50	3	1.7	2	5.6	<0.001
	18.50-24.99	71	39.9	30	83.3	
	25.00-29.99	43	24.2	2	5.6	
	≥30	61	34.3	2	5.6	
	Total	178	100	36	100	
	Mean□SD	27.66□5.77		22.80□4.56		
HbA$_1$C (%)	<7	16	9	8	22.2	<0.001S
	7 to 8	63	35.4	23	63.9	
	>8	99	55.6	5	13.9	
	Total	178	100	36	100	
	Mean□SD	8.46□1.34		7.49□0.71		

Table No3

Mild cognitive impairment (MCI) with lipid profile

		Mild cognitive impairment (MCI)				Total		
		Present (MoCA score<26)		Absent (MoCA score≥26)				
		No.	%	No.	%	No.	%	
TC (mg/dl)	<200	49	27.5	19	52.8	68	31.8	<0.001
	>200	129	72.5	17	47.2	146	68.2	
TG (mg/dl)	<150	9	5.1	7	19.4	16	7.5	<0.001
	>150	169	94.9	29	80.6	198	92.5	
	Mean□SD	268.12□65.16		216.38□69.49				
HDL Cholesterol (mg/dl)	≤50 female	84	47.2	17	47.2	101	47.2	>0.05NS
	>50 female	0	-	2	5.6	2	0.9	
	<40 male	58	32.6	8	22.2	66	30.8	0.087NS
	>40 male	36	20.2	9	25	45	21	
	Mean□SD	38.24□5.48		39.78□6.65				0.141NS
LDL Cholesterol (mg/dl)	<70	12	6.7	5	13.9	17	7.9	0.007
	70-100	29	16.3	5	13.9	34	15.9	
	>100	137	77	26	72.2	163	76.2	
	Mean□SD	148.26□64.06		117.84□43.46				
VLDL Cholesterol (mg/dl)	<40	26	14.6	17	47.2	43	20.1	<0.001
	>40	152	85.4	19	52.8	171	79.9	
	Mean□SD	53.62□13.03		43.28□13.89				

Table no 4

Correlation coefficient of different components of MoCA test with components of lipid profile in relation to type 2 diabetics

MoCA Test Components		TC	TG	HDL	LDL	VLDL
Visuospatial/ Executive	Pearson Correlation	-0.298	-0.158	0.053	-0.280	-0.158
	Sig. (2-tailed)	<0.001	0.021	0.443	<0.001	0.021
Naming	Pearson Correlation	-0.310	-0.230	0.046	-0.275	-0.230
	Sig. (2-tailed)	<0.001	0.001	0.499	<0.001	0.001
Attention	Pearson Correlation	-0.258	-0.260	0.173	-0.227	-0.260
	Sig. (2-tailed)	<0.001	0.000	0.011	0.001	<0.001
Language	Pearson Correlation	-0.237	-0.286	0.091	-0.192	-0.286
	Sig. (2-tailed)	<0.001	0.000	0.187	0.005	<0.001
Abstraction	Pearson Correlation	-0.245	-0.162	-0.114	-0.208	-0.162
	Sig. (2-tailed)	<0.001	0.018	0.095	0.002	0.018
Delayed recall/ memory	Pearson Correlation	-0.400	-0.309	0.142	-0.360	-0.309
	Sig. (2-tailed)	<0.001	0.000	0.038	<0.001	<0.001
Orientation	Pearson Correlation	-0.268	-0.001	0.020	-0.280	-0.001
	Sig. (2-tailed)	<0.001	0.984	0.775	<0.001	0.984

Discussion:

 Cognitive dysfunction in diabetics was first noted in 1922, when diabetics with diabetes, who were "free from acidosis but usually not sugar-free," were noted to have impaired memory and attention on cognitive testing compared with controls .[6] Action to Control Cardiovascular Risk in Diabetes-Memory in Diabetes (ACCORD-MIND) trial,[7] whose aim was intensive glycemic control in type 2 diabetics, even observed a decline in cognitive function over time. Given the prevalence of dyslipidemia in diabetics, it appears likely that even degree of dyslipidemia may also contribute to cognitive impairments. Hence, this study was undertaken at Department of Medicine, S.P. Medical College and PBM group of Hospitals and Research Centre, Bikaner from 1st January 2015 to 31st December 2015. This study was a cross-sectional study and includes 214 non-elderly diabetics attending medical outdoor and those admitted in the hospital. In this study, out of 214 type 2 diabetics, 178 had MCI. It was seen that type 2 diabetics (8.42±5.56yrs.) had a short duration of disease before cognitive impairments arise in them. 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.

Our findings are further supported by the fact quoted by   Ruis, Carla, et al.[8] 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]). This study shows that modest cognitive decrements are already present at the early stage of type 2 diabetics.

It was evident that a higher prevalence of MCI in type 2 diabetics (178 out of 214). This can be explained due to the fact that higher number of risk factors presence such as obesity, undiagnosed long standing hyperglycemia and a greater degree of dyslipidemia at the time of diagnosis. Moreover, most type 2 diabetics often have some micro or macrovascular complications at the time of diagnosis and are also at increased risk of developing dementia chiefly Alzheimer's that may play as a confounding factor that cannot be nullified in my study and may be a thread for future studies. It was observed that cognitive impairments appeared in diabetics irrespective of their age and type of DM. However, Ryan et al showed[9] 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.

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 al[10] and Kataria, L., et al.[11] 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.

In our study, we observed a statistically significant correlation of MCI with duration of diabetes The mean duration of diabetes in type 2 diabetics with MCI was 8.42±5.56 years 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.[12]Similar results were obtained by Roberts RO et al[13] and Ruis, Carla, et al.[8] 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. It was also seen that lesser mean duration of type 2 DM was associated with MCI can be explained as long-standing undiagnosed hyperglycemia is quite common in type 2 diabetics and during this interval of incipient diabetes, hyperglycemia causes oxidative stress and glycation of important functional and structural proteins, [14]which can have a direct detrimental effect on brain cells and the microcirculation in the brain. Thus considering that cognitive decrements can be found in the early stages of type 2 diabetes, this finding may have implications for diabetes education and self-management behavior in diabetics.

The mean systolic BP of type 2 diabetics with MCI was 130.59±9.90 mm Hg this has a significant impact on cognition in case of type 2 diabetics. This finding is in line with the specifications suggested by recent studies on the potential benefit of cognitive functioning with intensive BP control.[15]

In our study, Pearson's correlation showed a highly significant positive correlation (p<0.001) between HbA$_1$C and cognitive dysfunction in type 2 diabetics which is consistent with results of different studies published earlier. Biessels et al.[16] showed diabetes-related factors, such as insulin resistance and chronic hyperglycemia to be associated with impaired cognitive function.

In our study, we reported a high prevalence of dyslipidemia in type 2 diabetics .This is in line with the results of recent studies that indicated high incidences of dyslipidemia in young and non-elderly adults. 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 2 diabetics although the correlation among type 2 diabetics ($p<0.001$) were more significant HDL cholesterol failed to show any impact on cognitive impairment of diabetics ($p>0.05$).

However, the results of the different neuropsychological studies are heterogeneous with respect to the affected cognitive domains and the severity of the reported cognitive deterioration. This heterogeneity is probably caused by differences in patient characteristics and the psychometric paradigms used. Significant impairments were seen in all domains of cognitive functioning. The most significant parameters that were affected was naming, attention and language ($P<0.001$) whereas abstraction, delayed recall, orientation and visuospatial functioning were impaired in a statistically significant manner ($p<0.05$). These findings are in line with earlier (Stewart and Liolitsa, 1999; Strachan et al., 1997) studies conducted in type 2 diabetics. Ryan, Christopher M, et al., [9] conducted that middle-aged adults with type 2 diabetes manifest psychomotor slowing that is associated with poorer metabolic control, whereas learning, memory, and problem-solving skills appear to be largely intact. The development of psychomotor slowing may be a manifestation of a "central neuropathy" induced by chronic hyperglycemia.

Sinclair et al.[17]found that Type 2 diabetics with MCI also displayed an increased need for personal care and increased rates of hospitalization when compared with controls. Patients with diabetes also have been found to have slower walking speed, lack of balance, and increased falling tendency associated but whether the cerebral effects of diabetes contributed to these abnormalities is debatable.[18] Complicating the impact of mild neurocognitive dysfunction secondary to diabetes on daily living is the observation that patients with diabetes are twice as likely to have depression which will also negatively affect cognitive function and daily activities.

There were certain limitation of my study, 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. Further studies are required to determine the significance and potential public health benefit of this association.

Conclusion:

 To conclude, This study indicated that even non-elderly type 2 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.

Conflict of interest :None

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