Original Article

Cognitive Impairment and its Association with Glycemic Control in Type 2 Diabetes Mellitus Patients

Coredath Venugopal Lalithambika, Chankramath S. Arun[1], Lakshmi Ammal Saraswathy, Renjitha Bhaskaran[2]

Departments of Physiology, [1]Endocrinology and [2]Biostatistics, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi, Kerala, India

Abstract

Introduction: Type 2 diabetes mellitus is one of the major causes of increasing morbidity worldwide. Effective screening is carried out routinely for diabetic retinopathy, neuropathy, and nephropathy. Of late, studies have reported that cognitive decline can occur in people with diabetes, which could go undetected for a long period, and hence routine screening could be warranted. **Methodology:** Our objective was to study the prevalence of previously unknown mild cognitive impairment (MCI) in type 2 diabetic patients visiting a tertiary care center with the Montreal Cognitive Assessment (MoCA) test and to study the correlations of HbA1c, fasting blood sugar (FBS), postprandial blood sugar (PPBS), age, and duration of diabetes with the MoCA scores. Seventy patients with type 2 diabetes mellitus were included in the study. Patients with MoCA scores ≥26 were considered to have normal cognition (NC) and those with <26 MCI. **Results:** MCI was noted in 38 (54.29%) type 2 diabetes mellitus patients and NC in 32 (45.71%). Those with MCI had higher HbA1c (8.79 ± 1.85 vs. 7.78 ± 1.60), higher FBS (177.05 ± 62.48 vs. 149.38 ± 54.38), and PPBS (282.03 ± 85.61 vs. 214.50 ± 82.43), which were statistically significant. The cognitive domains of executive function, naming, attention, language, and memory showed a statistically significant difference between those with MCI and NC. There were no differences in the mean age, duration of diabetes, and educational status between the groups. **Conclusion:** The high prevalence of MCI in type 2 diabetic patients highlights the importance of implementing routine cognitive testing. The correlation of cognitive impairment with poor glucose control needs further studies to find out whether improving glycemic control will help improve cognition.

Keywords: Mild cognitive impairment, Montreal Cognitive Assessment, normal cognition, type 2 diabetes mellitus

Introduction

Type 2 diabetes mellitus is a leading cause of morbidity and mortality worldwide. The incidence is on the rise and it is seen that the age of onset of type 2 diabetes is also earlier. Screening tests are now routinely employed for early detection of diabetic retinopathy, peripheral neuropathy, and nephropathy.

It is well known that type 2 diabetes is also associated with cognitive impairment.[1-3] The spectrum of cognitive impairment could range from mild to severe dementia with the delay in detection of the problem. Early identification of cognitive decline in previously undetected cases could help deal with this better. Over the years, researchers have used many tools like Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Hopkins verbal learning test, Addenbrooke's cognitive examination-revised, clock-drawing test, six-item cognitive impairment test, and others for assessing the cognitive function.[4]

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A few studies from India have shown cognitive impairment in type 2 diabetes mellitus.[5-7] A correlation between glycemic control and cognition has also been well documented in the literature.[5] However, there are no studies from India using MoCA score, which is regarded by many as the best tool to assess subjects for mild cognitive impairment (MCI).

Methodology

Our main objective was to find the prevalence of cognitive impairment in type 2 diabetes mellitus patients in the age group 35–65 years attending the endocrinology outpatient

Address for correspondence: Dr. Chankramath S. Arun, Department of Endocrinology, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Edapally, Kochi - 682 041, Kerala, India.
E-mail: csarun2003@yahoo.co.uk

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department in a tertiary care center. Secondary objectives were to find if there is an association between HbA1c levels, duration of diabetes, and cognitive impairment and to see if there is a correlation between blood glucose levels and MoCA scores.

Our study design was cross-sectional. Based on the prevalence rate observed in an earlier publication,[8] and with 95% confidence and 20% allowable error, minimum sample size obtained was 66. We included 70 patients with type 2 diabetes mellitus of age group 35–65 years attending endocrinology outpatient department in a tertiary care hospital. Patients who are illiterate, who had significant hearing or visual impairment, patients with acute illness, psychiatric problems, epilepsy, Alzheimer's disease (AD), stroke, and those who were unable to consent for participation were excluded from the study.

As MoCA is a cognitive screening tool with high sensitivity and specificity for detecting MCI, we selected this to use for the study.[9] We used the English version of MoCA, which is a test with 30-point score.

Clearance was obtained from the Institutional Ethics Committee. Patients were recruited from June 2017 to February 2018 after written informed consent. MoCA screening tool was administered to the patients who were asked to follow a set of instructions and scored according to their performance.

Most recent value of HbA1c, fasting blood sugar (FBS), and postprandial blood sugar (PPBS) values on the day of administering the MoCA test were taken from the electronic medical records. Patients with MoCA scores ≥26 were considered to have normal cognition (NC) and those with <26 MCI.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 20.0 software. Means and standard deviations were calculated for the continuous variables, counts, and percentages for the categorical variables. To estimate the prevalence of cognitive impairment in type 2 diabetes mellitus, frequency and percentage were calculated. To test the statistical significance of the association of categorical variables with cognitive impairment, Chi-square test was used. To test the significance of the correlation of HbA1c and duration of diabetes with MoCA scores, Pearson's correlation method was used. To test the statistical significance of the differences in the mean values of continuous variables between those with MCI and NC, Student's *t*-test was used.

Results

There were 70 participants in this study, of whom 57 (81.4%) were males [Table 1].

Thirty-eight (54.29%) type 2 diabetes mellitus patients had MCI (MoCA score <26) and 32 (45.71%) had normal cognitive function (MoCA score ≥26). The HbA1c, fasting, and PPBS levels were significantly higher in patients with MCI [Table 2]. There were no significant differences in mean age and the duration of diabetes between the groups. HbA1c, FBS, and PPBS levels showed a negative correlation with the MoCA scores [Table 3]. Of the domains tested, executive function, naming, attention, language, and memory showed a statistically significant difference between those with NC and MCI [Table 4].

Twenty-five percent of those with normal scores named all the five words used for testing memory correctly, whereas only 2.6% of those with abnormal scores could do it in the MCI group. Around 53.1% of those with NC could repeat both the administered questions, whereas in MCI group, only 10.5% could do it. Orientation scores between the groups showed borderline significance. Abstraction scores were not statistically significant between the two groups.

Discussion

The present study examined the prevalence of MCI in patients with type 2 diabetes in South India. The prevalence

Table 1: Baseline characteristics of patients with type 2 diabetes included in the study (*n*=70)

Variables	*N* = 70
Age (years)	53.30±7.69
Sex (M/F)	57/13
Height (cm)	165.66±7.80
Weight (kg)	72.27±12.66
BMI (kg/m^2)	26.56±4.18
Type 2 diabetes duration (years)	12.04±6.04
MoCA score	24.91±2.69
HbA1c* (%)	8.33±1.8

*Mean±standard deviation

Table 2: Comparison of means and *P* values of variables between those with mild cognitive impairment and normal cognition

Variable	MCI (*n*=38) mean±SD	NC (*n*=32) mean±SD	*P*
Age	54.82±6.82	51.50±8.37	0.072
HbA1c	8.79±1.85	7.78±1.60	0.013*
FBS	177.05±62.48	149.38±54.38	0.034*
PPBS	282.03±85.61	214.50±82.43	0.001*
Duration of diabetes	12.79±6.28	11.16±5.71	0.318

*Statistically significant

Table 3: Correlations between HbA1c, FBS, PPBS, duration of diabetes, and MoCA scores

Variables	MoCA score		
	Pearson correlation coefficient	*P*	*n*
HbA1c	−0.287	0.016*	70
FBS	−0.309	0.009*	70
PPBS	−0.400	0.001*	70
Duration of diabetes	−0.142	0.240	70

*Statistically significant

Table 4: Cognitive domains in normal cognition and mild cognitive impairment group

Cognitive domain	Score (number of patients)	Mild cognitive impairment *n* (%)	Normal cognition *n* (%)	*P*
Executive function	2 (3)	3 (100)	0 (0)	
	3 (24)	19 (79.2)	5 (20.8)	
	4 (25)	12 (48)	13 (52)	0.001*
	5 (18)	4 (22.2)	14 (77.8)	
Naming	2 (18)	15 (83.3)	3 (16.7)	
	3 (52)	23 (44.2)	29 (55.8)	0.009*
Attention	2 (1)	1 (100)	0 (0)	
	3 (3)	3 (100)	0 (0)	
	4 (6)	5 (83.3)	1 (16.7)	0.009*
	5 (19)	14 (73.7)	5 (26.3)	
	6 (41)	15 (36.6)	26 (63.4)	
Language	0 (7)	6 (85.7)	1 (14.3)	
	1 (25)	18 (72)	7 (28)	0.001*
	2 (20)	11 (55)	9 (45)	
	3 (18)	3 (16.7%)	15 (83.3)	
Abstraction	1 (3)	3 (100)	0 (0)	
	2 (67)	35 (52.2)	32 (47.8)	0.302
Memory	1 (6)	6 (100)	0 (0)	
	2 (17)	14 (82.4)	3 (17.6)	0.001*
	3 (19)	10 (52.6)	9 (47.4)	
	4 (19)	7 (36.8)	12 (63.2)	
	5 (9)	1 (11.1)	8 (88.9)	
Orientation	5 (12)	10 (83.3)	2 (16.7)	0.057#
	6 (58)	28 (48.3)	30 (51.7)	

*Statistically significant. #Borderline significance

of MCI was found to be 54.3% in our study population. This is higher than that shown in the previous studies from India, which range from 19.5% to 48.0%.[5-7] However, previous studies used MMSE, trail-making tests, modified MMSE, and other neuropsychological tests like digit span test, digit symbol substitution test, and others, which are less sensitive in detecting MCI and hence could have contributed to the difference. As MoCA is a more sensitive test, it might have helped detect MCI more accurately.

In our study, patients with cognitive impairment had significantly higher FBS, PPBS, and HbA1c, which negatively correlated with MOCA scores. In a study by Roy *et al*., cognitive impairment was observed in 11.6% of the patients who had optimal glycemic control (HbA1c under 7%) and 30.2% with HbA1c 7% or above.[5] Khullar *et al*. showed that subjects having glucose levels >125 mg/dl had 1.73 times higher risk of developing neurocognitive impairment.[6,7] ACCORD-MIND trial done on 2977 type 2 diabetes subjects found a statistically significant age-adjusted association between HbA1c level and score on four cognitive tests.[10] Both clock in a box and clock-drawing test have been shown to inversely correlate with HbA1c.[11] Hence, our results are consistent with existing literature that poor glycemic control in type 2 diabetes is associated with cognitive decline.

While there is vast epidemiologic data linking poor glycemia and cognitive impairment, it is not clear whether improving glucose control leads to improvement in cognition. The diabetes control and complications trial in type 1 diabetes demonstrated that improved HbA1c was related to improved cognition in nonamnestic domains.[12] Luchsinger *et al*. showed that improving HbA1c levels in an elderly population over a period of 5 years was associated with slowing down of global cognitive decline.[13]

Being a woman and longer duration of diabetes have been shown to be independent risk factors in previous studies.[6] Our study did not find any difference between sex or any relation to duration of diabetes perhaps because of inadequate sample size.

The MoCA is now accepted as an excellent tool for brief cognitive screening measure and is freely available with multiple editions in various languages. The original MoCA reported a sensitivity of 100% and specificity of 87% in detecting mild AD using a cutoff score of 26.[9] Amnestic MCI (aMCI) is said to have a high likelihood of progressing to AD.[10] It has previously been shown that the total score of the MoCA was a better discriminator for aMCI and had a modest accuracy in differentiating Nonamnestic MCI (naMCI) patients from healthy controls that were better than the MMSE.[14] Hence, the differences noted in the MOCA scoring in our study could be suggestive of risk for development of AD in the future.

In the present study, executive function, naming, attention, language, and memory showed a statistically significant difference between those with NC and MCI. It has been shown that attention, language, orientation, visual perception,

organization of visual movement, and logical questioning improved with proper cognitive training in patients with MCI.[15] A study on the effectiveness of cognitive training program in people with MCI underlines the importance of early detection of MCI.[16]

We used the English version of MOCA as the local language version is not available. However, all patients understood English and were comfortable using it for the study. The level of education among subjects in both groups was similar.

In summary, our study shows a high prevalence of undetected MCI in type 2 diabetes mellitus patients attending an outpatient clinic setting. A strong negative correlation was noticed between all parameters of glycemic control and MOCA scores representative of cognitive function. These observations make a strong case for routine screening of type 2 diabetes mellitus patients to detect MCI with a sensitive tool such as MoCA. Studies on the benefits of improved glycemic control on cognitive function would need to be performed in the future to help us understand the significance of our finding in the long-term management of these patients.

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Conflicts of interest

There are no conflicts of interest.

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