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Original Research Article

IMPACT OF TYPE 2 DIABETES MELLITUS ON COGNITIVE FUNCTION: A COMPARATIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Diabetes mellitus (DM) is a chronic condition which is characterized by persistent hyperglycemia. Long standing DM may lead to metabolic dysregulation and end-organ damage. Type 2 diabetes mellitus (T2DM) is associated with microvascular and macrovascular complications such diabetic neuropathy and cognitive dysfunction. Cognitive impairment in T2DM is linked to hyperglycemia insulin resistance and neuroinflammation.

Material and Methods: This comparative observational study involved 50 Type 2 Diabetes Mellitus (T2DM) patients and 50 age-matched healthy controls. Assessment of cognitive function was done using the Mini-Mental State Examination (MMSE). Demographics, duration of diabetes, presence of other co-morbidities and glycemic control (HbA1c) were recorded. MMSE score was used to assess cognitive function. Both the groups were compared and correlated with diabetes-related factors such as HbA1c and duration of disease. P value less than 0.05 was considered as statistically Significant.

Results: Gender and age distributions were comparable in both the groups. Most participants were between 51-60 years of age. Group A (Individuals with T2DM) demonstrated significantly lower MMSE scores across cognitive domains except for registration. The total MMSE score was notably higher in Group B (27.9 ± 2.1) as compared to Group A (25.4 ± 2.2) and the difference was statistically significant ($P<0.05$). Greater cognitive decline was seen in T2DM patients with Poor glycemic control (HbA1c > 7%) and individuals with longer diabetes duration.

Conclusion: Cognitive dysfunction is a common complication of Type 2 Diabetes Mellitus. Early detection and effective management of glycemic levels are crucial to prevent significant cognitive impairment and improve patient outcomes. Regular cognitive assessments should be conducted in individuals with type 2 diabetes mellitus (T2DM), particularly in cases of poor glycemic control or a long duration of the T2DM.

Key Words: Cognitive Dysfunction, Diabetic Neuropathy, Glycemic Control, Type 2 Diabetes Mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting either from defects in insulin secretion or insulin action or in some cases both.[1] Over recent decades the incidence and prevalence of diabetes mellitus have risen to alarming levels worldwide. Sedentary lifestyle and unhealthy dietary patterns are major factors behind global rise in Type 2 diabetes mellitus (T2DM) incidence. Moreover, aging population and improved healthcare access have led to earlier diagnoses thereby further contributing to the increasing prevalence of diabetes.[2]

Chronic hyperglycemia Is the hallmark of T2DM and metabolic dysregulation which contribute to end-organ damage over time. Persistent hyperglycemia induces oxidative stress, chronic inflammation and

microvascular and macrovascular changes. These changes cumulatively impair the structure and function of vital organs.[3] The end-organ damage in T2DM typically manifests as microvascular complications such as diabetic retinopathy, nephropathy and neuropathy. Macrovascular complications include cardiovascular disease, peripheral arterial disease, and cerebrovascular accidents. These complications not only significantly affect the quality of life for patients but also significantly increase morbidity, mortality and healthcare costs. Among these, diabetic neuropathy is a particularly debilitating condition that is associated with long standing T2DM.[4]

Neurological manifestations of T2DM include short term and long term neurological complications. The short term neurological complications are usually acute and catastrophic in nature whereas the long term complications are subtle in nature. The acute complications include hypoglycaemia and hyperglycemia and hyperosmolar hyperglycemic state (HHS).[5] All these pathologies are associated with acute neurological manifestation that may range from confusion to convulsion and in un-treated cases progression to coma. The long term complications include diabetic neuropathy that may manifest as tingling and numbness and neurological pain. Additionally, autonomic neuropathy may result in gastrointestinal dysmotility, orthostatic hypotension, and cardiac arrhythmias. In addition to these patents of T2DM are also prone to develop catastrophic conditions such as cerebrovascular accidents.[6]

Among the CNS complications of T2DM cognitive dysfunction is an area of growing concern. Patients with T2DM are at an increased risk of developing mild cognitive impairment (MCI), vascular dementia, and Alzheimer's disease. The mechanism underlying cognitive dysfunction in T2DM is multifactorial and includes chronic hyperglycemia, insulin resistance, microvascular disease and neuroinflammation.[7] These factors contribute to structural and functional changes in the brain such as hippocampal atrophy and reduced cerebral perfusion. Cognitive dysfunction not only diminishes the quality of life for individuals but also is responsible for complicating diabetes management by impairing patients ability to take proper care which is essential part of overall management of T2DM. It is important to diagnose cognitive dysfunction in T2DM cases and start appropriate intervention to mitigate the progression of cognitive decline and improve overall outcomes.[8]

Despite growing evidence linking T2DM to cognitive dysfunction significant gaps remain in our understanding of this association. Existing studies often lack standardized methods for cognitive assessment. This study aims to address these knowledge gaps by systematically evaluating cognitive dysfunction in T2DM patients. By doing so we seeks to provide insights that will help in earlier detection and targeted interventions to reduce the burden of cognitive decline in this population.

MATERIALS AND METHODS

This was a comparative observational study conducted in the Department of Neurology of a tertiary care medical institute. Fifty patients having Type 2 Diabetes Mellitus (T2DM) were included in this study based on predefined inclusion and exclusion criteria. Fifty age-matched healthy individuals were enrolled as the control group. The sample size was determined using the formula $N=(Z\alpha^2)\times SD^2/d^2$ calculated with the OPENEPI-3 version. The sample size was determined based on the number of cases in a pilot study done on the topic of cognitive dysfunction in patients with T2DM. Assuming a statistical power of 90% and a confidence interval of 95% the required sample size was 45 patients with T2DM; therefore, we included 50 cases of diabetes mellitus along with an equal number of age matched healthy individuals serving as the control group.

Group A: Fifty adults diagnosed with Type 2 Diabetes Mellitus.

Group B: Fifty age matched healthy individuals.

Demographic details such as age, gender as well as occupation was recorded. For the case group, the duration of diabetes and the specific antidiabetic medications being used were noted. The presence of coexisting medical conditions such as hypertension, asthma or any other systemic illnesses was also noted. A comprehensive general and systemic examination was carried out for all participants. Routine investigations, including blood sugar levels, complete blood count, and glycosylated hemoglobin, were performed in all cases. Cognitive function was assessed in all participants using the Mini-Mental State Examination (MMSE).[9] The MMSE evaluated parameters such as orientation, registration, attention and calculation, recall, and language skills. Scores were categorized to indicate normal cognition, mild cognitive impairment or significant cognitive dysfunction. After collecting data, the mean MMSE scores of Group A (patients with T2DM) and Group B (healthy controls) were compared to evaluate cognitive performance. Additional comparisons were made to identify any correlations between MMSE scores and factors such as duration of diabetes, glycemic control (HbA1c levels), and presence of co-morbidities.

Statistical analysis was performed using SPSS version 23.0 software. Quantitative data, such as MMSE scores, were presented as mean and standard deviation. Qualitative data, such as the incidence of cognitive dysfunction were presented in incidence and percentage tables. For comparisons of quantitative data between the two groups (Group A: T2DM patients and Group B: healthy controls) the chi-square test was applied. A p-value of less than 0.05 was considered statistically significant.

Inclusion Criteria

1. Diagnosed cases of Type 2 Diabetes Mellitus.
2. Age above 18 years.

3. Willingness to provide informed and written consent to participate in the study.
4. Equal number of healthy individuals enrolled as the control group.

Exclusion Criteria

1. Age less than 18 years.
2. Refusal to provide consent for participation.
3. Patients with conditions that may independently affect cognitive function, such as significant psychiatric illnesses or neurodegenerative diseases.
4. Patients on medications known to impair cognitive function.

RESULTS

The analysis of gender distribution of studied cases showed that there were 29 (58%) males and 21 (42%) females in group A whereas in group B there were 28 (56%) males and 22 (44%) females. Overall, there was a male preponderance in studied cases. However overall gender distribution was found to be comparable in both the groups without any statistically significant difference between study and control groups. [Table 1]

Majority of participants in both groups were in the 51-60 years age range, accounting for 40% (20 individuals) in Group A and 36% (18 individuals) in Group B. The next most common age group was 41-50 years, with 28% (14 individuals) in Group A and 26% (13 individuals) in Group B. The mean age of patients in group A and group B was 52.4 ± 10.8 years and 51.6 ± 11.1 years respectively. The mean age in both the groups was found to be comparable in both the groups with no statistically significant difference (P= 0.7157). [Table 2]

Most of the patients (42%) were having diabetes since more than 5 years to 10 years. 13 (26%) patients had T2DM of less than 5 years duration whereas 11 (22%) and 5 (10%) patients had diabetes for 11-15 years and more than 15 years respectively. [Table 3]

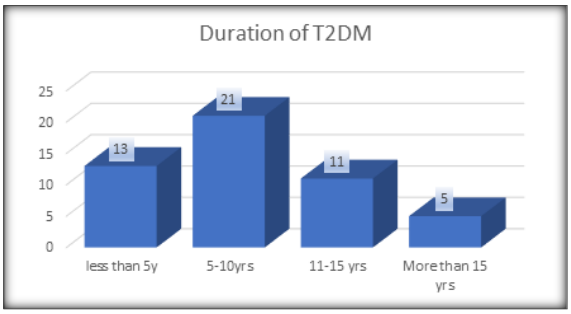

Figure 1: Duration of Type 2 Diabetes Mellitus in studied cases

In 26 (52%) cases there was no other co-morbidity other than T2DM. In 15 (30%) cases hypertension was also present in addition to T2DM. in 7 (14%) cases bronchial asthma was present and in 2 (4%) cases rheumatoid arthritis and psoriasis was present.

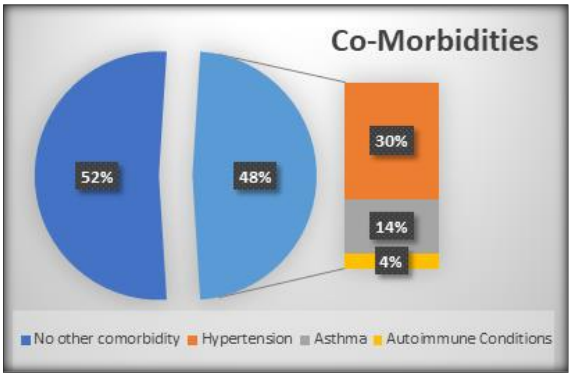

Figure 2: Presence of co-morbidities in studied cases.

The analysis of MMSE domain scores between Group A (individuals with T2DM) and Group B (healthy individuals) demonstrated statistically significant differences across most cognitive domains. In the orientation, attention/calculation, recall, language and as well as skill domains Group B scored higher compared to Group A. And the difference was found to be statistically significant (P<0.05). The registration domain showed minimal differences between the groups with Group A scoring 2.9 ± 0.5 and Group B scoring 3.0 ± 0.3 and this difference was not statistically significant (p = 0.2282). The total MMSE score was notably higher in Group B (27.9 ± 2.1) as compared to Group A (25.4 ± 2.2) and the difference was statistically highly significant. [Table 3]

The analysis of HbA1c levels in relation to glycemic control and MMSE scores among individuals with T2DM revealed a significant association between glycemic control and cognitive performance. Among those with good glycemic control (HbA1c < 7%) the mean MMSE score was 27.8 ± 2.1. Conversely, individuals with suboptimal or poor glycemic control (HbA1c > 7%) showed a lower mean MMSE score of 23.1 ± 2.5. Those with good glycemic control (HbA1c < 7%) were found to have better cognition as compared to those who had suboptimal glycemic control (HbA1c > 7%). This difference was found to be statistically highly significant (P < 0.0001). [Table 4]

The analysis of MMSE scores based on the duration of diabetes showed a declining trend in cognitive performance with increasing duration of the disease. Individuals with a diabetes duration of less than 5 years had the highest mean MMSE score of 26.8 ± 1.5, followed by those with a duration of 6-10 years and 11-15 years. Mean MMSE score was lowest for those with a duration greater than 15 years. The overall mean MMSE scores in studied cases was 25.4 ± 2.2. [Table 5]

There was a strong negative correlation between the duration of diabetes and cognitive function as assessed by MMSE scores. The correlation coefficient (R) was -0.9165 indicating an inverse relationship between durations of diabetes and Cognitive functions. This relationship was found to

be statistically highly significant (P< 0.00001). [Table 6]

Table 1: Gender Distribution of the studied cases

Gender	Group A (T2DM) - Number (%)	Group B (Healthy) - Number (%)
Male	29 (58%)	28 (56%)
Female	21 (42%)	22 (44%)
Total	50 (100%)	50 (100%)
P =1.00 (Not Significant)		

Table 2: Comparison of age distribution of studied cases

Age Group (years)	Group A (T2DM) - Number (%)	Group B (Healthy) - Number (%)
18-30	3 (6%)	4 (8%)
31-40	6 (12%)	7 (14%)
41-50	14 (28%)	13 (26%)
51-60	20 (40%)	18 (36%)
>60	7 (14%)	8 (16%)
Total	50 (100%)	50 (100%)
Mean Age	52.4 ± 10.8	51.6 ± 11.1
P = 0.7157 (Not Significant)		

Table 3: Comparison of cognitive functions in studied groups

MMSE Domain	Group A (T2DM) - Mean ± SD	Group B (Healthy) - Mean ± SD	95% CI	P-Value
Orientation	9.1 ± 1.2	9.8 ± 0.8	0.2952 to 1.1048	0.003*
Registration	2.9 ± 0.5	3.0 ± 0.3	-0.0636 to 0.2636	0.2282
Attention/Calculation	3.4 ± 0.7	3.8 ± 0.4	0.1737 to 0.6263	0.0007*
Recall	2.2 ± 0.9	2.8 ± 0.6	0.2964 to 0.9036	0.0002*
Language and related Skills	7.8 ± 1.1	8.5 ± 0.7	0.3341 to 1.0659	0.0003*
Total MMSE Score	25.4 ± 2.2	27.9 ± 2.1	1.4258 to 3.5742	0.0002*

Table 4: Correlation of HbA1c level and cognitive functions

HbA1c Category	HbA1c (%)	No Of cases	Glycemic Control	Mean MMSE Score (Mean ± SD)
Good Control	<7	22	Good	27.8 ± 2.1
Suboptimal/poor Control	> 7	28	Suboptimal	23.1 ± 2.5
P < 0.0001 (Significant) *				

Table 5: Correlation of Duration of diabetes and cognitive functions

Duration of Diabetes (years)	Mean MMSE Score (Mean ± SD)
<5	26.8 ± 1.5
6-10	26.5 ± 2.2
11-15	25.1 ± 2.4
>15	23.5 ± 2.7
Overall	25.4 ± 2.2

Table 6: Correlation coefficient for Duration of diabetes and cognitive functions

Parameter	Value
Correlation Coefficient (R)	-0.9165
P-Value	< 0.00001*
Correlation	Strong negative correlation

DISCUSSION

Cognitive dysfunction in Type 2 Diabetes Mellitus (T2DM) has emerged as an important area of research due to its substantial implications on overall disease management. Previous research has suggested that in cases of T2DM chronic hyperglycemia, insulin resistance and inflammation contribute to cognitive impairment.10 Prolonged hyperglycemia can lead to microvascular and macrovascular complications such as cerebral microangiopathy which is associated with cognitive decline. Another mechanism by which cognition is affected in these cases include insulin resistance and resultant neuronal dysfunction that may impair synaptic plasticity which is crucial for memory and learning. Additionally advanced glycation end products (AGEs) also have a detrimental effect on neural tissue which explains the observed deficits in specific cognitive domains among patients with T2DM.[11]

In this study MMSE domain scores between Group A (individuals with T2DM) and Group B (healthy individuals) demonstrated statistically significant differences across most cognitive domains including orientation, attention/calculation, recall, language and as well as skill domains. The registration domain showed minimal differences between the groups.

Shuba N et al conducted a cross-sectional study to assess cognitive function in individuals with diabetes mellitus.[12] For this purpose, the authors undertook a study comprising 50 diabetic patients and 50 age-matched non-diabetic controls. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE) and a battery of neuropsychological tests assessing memory, attention, and executive functions. The study found that diabetic patients had significantly lower MMSE scores compared to controls (mean score: 25.3 vs. 28.5, $p < 0.001$). Additionally, diabetic patients performed worse on tests of memory recall, attention, and executive function, with 40% exhibiting mild cognitive impairment compared to 12% of controls. On the basis of these findings, the authors concluded that diabetes mellitus is associated with impaired cognitive function, particularly affecting memory, attention, and executive abilities. Similar Cognitive dysfunction in cases of T2DM was also reported by the authors such as Kodl CT et al,[13] and Kim HG et al.[14]

We found a clear and significant link between glycemic control and cognitive performance in individuals with T2DM. People who maintained good glycemic control (HbA1C < 7%) consistently showed better cognitive abilities compared to those with poorly managed blood sugar levels (HbA1C > 7%). Fanfan Zheng et al conducted a prospective cohort study to investigate the association between HbA_{1c} levels, diabetes status, and cognitive decline in older adults.[15] For this purpose, the authors analyzed data from 5,189 participants aged 50 years and older from the English Longitudinal Study of Ageing, assessing their HbA_{1c} levels, diabetes status, and cognitive function over a 10-year follow-up period. The study found that higher HbA_{1c} levels were associated with a greater rate of cognitive decline, with each 1 mmol/mol increase in HbA_{1c} corresponding to a 0.012 standard deviation decrease in global cognitive z scores (95% CI -0.018, -0.006; $p<0.001$). Additionally, individuals with diabetes experienced a more rapid cognitive decline compared to those without diabetes, with a difference in global cognitive z scores of -0.06 (95% CI -0.10, -0.02; $p=0.002$). On the basis of these findings, the authors concluded that higher HbA_{1c} levels and diabetes are associated with accelerated cognitive decline in older adults. Similar correlation between HbA1c levels was also reported by the authors such as Yu ZB et al,[16] and Song J et al.[17]

In this study cognitive performance was observed to deteriorate progressively with the duration of diabetes. Individuals who had been living with the condition for a shorter period (Less than 5 years) displayed relatively better cognitive function as compared to those with longer disease durations showed greater cognitive impairment. Astrid C.J. Nooyens et al conducted a cohort study to investigate the association between type 2 diabetes and cognitive decline in middle-aged individuals.18 For this purpose, the authors undertook a study comprising 2,613 men and women aged 43–70 years from the Doetinchem Cohort Study, assessing cognitive function over a 5-year follow-up period. The study found that individuals with type 2 diabetes experienced a greater decline in cognitive function compared to those without diabetes, with an average additional decline of 0.2 points on a standardized cognitive test. On the basis of these findings, the authors concluded that type 2 diabetes is associated with accelerated cognitive decline in middle-aged men and women. Similar cognitive decline in cases of T2DM over a period of time was also reported by the authors such as Spauwen PJ et al,[19] and Zilliox LA et al.[20]

CONCLUSION

There was a significant association between Type 2 Diabetes Mellitus (T2DM) and cognitive dysfunction. Poor glycemic control (HbA1c > 7%) and longer diabetes duration correlated strongly with greater cognitive decline. The findings emphasize the importance of early detection and effective management of glycemic levels to mitigate cognitive impairment in T2DM patients. Regular cognitive assessments should be integrated into diabetes care to improve overall patient outcomes and quality of life.

Conflict of Interest: None.

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