Original Article

"Do Diabetics Cherish Memories" A Study Of Cognitive Status In Type 2 Diabetics

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Abstract

Background and aims: Type 2 diabetes, the modern epidemic has recently known to be associated with cognition dysfunction and dementia, the detection of which appears to be the tip of the iceberg as majority of the cases still remains undiagnosed. With the increase in the prevalence of type 2 diabetes mellitus and neurodegenerative diseases,it is worthwhile to warrant a screening for cognition function in type 2 diabetes mellitus. The study was done to evaluate the cognition status using MoCA score in type 2 diabetes mellitus and age and sex matched control and to correlate the MoCA score with Glycemic status and BMI.

Material and method: The study involved 41 cases of type 2 diabetes mellitus and 41 controls. Cognition status was assessed using MoCA score. A score of > 26 was considered as normal cognition. Fasting Plasma Glucose (FPG) was measured by Hexokinase method. HbA1c was assessed by Turbidimetric inhibition method BMI was Calculated as weight (kg)/ height2 (m).

Data was expressed as mean ± SD. Comparison of the data was done by using unpaired t test. Correlation of the parameters was done by using Pearson's correlation test. $p < 0.05$ was considered statistically significant.
Conclusions: Cognitive decline observed emphasis the need for a routine screening of cognition status in type 2 diabetes mellitus and to identify sensitive and specific biomarkers for early detection of cognitive decline in type 2 diabetic patients.

Keywords: Type 2 diabetes mellitus, MoCA score, cognitive status

BACKGROUND AND AIMS

Type 2 Diabetes mellitus, characterized by hyperglycemia, is emerging as a leading health challenge (1). Type 2 diabetes mellitus cases are expected to increase to over 134 million by 2045 (2). Aging is an intrinsic phenomenon. With the increase in the ageing population, there is a substantial increase in the incidence of neurodegenerative diseases. Type 2 diabetes, the modern epidemic, has recently been known to be associated with cognition dysfunction and dementia, which appears to be the tip of the iceberg as most cases still remains undiagnosed (3). Cognitive impairment is defined as difficulty in learning, decision making, poor memory, and lack of concentration. Studies have demonstrated that diabetes patients, especially those with type 2 diabetes, develop cognitive problems such as dementia and Alzheimer's disease, irrespective of gender. Compared to those without diabetes, diabetes is associated with ~~a~~ 60% increased risk of dementia and 19 % greater cognitive decline (4). Diabetes is, therefore a potential risk factor for both vascular dementia and Alzheimer's disease due to the development of unique brain-specific insulin resistance and impaired glucose regulation (5). Brain abnormalities such as reduced hippocampal volumes provide evidence for this in both animal (6) and human models (7-9). Complex interactions such as hyperglycemia, hyperinsulinemia, hypertension, dyslipidemia, and micro and macro vascular complications of type 2 diabetes mellitus are involved in the pathogenesis of Diabetic cognitive impairment (DCI) (10-11). Hyperglycemia and insulin resistance promotes dysfunction of the blood -brain barrier and enhances neuronal loss by facilitating harmful substance (e.g., AGEs and endotoxin) to access the neurons, thus contributing to Diabetic cognitive impairment(DCI) (12). The present study was conducted to determine the cognitive status by assessing the MoCA score and its correlation with age, Body Mass Index(BMI), fasting plasma glucose and glycated hemoglobin in type 2 diabetics and age and sex matched controls.

MATERIAL AND METHOD

This cross-sectional study involved 82 subjects (41 cases and 41 controls) based on universal sampling method, visiting Justice KS Hegde Charitable Hospital Mangaluru, Karnataka, India from April 2022 –August 2022. The study was approved by the Institution Ethical Committee(INST.EC/EC/017/2022)

The sample size was calculated based on the standard deviation of I-FABP (0.83 in control group and 1.96 in Type II Diabetes Mellitus (5)), mean difference 1, effect size 0.7168, alpha error 5%, power 85%, the sample required per group is 41. i.e., total of 82. This was calculated using nMaster software version 2.

Cases included subjects with confirmed type II diabetes aged more than 30 years and less than70 years. Controls were age and sex matched non-diabetic subjects. Subjects with Type 1 Diabetes Mellitus, pregnancy, acute or chronic infectious disease, hypertension, heart failure, hepatic or renal disease, cancer, history of primary disease of digestive system such as Inflammatory Bowel Disease, pancreatitis or liver cirrhosis, history of autoimmune disease, history of malignancy, history of abdominal surgery in recent 6 months, treatment for anxiety or depression, patients treated with corticosteroids or immunosuppressant, neurodegenerative disorders and neurovascular disorders were excluded Subjects vaccinated for COVID-19 within past two were also excluded from the study. Informed consent was obtained from the study subjects who were willing to participate in the study. 2 ml of fasting blood sample (8-12 hrs of fasting) was collected in fluoride vacutainer for estimating Fasting plasma glucose. 2 ml of blood was collected in EDTA vacutainer for estimation of glycated hemoglobin (HbA1c)

Body weight was measured using standard analogue weighing scale to the nearest kilogram.

BMI was Calculated as weight (kg)/ height(m)^2. Cognitive analysis was done by using Montreal Cognitive Assessment Chart. Total possible score is 30.A MoCA score of 26 or above indicates normal cognitive function. A MoCA score <26 indicates Cognitive impairment. A score of 18-25 indicates mild cognitive impairment. 10-17 – moderate cognitive impairment and less than 10 – severe cognitive impairment. Fasting Plasma Glucose (FPG) was measured by Hexokinase method. HbA1c was assessed by Turbidimetric inhibition method. Statistical analysis was done using SPSS version 20. Data was expressed as mean ± SD. Comparison of the data was done by using unpaired t test. Correlation of the parameters was done by using Pearson's correlation test.

$p < 0.05$ was considered statistically significant.

RESULTS

The present study included 41 cases and 41 controls. FPG and HbA1c were significantly higher in cases than in controls. ($p<0.001$). The MOCA score was significantly lower in cases than in controls. ($p<0.001$). No significant difference was observed in the mean BMI levels between cases and controls.(Table 1)

Table 1: Comparison of parameters between cases and controls

Parameters	**Cases (n=41)**	**Controls (n=41)**	**P value**
	Mean ± SD (Min-Max)		
BMI	24.22 ± 4.68 (17.72 – 41.38)	22.69 ± 3.94 (7.80 – 28.58)	0.114
Fasting Plasma Glucose	186.17 ± 71.54 (106.00 -426.00)	95.49 ± 11.59 (75.00 – 129.00)	<0.001
HbA1c	8.48 ± 1.93 (6.02 – 14.40)	5.71 ± 0.39 (4.70 – 6.50)	<0.001
MOCA score	21.90 ± 4.59 (7.00 – 28.00)	26.93 ± 2.61 (20.00 – 30.00)	<0.001

Figure 1: Distribution of diabetic subjects based on cognition and glycemic control

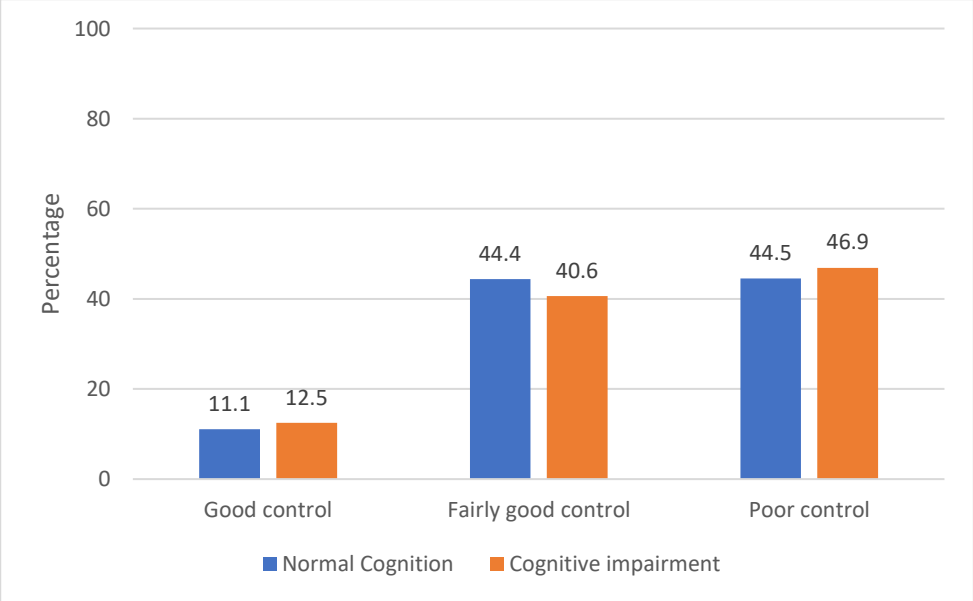
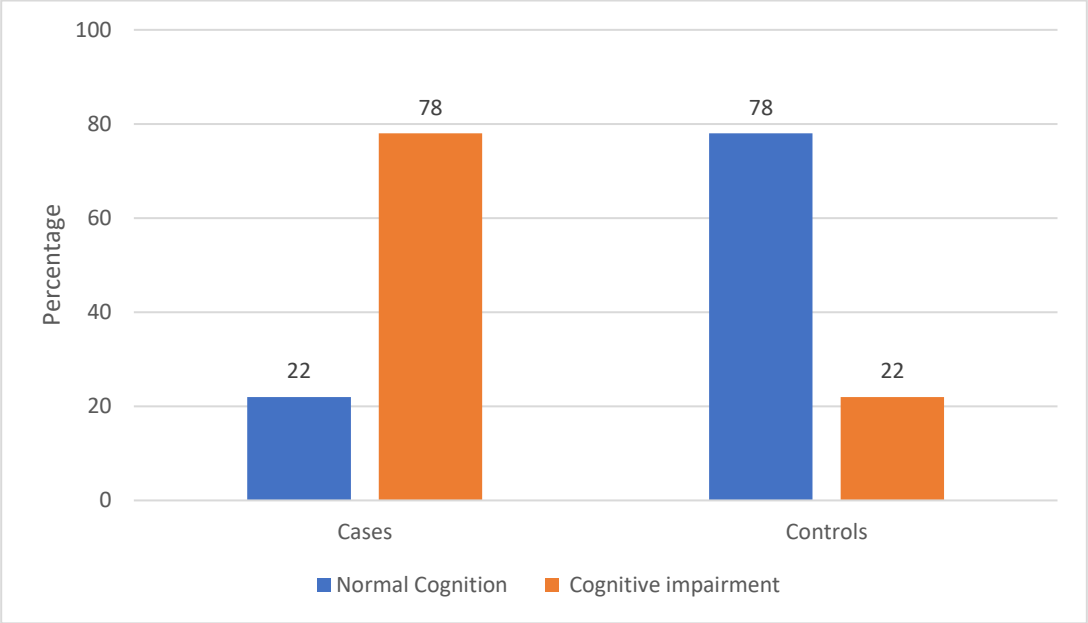


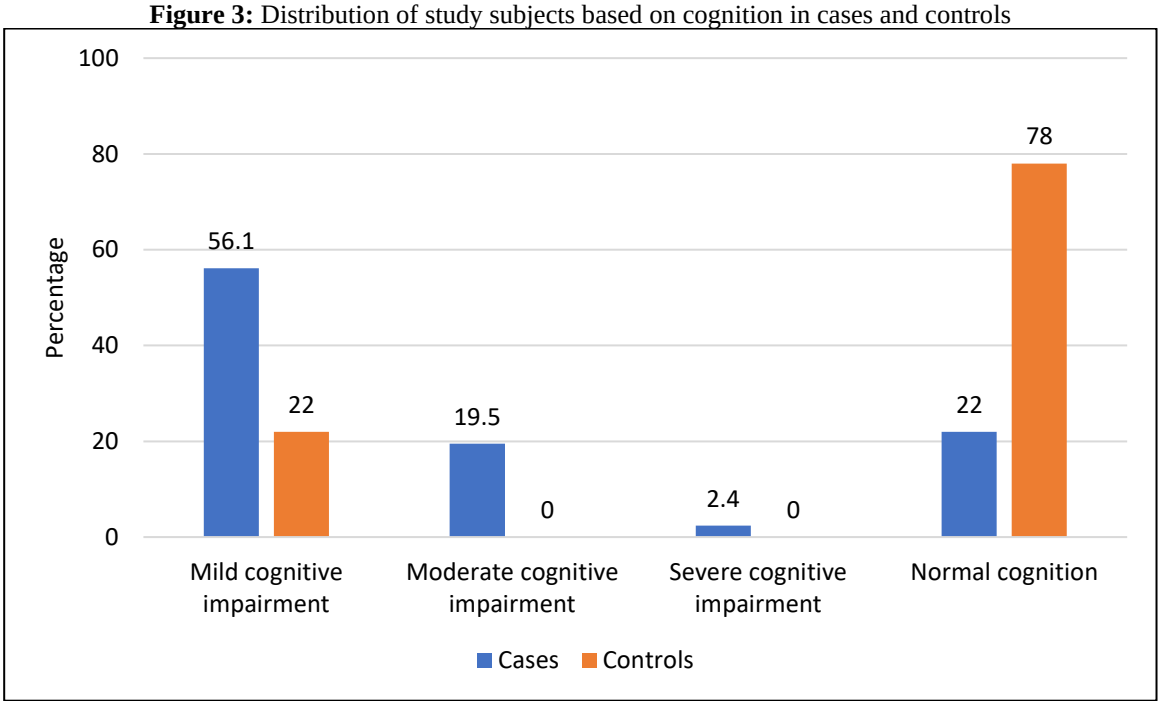
Figure 2: Distribution of cognitive status among study participants.



The percentages of diabetic patients with NC and MCI were 22% (n=9) and 78% (n=32) respectively.

- The percentages of healthy controls with NC and MCI were 78% (n=32) and 22% (n=9) respectively.
- MCI was strongly associated with DM and NC was associated with normal individuals (p<0.001)(Figure 2)

Figure 3: Distribution of study subjects based on cognition in cases and controls



The percentages of cases with mild, moderate and severe cognitive impairment were 56.1% (n=23), 19.5% (n=8) and 2.4% (n=1) respectively. The remaining 22.0% of the cases (n=9) had normal cognition. The percentages of controls with mild, moderate and severe cognitive impairment were 22.0% (n=9), 0% (n=0) and 0% (n=0). The remaining 78% of the controls (n=32) had normal cognition. Significant association was seen between cognition status and study groups. (p<0.001) (Figure 3)

Table 2: Correlation of parameters with MOCA score

		AGE	BMI	FPG	HBA1C
MOCA SCORE	Pearson Correlation	-0.356	-0.021	-0.405	-0.489
	p value	0.001	0.851	<0.001	<0.001
	n	82	82	82	82

MOCA SCORE showed a negative and moderate correlation with age, fasting plasma glucose and glycated hemoglobin which was statistically significant. ($p<0.05$) (Table 2)(Figure 4,5 and 6)

Figure 4: Correlation between MOCA score and age (in years)

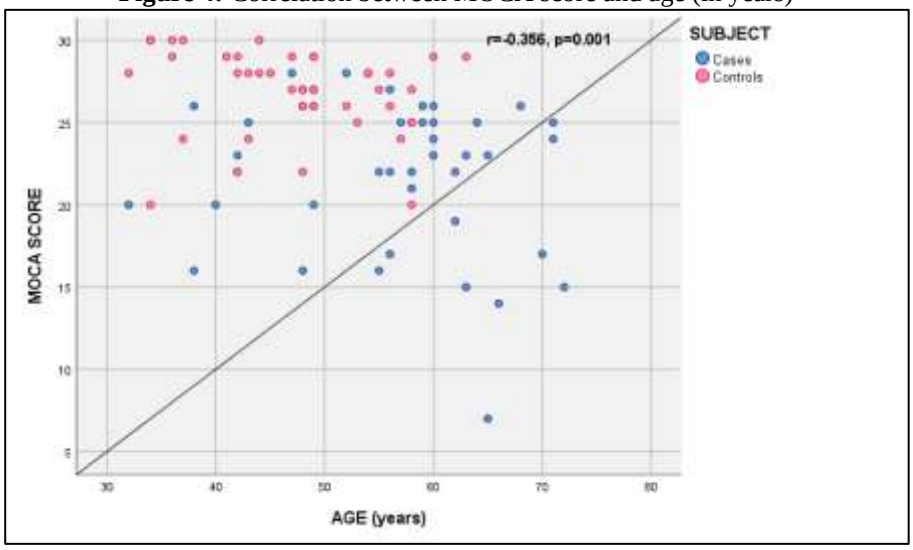


Figure 5: Correlation between MOCA score and fasting plasma glucose

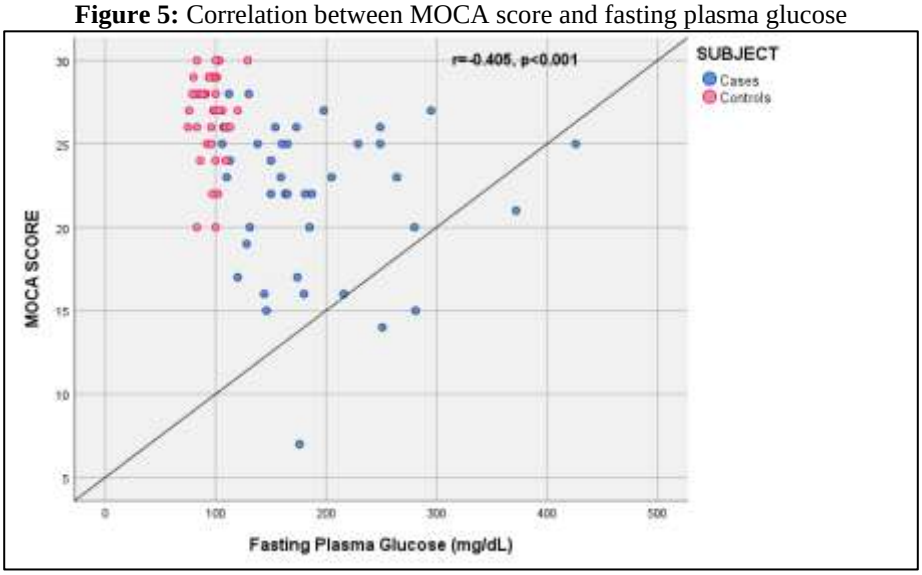
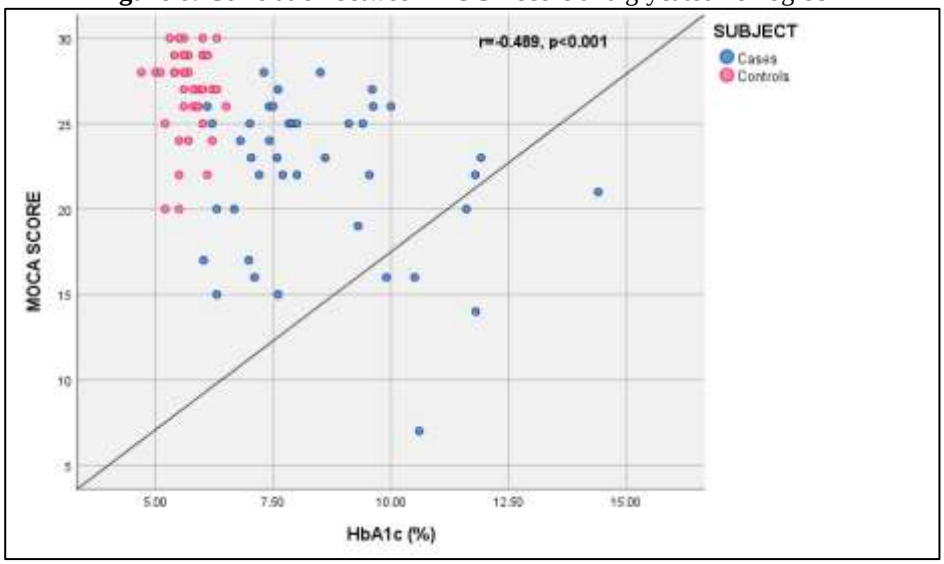


Figure 6: Correlation between MOCA score and glycated hemoglobin



DISCUSSION

The present study showed that the MOCA score was significantly lower in cases than in controls. ($p<0.001$). MCI was present in 78% of type 2 diabetics and 22 % of controls. MOCA score showed a negative and moderate correlation with fasting plasma glucose ($r=-0.405$ $p= <0.001$) and HbA1c ($r= -0.489$ $p=<0.001$) which was statistically significant. ($p<0.05$). MOCA score showed a negative correlation with BMI ($r= -0.021$ $p=0.851$), which was not statistically significant. Bashir J et al. conducted a study on 61 type 2 diabetics and 32 non-diabetic controls. About 88.5% of the diabetic subjects had MCI, in contrast with only 50% of the non-diabetic controls (13). A study by Naguib et al. on 269 type 2 diabetics showed that 80.3% had cognitive impairment while 33.8% had severe impairment (14). A study on 1,012 type 2 diabetics and 19,302 healthy control UK participants by Antal B et al. showed that Type 2 diabetics had accelerated atrophy of gray matter and brain aging, which increased with advanced age. Type 2 Diabetes Mellitus was associated with a defect in executive functioning and processing speed (15). Insulin possesses a neuromodulatory effect and promotes neuronal plasticity, an essential factor for normal cognitive function. Type 2 diabetes mellitus results in insulin dysregulation, thus promoting neuroinflammation (16). The severity of cognitive dysfunction increases with age and can be linked to decreased energy availability due to insulin deficiency or insulin action. Persistent hyperglycemia overproduces advanced glycation end products that cause oxidative damage and injury to neurons (17). Insulin resistance may be promoted by the inflammatory cytokines produced by adipose tissue cells and macrophages. These inflammatory cytokines may cross the blood-brain barrier and activates stress kinases promoting neuronal insulin resistance, which damages the synaptic function and promotes neurodegeneration, thus contributing to diabetic cognitive impairment (18). The human brain is considered to be a vulnerable organ to the effects of Type 2 diabetes mellitus. Evidence of hippocampal region atrophy was reported by Moulton et al. (19). Disruptions in the white matter within the body of the corpus callosum, with interferences in the functional connectivity between the hippocampal regions and other critical areas of brain, was demonstrated by Sun et al. (20). Insulin resistance may affect acetylcholine release, an important neurotransmitter, thus contributing to neurocognitive impairment of type 2 diabetes mellitus (21).

CONCLUSIONS

Cognitive decline observed emphasis the need for a routine screening of cognition status in type 2 diabetes mellitus as a recommendation for good care and to identify sensitive and specific biomarkers for early detection of cognitive decline in type 2 diabetic patients.

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