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Impact of Glycated Hemoglobin (HbA1c) on cognitive functions in Type 2 diabetic patients

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Abstract. – OBJECTIVE: Diabetes mellitus is a highly challenging worldwide epidemic affecting the health of millions of people. This study investigates the impact of glycated hemoglobin (HbA1c) and duration of diabetes on cognitive functions in type 2 diabetic patients and evaluates whether high HbA1c or duration is more harmful to impair cognitive functions.

PATIENTS AND METHODS: In this study, 202 participants, 101 patients with type 2 diabetes mellitus (T2DM), and 101 age, gender, height, and weight-matched controlled subjects were enlisted. The HbA1c was determined using a clover analyzer, and cognitive functions were evaluated using "Cambridge Neuropsychological Test Automated Battery (CANTAB).

RESULTS: The results revealed that AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors, SWM Strategy, PRM Percent correct responses were meaningly delayed in the diabetic group as compared to the control group ($p < 0.0001$).

CONCLUSIONS: High HbA1c or uncontrolled DM and duration of diabetes cause cognitive function impairment. Moreover, the cognitive functions declined were significantly linked with the duration of the disease and high HbA1c. While treating diabetic patients, physicians must monitor the HbA1c level as reasonable glycemic control is vital to curtail the complications of DM, including cognitive function impairment.

Key Words:
Diabetes mellitus, Glycated hemoglobin, HbA1c, Cognitive functions.

Introduction

Diabetes mellitus (DM) throughout the world is becoming a threatening pandemic due to a rapid rise in population, aging[1], sedentary lifestyle[2], obesity, unplanned urbanization, industrialization, and environmental pollution[3,4]. Diabetes mellitus affects all the organs in the human body and accounts for the economic burden of patients and societies[5]. The present prevalence of DM is 463 million, out of which 374 million people are currently suffering from impaired glucose tolerance, while 232 million people are still unaware that they have a disease. This disease has caused 760 billion dollars in health expenditure[5].

The literature highlights that hyperglycemia and the duration of the DM are leading risk factors for multiple microangiopathic complications[6]. In uncontrolled diabetes, dysglycemia rapidly increases reactive oxygen species, and variations in signaling pathways cause various vascular dysfunctions[7]. In addition, it causes numerous physiological problems in all organs, including brain biology[8].

The brain is one of the targeted organs in diabetes mellitus, in which cognitive impairment is relatively subclinical and often ignored by patients and physicians. However, the nervous system is the most vulnerable human body and is susceptible to diabetic microvascular complications[9]. The biochemical and micro-angiopathic alterations in neuronal characteristics cause brain damage in the diabetic population[9,10].

The literature demonstrated that the duration of the disease is the prime cause of various complications of diabetes mellitus and mortalities[11]. There is debate in the scientific community that the development of multiple complications is mainly due to the duration of diabetes, but uncontrolled diabetes is also involved in various body function impairments. At the same time, cognitive functioning is not well acknowledged as a complication of DM, and the relationship of T2DM with cognition is less likely characterized. Moreover, it is unclear which one is more toxic, the duration of diabetes mellitus or high hyperglycemic due to increased glycated hemoglobin (HbA1c). Therefore, this study explores the im-

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pact of diabetes and HbA1c on cognitive dysfunction in T2DM patients and recognizes that either the high HbA1C or duration of DM is more toxic to damage the cognitive physiology.

Patients and Methods

In this matched case-controlled cross-sectional study, T2DM patients aged between 30-65 ys, BMI less than 30 kg/m^2, fasting blood glucose ≥7.0 mmol/lit, or HbA1c > 6.5% were recruited. The control group was free from chronic diseases, such as DM, hypertension, dyslipidemia, and cardiorespiratory conditions.

Exclusion Criteria

Subjects with BMI > 30 kg/m², diabetic patients with a known history of heart diseases, neuropathy, retinopathy, cerebrovascular diseases, malignancy, type 1 diabetic patients, abnormality in the vertebral column, were excluded from the study. Participants who use cigarettes, shisha, alcohol, or other addictive, and suffering from obesity, anemia, difficulty in vision, attention, psychiatric problems, seizures, musculoskeletal disorders, and disturbed sleep history were excluded from the study[12,13].

Considering the inclusion and exclusion criteria, we recruited 101 type-2 diabetic patients. The diabetic patients were matched with 101 control subjects for age, height, weight, BMI, ethnicity, and socioeconomic status. The healthy control subjects were university staff, including technicians and clerical staff. There were no substantial variances in the anthropometric means between the groups (Table I).

Measurements of HbA1c

HbA1c was measured using a device Clover A1c system (Inforpia, Kyunggi, Korea), an automated boronate affinity assay to determine the percentage of HbA1c % in blood[14]. The Clover A1c system is well acknowledged in the measurement of HbA1c both in clinical medicine and research. In addition, HbA1c is a reliable indicator of glycemic measures for diagnosing diabetes mellitus[15].

Measurements of Cognitive Functions

The neuropsychological assessment was executed using the Cambridge Neuropsychological Test Automated Battery (CANTAB) to perform different tests. It consisted of various tasks distributed in four different modules, but the investigator chose five to evaluate different modules in all subjects. A senior lab technologist and research team member briefed both experimental and control subjects on how the entire cycle of the test would take place. The subjects were informed that these tests required around 30 to 35 minutes to be completed. Subjects were sat comfortably on a chair with a 25 cm distance between the subject and screen, then instructed to respond by pressing the buttons in the press pad with the dominant hand's index finger.

The subjects were instructed about the techniques, explained the procedure, and asked to perform the cognitive tasks in a relaxed mood. The cognitive function test parameters were based on the cognitive domains attention switching task (AST), pattern recognition memory (PRM), choice reaction time (CRT), special working memory (SWM), and motor screening (MOT). The cognitive function tests parameters, including AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Motor screening mean latency, SWM Between errors, SWM Strategy, and PRM Percent correct, were recorded[13].

Statistical Analysis

The results were analyzed by using the Statistical Package for Social Sciences, SPSS. Ar-

Table I. Demographic and biochemical features of type 2 diabetic patients and control group.

Parameters	Control group (N = 101) mean ± SD	Diabetic group (N = 101) mean ± SD	*p*-value
Age (years)	54.88 ± 6.76	55.50 ± 5.99	0.489
Height (cm)	166.11 ± 6.04	166.02 ± 6.44	0.919
Weight (kg)	68.21 ± 5.77	68.84 ± 4.64	0.653
BMI (kg/m^2)	24.34 ± 1.33	25.04 ± 2.11	0.319
HbA1c (%)	6.01 ± 0.24	8.19 ± 1.48	< 0.001*
Fasting Blood Glucose (mmol/lit)	5.21 ± 0.11	9.12 ± 3.12	< 0.001*

*Significance level.

monk, NY, USA. Mean + SD is reported for quantitative variables like cognitive parameters. A two-independent sample *t*-test was employed to compare the variances between diabetic and control groups with cognitive functions and then in the stratified analysis, i.e., duration of diabetes (up to 5 years, 6-10 years, and more than 10 years), and HbA1c less than eight and more than eight. Pearson Correlation was also applied to identify the complete and stratified relationship of HbA1c and duration of DM with cognitive function parameters. A p-value < 0.05 was considered statistically significant.

Results

Demographic and Biochemical Characteristics

For this study, 202 subjects, 101 patients with T2DM, and 101 age, gender, height, and weight-matched control subjects were enlisted. The mean age of the T2D patients was 55.50 ± 5.99 ys, and for the control group was 54.88 ± 6.76 ys (Table I). The male participants were 71 (70.29%), and females were 30 (29.71%). The mean duration of disease was 17 ± 7.64 ys, ranging from 1-30 ys. However, among 101 control males were 70 (69.30%), and females were 31 (30.70%). No substantial variance was noticed for the age, height, weight, and BMI of diabetics and controls (Table I). The HbA1c and fasting blood glucose were significantly increased in the diabetic group compared to the control group (Table I).

Cognitive Functions Parameters

Motor Screening Task shows response speed and pointing precision that displayed as latency and mean error. Pattern Recognition Memory test expressed as a percentage of correct patterns while Spatial Working Memory measures mistakes and strategy. Attention switching task outcome assessed by response latency, and choice reaction time outcome was determined by latency, correct and incorrect response.

The cognitive functions were compared between the diabetics and controls. The results showed that attention-switching task (AST), AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors and SWM Strategy were significantly delayed in the diabetic group as compared to the control group ($p < 0.001$), whereas PRM Percent correct was significantly decreased in the diabetic group compared to the control group ($p < 0.001$) (Table II).

Analysis Based on the Duration of Diabetes

Duration of Diabetes up to 5 Years (Cognitive Tests)

The cognitive functions were compared between the diabetics and matched controls. The mean difference between the AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors, and SWM Strategy was delayed in the diabetic group as compared to the control group ($p < 0.001$). The PRM percent correct were meaningfully reduced in the control group compared to the diabetic group ($p < 0.001$). Results are presented in Table III.

Table II. Cognitive functions for type 2 diabetic patients and control group.

Parameters	Control group N = 101 mean ± SD	Diabetic group N = 101 mean ± SD	*p*-value
AST Mean correct latency (ms)	503.65 ± 122.83	938.52 ± 163.64	< 0.001*
AST Mean correct latency (congruent) (ms)	471.30 ± 107.55	887.95 ± 471.30	< 0.001*
AST Mean correct latency (incongruent) (ms)	498.98 ± 126.82	997.73 ± 166.51	< 0.001*
CRT Mean correct latency (ms)	418.47 ± 71.78	720.43 ± 218.89	< 0.001*
MOT Mean latency (ms)	522.15 ± 47.27	1031.89 ± 331.24	< 0.001*
PRM Percent correct (%)	96.48 ± 3.77	75.16 ± 11.71	< 0.001*
SWM Between errors	4.50 ± 3.52	40.50 ± 17.98	< 0.001*
SWM Strategy	27.18 ± 2.88	36.57 ± 5.11	< 0.001*

AST: Attention switching task; CRT: Choice reaction time, PRM: Pattern recognition memory; SWM: Special working memory, ms: millisecond. *Significance level.

Table III. Cognitive functions data for type 2 diabetic patients with a duration of disease up to 5 years, compared with their matched controls.

Parameters	Control group N = 14 mean ± SD	Diabetic group N = 14 mean ± SD	*p*-value
AST Mean correct latency (ms)	562.08 ± 144.27	855.28 ± 178.60	< 0.001*
AST Mean correct latency (congruent) (ms)	491.74 ± 103.87	799.92 ± 173.66	< 0.001*
AST Mean correct latency (incongruent) (ms)	515.51 ± 124.82	920.54 ± 194.74	< 0.001*
CRT Mean correct latency (ms)	436.30 ± 69.39	658.64 ± 271.19	< 0.001*
MOT Mean latency (ms)	527.53 ± 46.77	996.09 ± 418.08	< 0.001*
PRM Percent correct (%)	95.13 ± 4.69	75.59 ± 10.57	< 0.001*
SWM Between errors	4.43 ± 3.97	39.79 ± 18.67	< 0.001*
SWM Strategy	28.07 ± 2.65	35.64 ± 5.34	< 0.001*

AST: Attention switching task; CRT: Choice reaction time, PRM: Pattern recognition memory; SWM: Special working memory, ms: millisecond. *Significance level.

Duration of Diabetes 6-10 Years (Cognitive Tests)

The cognitive functions were compared between the diabetics with 6-10 years duration and matched controls. The mean difference between the AST mean correct latency, AST mean correct latency (congruent), AST mean correct latency (incongruent), MOT mean latency, SWM between errors, and SWM strategy were significantly delayed in the diabetic group as compared to the control group ($p < 0.001$), whereas, the PRM percent correct was decreased considerably in people with diabetes related to control group ($p = 0.001$). Results are presented in Table IV.

Duration of Diabetes >10 Years (Cognitive Tests)

The cognitive functions were compared between the diabetics with a duration of disease > 10 years and matched controls, the mean difference between the AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors and SWM Strategy were significantly delayed in the diabetic group as compared to the control group ($p < 0.001$), whereas, PRM Percent correct were significantly decreased in the diabetic group compared to the control group ($p < 0.001$). Results are presented in Table V.

Analysis Based on HbA1c < 8 (Cognitive Tests)

When the cognitive functions were compared between the people with diabetes with HbA1c < 8 and matched controls, the mean difference between the AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors and

Table IV. Cognitive functions data for type 2 diabetic patients with duration of disease between 6-10 years, compared with their matched controls.

Parameters	Control group N = 14 mean ± SD	Diabetic group N = 14 mean ± SD	*p*-value
AST Mean correct latency (ms)	520.79 ± 145.5	950.63 ± 178.25	< 0.001*
AST Mean correct latency (congruent) (ms)	474.17 ± 125.92	897.73 ± 179.64	< 0.001*
AST Mean correct latency (incongruent) (ms)	510.76 ± 130.33	1011.36 ± 186.08	< 0.001*
CRT Mean correct latency (ms)	424.73 ± 70.87	730.85 ± 172.88	0.171
MOT Mean latency (ms)	534.86 ± 46.46	1083.81 ± 336.40	< 0.001*
PRM Percent correct (%)	96.57 ± 3.61	77.24 ± 13.13	< 0.001*
SWM Between errors	27.27 ± 3.09	39.96 ± 19.50	< 0.001*
SWM Strategy	27.27 ± 3.90	36.38 ± 5.74	< 0.001*

AST: Attention switching task; CRT: Choice reaction time, PRM: Pattern recognition memory; SWM: Special working memory, ms: millisecond. *Significance level.

Table V. Cognitive functions data for type 2 diabetic patients with duration of disease >10 years, compared with their matched controls.

Parameters	Control group N = 61 mean ± SD	Diabetic group N = 61 mean ± SD	*p*-value
AST Mean correct latency (ms)	506.26 ± 118.14	952.46 ± 150.33	< 0.001*
AST Mean correct latency (congruent) (ms)	474.05 ± 104.65	903.99 ± 158.39	< 0.001*
AST Mean correct latency (incongruent) (ms)	496.21 ± 121.30	1009.64 ± 148.25	< 0.001*
CRT Mean correct latency (ms)	423.74 ± 71.85	730.17 ± 224.55	< 0.001*
MOT Mean latency (ms)	523.44 ± 47.77	1017.97 ± 310.13	< 0.001*
PRM Percent correct (%)	96.51 ± 3.57	74.18 ± 11.38	< 0.001*
SWM Between errors	4.36 ± 3.59	40.85 ± 17.44	< 0.001*
SWM Strategy	27.21 ± 3.01	36.87 ± 4.81	< 0.001*

AST: Attention switching task; CRT: Choice reaction time, PRM: Pattern recognition memory; SWM: Special working memory, ms: millisecond. *Significance level.

SWM Strategy delayed in the diabetic group as compared to the control group ($p < 0.001$), whereas, PRM Percent correct were decreased in the diabetic group compared to the control group ($p < 0.001$). Results are presented in Table IV.

Analysis Based on HbA1c > 8 (Cognitive Tests)

The cognitive functions were compared between the people with diabetes with HbA1c >8 and matched controls. The mean difference between the AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors and SWM Strategy were significantly delayed in the diabetic group as compared to the control group ($p < 0.001$), However, PRM Percent correct were significantly reduced in the diabetic group as compared to the control group ($p < 0.001$). Results are presented in Table VII.

Overall Correlation Analysis (HbA1c and Cognitive function Parameters)

A positive correlation was identified between increased HbA1c and increased delayed in AST Mean correct latency (r= 0.570, $p < 0.001$), AST Mean correct latency (congruent) (r= 0.563, $p < 0.001$), AST Mean correct latency (incongruent) (r= 0.598, $p < 0.001$), CRT Mean correct latency (r= 0.465, $p < 0.001$), MOT Mean latency (r= 0.561, $p < 0.001$), SWM Between errors (r= 0.650, $p < 0.001$) and SWM Strategy (r= 0.575, $p < 0.001$), whereas, HbA1c had an inverse relation with Percent correct trials (r= -0.434, $p < 0.001$), and PRM Percent correct (r= -0.610, $p < 0.001$).

Correlation Analysis (Duration of Diabetes and Cognitive Function Parameters)

A significant positive correlation was found due to the increased duration of diabetes, and

Table VI. Cognitive functions data for type 2 diabetic patients with HbA1c < 8, compared with their matched controls.

Parameters	Control group N = 58 mean ± SD	Diabetic group N = 58 mean ± SD	*p*-value
AST Mean correct latency (ms)	503.54 ± 119.8	942.24 ± 158.29	< 0.001*
AST Mean correct latency (congruent) (ms)	470.46 ± 105.61	891.62 ± 162.46	< 0.001*
AST Mean correct latency (incongruent) (ms)	492.20 ± 121.87	999.91 ± 163.62	< 0.001*
CRT Mean correct latency (ms)	420.13 ± 72.37	714.04 ± 198.99	< 0.001*
MOT Mean latency (ms)	524.53 ± 47.04	1003.27 ± 281.09	< 0.001*
PRM Percent correct (%)	96.50 ± 3.62	76.50 ± 10.54	< 0.001*
SWM Between errors	4.40 ± 3.54	37.29 ± 18.41	< 0.001*
SWM Strategy	27.12 ± 2.98	36.02 ± 5.09	< 0.001*

AST: Attention switching task; CRT: Choice reaction time, PRM: Pattern recognition memory; SWM: Special working memory, ms: millisecond. *Significance level.

Table VII. Cognitive functions data for type 2 diabetic patients with HbA1c > 8, compared with their matched controls.

Parameters	Control group N = 43 mean ± SD	Diabetic group N = 43 mean ± SD	*p*-value
AST Mean correct latency (ms)	509.58 ± 129.94	933.50 ± 172.35	< 0.001*
AST Mean correct latency (congruent) (ms)	473.28 ± 115.57	883.01 ± 177.68	< 0.001*
AST Mean correct latency (incongruent) (ms)	492.94 ± 129.94	994.80 ± 172.23	< 0.001*
CRT Mean correct latency (ms)	425.02 ± 74.89	729.05 ± 245.35	< 0.001*
MOT Mean latency (ms)	527.61 ± 47.82	1070.48 ± 389.03	< 0.001*
PRM Percent correct (%)	96.38 ± 3.99	73.35 ± 13.02	< 0.001*
SWM Between errors	4.35 ± 3.67	44.77 ± 16.27	< 0.001*
SWM Strategy	27.14 ± 2.95	37.33 ± 5.08	< 0.001*

AST: Attention switching task; CRT: Choice reaction time, PRM: Pattern recognition memory; SWM: Special working memory, ms: millisecond. *Significance level.

MOT mean latency (r= 0.231, $p = 0.020$), and the remaining cognitive parameters were not significant ($p > 0.05$), respectively.

Discussion

Diabetes mellitus (DM) gradually affects various body organs and systems with multi-systemic complications. Presently, DM has a high priority rank on the global health program due to being a pandemic and a deathtrap to human health and worldwide economies[4]. The present study results demonstrated an association between the duration of disease, glycemic state, and impaired cognitive functions. The overall result reveals that the duration of diabetes, high HbA1c, or uncontrolled diabetes mellitus impairs cognitive functions.

Dybjer et al[16] studied diabetes associated with cognitive function, processing swiftness, and executive working abilities. They reported that long-standing diabetes was related to more significant cognitive deficits. Moreover, the associations were more robust in old-aged and physically less active individuals. Monette et al[17] conducted a meta-analysis based on twenty-five studies and concluded that T2DM leads to mild to moderate decline in cognitive capabilities. Similarly, Kálcza-Jánosi et al[18] demonstrated that type 1 and T2DM were linked with delayed performance in several cognitive domains.

In another meta-analysis, Palta et al[19] identified mild to moderate impairments in cognitive performance in people with diabetes relative to non-diabetic controls. Moreover, the motor function was most significantly affected, while the attention and concentration were exhibited the smallest effect size.

Alkethiri et al[20] determined the cognitive tests in patients with T2DM. The authors reported that Attention switching task (AST), AST congruent score, AST incongruent score were significantly higher in patients with poorly-controlled DM. Similarly, in the present study, we found that AST Mean correct latency, AST Mean correct latency (congruent), AST Mean correct latency (incongruent), CRT Mean correct latency, MOT Mean latency, SWM Between errors, and SWM Strategy was significantly delayed in the diabetic group. However, the pattern recognition memory (PRM) percent correct (number of correct responses) was considerably lower in people with diabetes than in the control group.

These studies' findings support the hypothesis that T2DM is a leading cause of cognitive functions impairment. In another study, Garfield et al[21] reported the cause related to incidence with vascular dementia (VD), Alzheimer's dementia (AD), hippocampal volume (HV), white matter hyperintensity (WMH), and cognitive function decline. The authors found that prediabetes and DM enhanced the risks of cognitive functions decline. Similarly, Tonoli et al[22] demonstrated that T1DM causes a decrease in cognitive performance related to non-diabetic controls. The findings suggest that cognitive functions declined was more severe in adults, indicating that age and diabetes duration contribute to the cognitive function impairment.

The present study findings also support the hypothesis between the HbA1c level, disease duration, and impaired cognitive function in T2DM. Moreover, the logistic regression revealed that high HbA1c was linked with an increased risk for poor cognitive function and indicated neuronal damage in a diabetic patient. Thus, our results

provide evidence that in diabetic patients, high HbA1c may be an essential clue to find the adverse effect on brain biology.

Possible Mechanism Linked to T2DM and Cognitive Functions Impairment

The average young adult brain is about 2% of the body weight and utilizes 20% of the body glucose (120 gm per day)[23]. The possible mechanism linked to T2DM and cognitive function is the duration and uncontrolled hyperglycemia. White matter hyperintensities were linked with impaired cognitive functions in people with an extended period of diabetes and uncontrolled T2DM. It has also been reported by Mankovsky et al[24] that cerebral small vessel disease is a causal mechanism of cognitive dysfunction.

Uncontrolled glycemia, high HbA1c is linked with delayed and declined cognitive functions and is a reliable predictor of poor cognitive function in patients with T2DM. Fluctuation in hyperglycemia gradually causes neuronal injury[25]. It can also be due to oxidative stresses, which disrupt neuronal functions. Oxidative stress plays an essential role in pathophysiologic changes of hyperglycemia-induced accentuation of ischemic injury and glucose neurotoxicity[26]. A single event of severe hyperglycemia may result in overt impairment of neurons. Moreover, the mismatch between altered glucose transporters (GLUTs) and swift blood glucose level changes can cause neuronal damage and cognitive functions impairment during glucose fluctuations[26].

Study Strengths and Limitations

There are a few limitations of this study. First, other confounding factors may have influenced cognitive function parameters such as genetics, environmental pollution, etc. Second, due to cross-sectional design, causality could not be established. Third, we were unable to classify further the diabetic patients based on HbA1c. Despite few potential limitations, this study has several strengths. First, the study participants were well matched based on their age, gender, weight, height, BMI, ethnicity, and educational and socioeconomic status. Second, this study quantifies cognitive dysfunction in adults with type T2DM across various cognitive domains. Third, the study findings are consistent with other studies of diabetic patients. Fourth, the results support the hypothesis that duration of diseases and poor glycemic control was related to cognitive function impairment in individuals with T2DM. Therefore, it is essential to maintain standard glycemic control to minimize cognitive function impairment in diabetic patients.

Conclusions

The findings conclude that the duration of diabetes and high HbA1c or poor glycemic control impairs cognitive functions in type 2 diabetic patients. The association between diabetes mellitus and cognitive function remains essential because of their potential clinical implications. Considering the present study findings, clinicians should understand the possibility of cognitive changes impacting T2DM management or require referral for neurological assessment. Cognitive function screening with other routine examinations should be carried out periodically to identify and manage abnormal cognitive functions in diabetic patients mainly the children and young adults. Standard glycemic control may improve cognitive functions and the overall health of diabetic patients. To reach a better conclusion, a sizeable sample-sized study would be conducted further to investigate the association between T2DM, duration of disease, glycemic control, and cognitive functions.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Institutional Review Board Statement

The study was approved by the "Institutional Review Board, Ethics Committee, College of Medicine, King Saud University, Riyadh, Saudi Arabia (Ref. E-18-3293)". A written consent was obtained from the participants.

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Authors' Contribution

HBM: research conceptualization, data collection, literature review, and manuscript writing. SAM, FAR overall supervision, review, and editing of the manuscript. IMUM, supports data collection. All authors have read and approved the manuscript.

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