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# Evaluation of Cognitive Functions in Type 2 Diabetes Mellitus Patients Attending Diabetic Clinic of Tertiary Care Hospital in India.

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**Received:** 11 December 2021
**Accepted:** 26 December 2021

## Abstract

**Objective:** To evaluate cognitive functions of diabetes type 2 patients and to assess whether they differentially vary between male and female patients attending diabetic care clinic of Tertiary Care Hospital in Vijayapura, Karnataka, India.

**Methods:** This cross- sectional clinical study was conducted on 94 Type 2 Diabetic patients, in the age range of 30 – 75 years, out of which 52 were males and 42 were females. Anthropometric and Physiological parameters were recorded. Blood sample was collected. Random blood sugar glucose, Postprandial blood sugar levels (Biosen S-Line Glucose and lactate analyzer) were measured and HbA1c testing was done by enzymatic assay. Assessment of Cognitive function was done using Mini-Mental State Exam (MMSE), Clock Drawing Test (CDT), Trail Making Test (TMT) and Wechsler Memory Scale (WMS).

**Results:** In comparing anthropometric parameters in male and female patients. There was a statistically significant difference in the Basal Metabolic Index ($P<0.05$), as females had a comparatively higher value than males. In evaluating cognitive functions, there was a significant decline in MMSC and CDT in both male and female patients but there no statistical significance between genders.

**Conclusion:** Overall, there was a significant correlation in P values between HbA1c and cognitive function tests in both genders.

**Keywords:** Type 2 Diabetes, Cognitive Functions, Anthropometric parameters, Mini-Mental State Exam (MMSE), Clock Drawing Test (CDT), Trail Making Test (TMT), Wechsler Memory Scale (WMS).

### Introduction

Diabetes Mellitus is a condition that develops over the years and disrupts normal metabolism, characterized by elevated blood glucose levels. It has been estimated by the World Health Organization (WHO) that around 220 million people around the world have diabetes.[1] A survey conducted in 2019 revealed that diabetes was the ninth leading cause of death globally and around 1.5 million deaths around the world were primarily caused by diabetes.1 The WHO and International Diabetes Federation (IDF) have predicted that the total number of people living with diabetes is expected to rise to 643 million by 2030 and 783 million by 2045.[2]

In humans, Diabetes Mellitus exist in 2 main forms - type 1 and type 2. The basic difference between the 2 types is based on the two classifications which differ from each other based on the cause of elevated blood sugar and the response of the individual to insulin. The incidence of type 2 diabetes mellitus (T2DM) is on the rise throughout the world , causing a significant health burden both on the population and economy of every country.[3] Diabetes can lead to many other complications, involving multiple organs throughout the body, including the eyes, kidney, heart, and brain. The end result of these complications ultimately leads to the death of the patients, effecting both the quality and quantity of life. One of the serious complication of diabetes is its neurological manifestations, which is due to its negative role on the functioning of neurons.[4]

Many studies have been conducted to demonstrate an association between diabetes mellitus and impairment in cognition. It is a well-known fact that poor control of blood sugar or prolonged episodes of hypo or hyperglycemia may damage the blood vessels leading to a condition called microangiopathy. It will moreover lead to damage of neurons leading to dementia.[5] Over the years, the incidence of diabetes mellitus increases with increase in age and accelerates the process of decline in cognition, leading to an increase in the prevalence of co-morbidities associated with diabetes. This fact has been documented by relevant studies conducted on aged patients suffering from type 2 diabetes who had a higher incidence of cognitive dysfunction or dementia.[6]

Even mild form of cognitive dysfunction can disturb day to day activities in all age groups and work situations. Every work performed requires specific domains of cognition and perception such as general intelligence, processing speed, psychomotor efficiency, attention, perception, learning, memory, and executive functions.[7] Diabetes is remarkably associated with risk of dementia with the passage of time. The more prolonged the incidence of diabetes, the more the level of cognitive impairment. It often goes unnoticed by the patient when it is a mild cognitive impairment,

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but when the episodes of memory deficit increases and start disrupting the ongoing daily activities, that is when the patient seeks medical help.

Dementia and impaired cognition have certain subtypes which are exaggerated by diabetes mellitus. It is quite unclear what is the underlying mechanism for causing impaired cognition leading to dementia in diabetes, but it is more likely that many physiological and non-physiological factors are involved, leading to dementia and other co-morbidities. In case of lack of effective treatments for dementia, the patients are at increased risk of serious consequences of this condition, ultimately leading to their death. Interventions to identify the stage of dementia at this point is essential to prevent progression from preclinical to clinical disease. Hence our study aimed to evaluate cognitive functions of diabetic patients by performing various procedures to assess their level of cognition and to assess whether cognitive functions of diabetic patients differentially vary between male and female patients.

### Methods

This cross-sectional clinical study was conducted between march – June, 2018, on 94 Type 2 Diabetic patients, out of which 52 were males and 42 were females, in the age range of 35 – 75 years, attending a Diabetic Clinic of tertiary care hospital in Vijayapura, Karnataka, India. All male and female patients included in this study were suffering from Type 2 diabetes mellitus for more than five years. Patients suffering from Diabetes for less than five years, hypertensive, patients suffering from type 1 DM or other endocrine disorders, patients on psychiatric treatment and chronic alcoholics were excluded from the study. Institutional ethical clearance was obtained (BLDE (DU)/ IEC/270/2017-18). After explaining the purpose of study to all the patients, written consent was obtained from all the participants who were then subjected to detailed history and physical examination. Anthropometric measures including age, height, weight and body mass index were recorded. Blood sample was collected and random blood sugar glucose, postprandial blood sugar levels (with the help of Biosen S-Line Glucose and lactate analyzer) were measured and HbA1c testing was done by enzymatic assay.

All the tests to evaluate the level of cognition were carried out by strictly following the standard protocols. Assessment of Cognitive function was performed using Mini-Mental State Exam (MMSE).[8] To interpret the level of reasoning and understanding of instructions conveyed to the patients, some tests were conducted in the form of Mini-Mental State Exam (MMSE). The purpose MMSE was to assess five specific areas of cognitive function, which included orientation, attention, calculus, recall and language. The highest attainable score in this test was 30 and a score of 24 or lower was marked as poor performance regarding cognitive skills. Clock Drawing Test (CDT)[9] was used as an assessment tool to check the cognition of the patient. The clock drawing test assessed cognitive or visuospatial impairment. In order to perform this test, each patient was directed individually to draw the face of a clock as well as the numbers inside the clock. Later the patient was instructed to place the hands of the clock to indicate certain time, such as "ten minutes after eleven." Clock drawing helped in identifying the short comings in executive functions of the patient, if any. The third assessment tool used in this study was the Trail Making Test (TMT).[10] The Trail Making Test is a pencil-and-paper test and it is used to evaluate psychomotor speed and executive function. Part A of this test involves one to connect 25 dots, as quickly as possible, which are randomly distributed, but during this process, the patient is required to remember the number of dots connected. Part B of this test engages the patient in connecting randomly distributed numbers and letters in an ascending alpha¬numeric sequence. Participants were allowed a maximum time of 240 seconds for the first part of this activity and 340 seconds for second part of this activity. To test the memory of the patients, the Digit forward and backward test was conducted and associate learning was assessed by using Wechsler Memory Scale (WMS).[11]

Results were expressed as Mean + SD and in the form of images. Data was analyzed using unpaired Student t test. Correlation between HbA1c and cognition scores for both male and female separately were evaluated.

### Result

Comparison anthropometric parameters in male and female patients has been shown in table 1. There is a statistically significant difference in the BMI (P<0.05), as females have a comparatively higher value than males.

**Table. I Anthropometric parameters in both genders.**

| Parameters | Male (n=52) | Female (n=42) | P - value |
|---|---|---|---|
| Age (Years) | 59.73 ± 8.86 | 57.15 ± 11.20 | 0.09 |
| Height (cm) | 160.77 ± 9.61 | 152.52 ± 7.55 | 3.51 |
| Weight (Kgs) | 62.18 ± 11.11 | 56.77± 10.34 | 0.017 |
| BMI (Kg/ $m^2$) | 22.96 ± 2.94 | 25.18 ± 3.8 | 0.04* |

*P<0.05 is significant. BMI – Basal Metabolic Index

Comparison of mean blood pressure (BP), random blood sugar (RBS), postprandial blood sugar (PPBS) and HbA1c has shown in table II. RBS, PPBS and HbA1c are high in both male and female patients but there is no statistical significance between groups based on gender.

**Table II. Blood pressure and blood glucose in both genders.**

| | Male(n=52) | Female(n=42) | P-value |
|---|---|---|---|
| Systolic BP (mmHg) | 126.25 ± 13.90 | 127.75 ± 14.06 | 0.62 |
| Diastolic BP (mmHg) | 73.55 ± 9.21 | 78.7 ± 9.54 | 0.88 |
| Random blood sugar | 141.00 ± 55.47 | 156.22 ± 43.72 | 0.20 |
| Postprandial blood sugar | 224.31 ± 74.71 | 222.3 ± 68.22 | 0.87 |
| HbA1c (4-5.6%) | 8.96 ± 1.80 | 9.53 ±1.93 | 0.086 |

Mean values for individual cognitive function tests of male and female has presented in table III in which we can observe alteration in MMSC and CDT in both male and female patients but there is no statistical significance between groups. There is statistically significant difference in WMS2 test among both genders.

**Table III. Cognitive Functions in both genders.**

| | HbA1c | MMSC | CDT | TMT A | TMT B | WMS1 | WMS2 |
|---|---|---|---|---|---|---|---|
| Male | 0.02* | 0.10 | -0.04* | 0.05* | 0.02* | 0.15 | -0.03* |
| R-value | - | 0.10 | 0.04* | 0.24 | 0.23 | 0.59 | 0.21 |
| Female | 0.02* | 0.10 | 0.13 | 0.06 | 0.08 | -0.06 | 0.05* |
| R-value | - | 0.10 | 0.13 | 0.19 | 0.18 | 0.31 | 0.23 |

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In Table IV correlation between HbA1c and cognitive functions is shown. In male patients there is negative correlation between CTD and HbA1c and is statistically significant. TMT A and B have positive correlation with HbA1c and statistically significant (P<0.05). In female patients there is positive correlation between HbA1c and WMS2 and is statistically significant (P<0.05).

**Table IV. Correlation in P values between HbA1c and cognitive function tests.**

| Cognitive Function Tests | Male(n=52) | Female(n=42) | P- value |
|---|---|---|---|
| MMSC (Normal 21-26) | 23.19 ± 2.61 | 23.15 ± 2.27 | 0.50 |
| CDT | 0.48 ± 0.50 | 0.37 ± 0.49 | 0.35 |
| TMT A (173/ sec) | 145.59 ± 18.09 | 150.39 ±24.10 | 0.81 |
| TMT B (273/sec) | 192.89 ± 27.39 | 198.91 ± 24.33 | 0.24 |

*P<0.05- significant

## Discussion

Patients included in this study were suffering from diabetes for a period of more than 5-years and were on treatment. In our study, both male and female diabetic patients receiving therapy showed a significant decline in cognitive functions. In contrast to these findings, a study conducted by van den Berg et al[12] in 2010 showed no difference in cognitive decline on several tests between individuals with and without diabetes when they were carefully monitored over a period of 4 years. However, our study differs from their study as we used different series of tests to determine cognitive functions. Different tests might reveal different pattern of decline. Tolit et al in 2020.[13] demonstrated unsatisfactory intellectual performance (Wechsler Logical Memory story recall) among old patients suffering from stroke.

There was a strong association found between type 2 diabetes and cognitive functions in a study conducted by Elias at al in 1997.[14] Literature indicates that there is a strong association of cognitive functions with the type of diabetes. One of such study was conducted by Espeland et al in 2011.[15]

A detailed epidemiological study was conducted on a large sample of population by Teixeira et al in 2020 to study if there was an association between diabetes and early changes in the cognitive performance of the Brazilian population and an alarmingly high association was observed between diabetes and cognitive performance of the sample population.[16] On the contrary, a study conducted by Papunen et al in 2020 revealed no association between diabetes and cognitive decline.[17]

The physiological processes ultimately leading to the decline in cognition in Diabetes Type 2 still remains to be explored. Many theories and hypothesis have been presented to define an association between the two, including Many hypotheses with supporting evidence exist, including amyloid deposition inside the brain cells, but evidence lacks.

## Conclusion

The explanation of association of T2DM with decline in cognitive functions and dementia is one step forward to the development of medication for this purpose. With the rise in the number of cases worldwide, T2DM-associated cognitive dysfunction and dementia are adding to the health burden. Developing better and urgent medical interventions are essential to preserve cognition.

## Limitation of study

We could not further subdivide groups based on their age and blood sugar levels due to time constraints and small sample size.

**Conflict of interest:** Nil

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