THE ASSOCIATION BETWEEN HBA1C LEVELS AND COGNITIVE FUNCTION IN GERIATRIC PATIENTS WITH TYPE 2 DIABETES MELLITUS

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THE ASSOCIATION BETWEEN HBA1C LEVELS AND COGNITIVE FUNCTION IN GERIATRIC PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is a significant global health concern, particularly in Indonesia. Recent studies suggest a link between T2DM and increased risk of cognitive impairment. However, the relationship between glycaemic control, as measured by HbA1c levels, and cognitive function in elderly diabetic patients remains unclear and requires further investigation. **Objective:** To investigate the association between HbA1c levels and cognitive impairment in geriatric patients with T2DM. **Method:** This observational analytic study with a cross-sectional approach was conducted at the Internal Medicine Clinic of Gotong Royong Hospital in Surabaya, Indonesia. Thirty-six geriatric T2DM patients were recruited using consecutive sampling. HbA1c levels were obtained from medical records, and cognitive function was assessed using the Montreal Cognitive Assessment-Indonesian Version (MoCA-INA). Data were analyzed using SPSS software, including normality tests and Spearman correlation analysis. **Result:** The majority of participants were female (77.8%) and aged 60-69 years (47.2%). Eleven participants (50%) of the 22 T2DM geriatric patients with good-controlled HbA1c levels had poor cognitive function (scores < 26). Meanwhile, among the 14 participants with poorly controlled HbA1c levels, 11 (78.6%) had poor cognitive function, and only 3 (21.4%) maintained good cognitive function. A significant negative correlation was found between HbA1c levels and MoCA-INA scores (p=0.013, r=-0.410), indicating that higher HbA1c levels were associated with lower cognitive function scores. **Conclusion:** This study demonstrates a significant relationship between HbA1c levels and cognitive function in elderly T2DM patients. Poor glycemic control is associated with a higher likelihood of cognitive impairment. These findings emphasize the importance of maintaining good glucose management to potentially prevent cognitive decline in this population. Further research with larger sample sizes and longitudinal designs is recommended to elucidate this relationship and its clinical implications.

Keywords: Type 2 Diabetes Mellitus, Geriatric, HbA1C, Cognitive function

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INTRODUCTION

Diabetes mellitus, particularly type 2 (T2DM), is a significant global health concern and a major burden among non-communicable diseases in Indonesia. Indonesia ranks among the top countries for diabetes prevalence according to the International Diabetes Federation.[1] The increasing incidence of diabetes, especially when uncontrolled, is associated with a higher risk of chronic complications, including cognitive impairment. As the global population ages, understanding the long-term consequences of T2DM becomes increasingly crucial. One area of particular concern is the potential impact of T2DM on cognitive function in older adults.

HbA1c plays a crucial role in the diagnosis and management of diabetes mellitus. It provides a reliable measure of chronic glycemia, reflecting average blood glucose levels over the previous 2-3 months and also correlates with the risk of long-term diabetes complications.[2,3] American Diabetes Association (ADA) recommends an HbA1c target of <7% for nonpregnant adults with diabetes, with more or less stringent goals for specific populations.[3]

T2DM is associated with numerous chronic complications affecting various organs, including the brain and nervous system. These complications frequently lead to impairments in cognitive function, particularly in memory and attention domains. Previous studies have demonstrated that individuals with T2DM exhibit poorer cognitive abilities and more frequent abnormalities in brain imaging results compared to non-diabetic individuals.[4,5] Recent studies suggest that individuals with diabetes have a substantially higher risk of developing various types of dementia, including Alzheimer's and vascular dementia.[6,7,8]

Cognitive function plays a crucial role in maintaining quality of life. As individuals age, cognitive decline can significantly impact their daily functioning and independence.[9] The Montreal Cognitive Assessment (MoCA) is a widely used standardized instrument for evaluating cognitive function.[10] Its Indonesian adaptation, the MoCA-Indonesian Version (MoCA-INA), provides a comprehensive assessment of various cognitive domains, including executive function, visuospatial abilities, language, attention and concentration, memory, calculation, and orientation. The MoCA-INA yields a maximum score of 30, with scores below 26 indicating cognitive impairment. This test offers several advantages, notably its quick and easy administration, coupled with a broad evaluation of cognitive domains that enables the detection of mild cognitive impairment. Furthermore, multiple studies have demonstrated that the MoCA-INA

exhibits high sensitivity and specificity in identifying mild cognitive dysfunction, attributed to its more extensive coverage of cognitive domains compared to other tools such as the Mini-Mental State Examination (MMSE). These characteristics make the MoCA-INA a valuable tool for cognitive assessment in both clinical and research settings, particularly in Indonesian populations.[11]

Cognitive impairment in elderly individuals with T2DM is a complex issue with significant implications for patient care and quality of life. The association between glycemic control, as measured by Glycated Hemoglobin (HbA1c) levels, and cognitive function in this geriatric population has been a subject of ongoing research, with some studies indicating a link between elevated HbA1c and increased risk of cognitive decline.[7,12] This research aims to explore the connection between HbA1c levels and cognitive impairment in elderly patients with type 2 diabetes, contributing to a better understanding of the long-term implications of diabetes on cognitive health, may inform more comprehensive management strategies and early identification of patients at higher risk of cognitive decline, allowing for timely interventions.

METHOD

This research was conducted at the Internal Medicine Clinic of Gotong Royong Hospital in Surabaya, Indonesia, using an observational analytic design with a cross-sectional approach. We assessed glycemic control through HbA1c levels and evaluated cognitive function using the Montreal Cognitive Assessment-Indonesian Version (MoCA-INA) instrument. The population consisted of geriatric patients with T2DM. Participants were recruited from the Internal Medicine Clinic of Gotong Royong Hospital in Surabaya using consecutive sampling, with the inclusion criteria included (1) patients aged over 60 years with T2DM who undergo HbA1c level assessment at the Internal Medicine Clinic of Gotong Royong Hospital and (2) willing to participate in the study by signing the informed consent form. Patients with anemia; have received a blood transfusion within the last 2 to 3 months; have a history of stroke, head trauma, or brain tumors; previously diagnosed with dementia, Alzheimer's disease, or Parkinson's disease, and suffering from depression were excluded. The independent variable was HbA1c levels, obtained from medical records, while the dependent variable was cognitive impairment, assessed using the MoCA-INA instrument. The study took place from July

14 to November 10, 2023. Data analysis was conducted using SPSS software, including normality tests and Spearman correlation analysis. The researchers aimed to determine if there was a significant correlation between HbA1c levels and cognitive impairment in elderly patients with type 2 diabetes mellitus, with p value less than 0.05.

RESULT

Table 1. Distribution of the participants

Characteristics	Frequency (n)	Percentage (%)
Gender		
Male	8	22,2%
Female	28	77,8%
Age group (years old)		
60 – 69	17	47,2%
70 – 79	15	41,7%
≥ 80	4	11,1%
HbA1c levels		
≤ 7,5	22	61,1%
> 7,5	14	38,9%
MoCA-INA score		
≥ 26	14	38,9%
< 26	22	61,1%

A total of 36 participants who met the eligible were studied. A higher number of female participants was seen (77.8%) and aged between 60-69 years (47.2%). Most participants (61.1%) had good glycemic control with HbA1c levels ≤7.5%, while 38.9% had HbA1c levels below 7.5%. Cognitive function assessment using the MoCA-INA instrument revealed that 61.1% of participants had cognitive impairment (scores <26), while 38.9% had normal cognitive function (scores ≥26).

Table 2. Distribution of HbA1c levels based on gender

Gender	HbA1c levels		Total
	≤ 7,5	> 7,5	
Male	3 (37,5%)	5 (62,5%)	**8 (100%)**
Female	19 (67,9%)	9 (32,1%)	**28 (100%)**

Among male participants, 62.5% had poor HbA1c control (> 7.5), while 37.5% had good HbA1c control (≤ 7.5). In contrast, the majority of female participants (67.9%) had good HbA1c control, with only 32.1% showing poor control. This analysis showed that male participants were more likely to have poor glycemic control and cognitive impairment compared to female participants.

Table 3. Distribution of HbA1c levels based on age group

Age	HbA1c levels		Total
	≤ 7,5	> 7,5	
60 – 69	10 (58,9%)	7 (41,1%)	**17 (100%)**
70 – 79	11 (73,3%)	4 (26,7%)	**15 (100%)**
≥ 80	1 (25%)	3 (75%)	**4 (100%)**

58.9% of participants had good HbA1c control (≤ 7.5), while 41.1% showed poor control (> 7.5) in the 60-69 age group. Among those aged 70-79, 73.3% maintained good HbA1c control, with only 26.7% showing poor control. For participants over 80 years old, the trend reversed, with 75% exhibiting poor HbA1c control and only 25% maintaining good control.

Table 4. Distribution of MoCA – INA score based on gender

Gender	MoCA-INA score		Total
	< 26	≥ 26	
Male	7 (87.5%)	1 (12,5%)	**8 (100%)**
Female	15 (53,6%)	13 (46,4%)	**28 (100%)**

For male participants, 87.5% (7 out of 8) demonstrated poor cognitive function (MoCA-INA < 26), while only 12.5% (1 out of 8) showed good cognitive function (MoCA-INA ≥ 26). Among female participants, 53.6% (15 out of 28) exhibited poor cognitive function, while 46.4% (13 out of 28) displayed good cognitive function.

Table 5. Distribution of MoCA – INA score based on age group

Age group (years)	MoCA-INA score		Total
	< 26	≥ 26	
60 – 69	9 (52,9%)	8 (47,1%)	**17 (100%)**
70 – 79	9 (60%)	6 (40%)	**15 (100%)**
≥ 80	4 (100%)	0 (0%)	**4 (100%)**

In the 60-69 age group, 52.9% of participants had poor cognitive function (< 26), while 47.1% maintained good cognitive function (≥ 26). This result worsened in the 70 – 79 age group, with 60% of participants had poor cognitive function. Notably, all participants (100%) aged 80 years old and older exhibited poor cognitive function.

Table 6. The association between HbA1c levels and MoCA-INA score

HbA1c levels	MoCA-INA score		Total
	< 26	≥ 26	
≤ 7,5	11 (50%)	11 (50%)	**22 (100%)**
> 7,5	11 (78,6%)	3 (21,4%)	**14 (100%)**

Among the 22 participants with good-controlled HbA1c levels (≤ 7.5), 11 (50%) had poor cognitive function (scores < 26) and 11 (50%) had good cognitive function (scores ≥ 26). Meanwhile, among the 14 participants with poorly controlled HbA1c levels, 11 (78.6%) had poor cognitive function, and only 3 (21.4%) maintained good cognitive function. These results indicated that participants aged 80 years old and older had the highest proportion of poor glycaemic control and cognitive impairment.

Table 7. The statistical analysis of the association between HbA1c levels and MoCA-INA score

Variable	Med	Min	Max	p value	r
HbA1c levels	7,1	5	14	0,013	-0, 410
MoCA-INA score	24,5	13	29		

Statistical analysis using the Spearman correlation test revealed a significant negative correlation between HbA1c levels and MoCA-INA scores (p=0.013, r=-0.410). This indicates a moderate strength correlation where higher HbA1c levels are associated with lower cognitive function scores.

DISCUSSION

Cognitive impairment in Type 2 Diabetes Mellitus (T2DM) patients is a complex phenomenon involving multiple interconnected pathophysiological mechanisms.[13] At the core of this relationship is the dysfunction of insulin signaling, which is considered the primary driver of cognitive decline in diabetic patients. Insulin and insulin-like growth factors (IGFs) play crucial roles in maintaining optimal brain function. When insulin signalling is impaired, it leads to a cascade of detrimental effects on brain health.[4,14] One of the key consequences of insulin signalling dysfunction is the disruption of glucose transport in the brain. Glucose transporter 4 (Glut4), responsible for mediating glucose uptake in brain tissue, becomes less effective, resulting in an energy imbalance that disturbs normal brain functions. This metabolic disturbance is further exacerbated by the overall reduction in glucose metabolism that occurs with aging, contributing to age-related cognitive decline and diminished executive functions.[4,14,15]

Oxidative stress emerges as another significant factor in the pathogenesis of cognitive impairment in T2DM. Hyperglycemia and insulin resistance increase oxidative stress, leading to the activation of proinflammatory networks, organelle dysfunction, and the production of neurotoxic fibrils. Additionally, the accumulation of advanced glycation end products (AGEs) due to chronic hyperglycemia further contributes to oxidative stress, cell damage, and the promotion of amyloid oligomer aggregation, which is associated with Alzheimer's disease neurotoxicity.[16,17]

The inflammatory component of T2DM also plays a crucial role in cognitive decline. Insulin resistance is associated with elevated levels of inflammatory cytokines such as IL-6, IL-1β, TNF-α, and C-reactive protein. This chronic low-grade inflammation contributes to neurodegenerative processes and exacerbates cognitive impairment. Furthermore, dysregulated lipid metabolism leads to the production of cytotoxic lipids that can cross the blood-brain barrier and initiate neurodegeneration, a process known as lipotoxicity.[4,18,19]

Vascular complications represent another significant mechanism underlying cognitive impairment in T2DM. Chronic microvascular injury, caused by persistent hyperglycemia and hyperinsulinemia, leads to endothelial cell proliferation, intima thickening, and fibrosis. These changes result in narrowed blood vessel lumens and an increased risk of microhemorrhages, compromising cerebral blood flow and

potentially contributing to cognitive decline. Moreover, diabetes compromises the integrity of the blood-brain barrier (BBB), increasing its permeability and disrupting neurovascular coupling. This BBB dysfunction is linked to altered astrocytic function and reduced nitric oxide availability, further exacerbated by oxidative stress from AGEs.[4,19,20]

Structural brain changes are also observed in T2DM patients, including diffuse brain atrophy and an increased risk of small-vessel disease. Specific regional volume abnormalities, particularly in the temporal lobes, hippocampus, and amygdala, have been noted. These structural alterations likely contribute to the cognitive deficits observed in diabetic patients.[17,18]

These various mechanisms interact and contribute to cognitive decline in T2DM patients, moreover, complicated by the high demands of diabetes self-management. Patients must engage in regular glucose monitoring, medication administration, and lifestyle adjustments, making any cognitive dysfunction particularly impactful on their ability to manage diabetes effectively. This creates a vicious cycle where poor diabetes control can further exacerbate cognitive issues.[4,15]

In conclusion, the mechanisms underlying cognitive impairment in T2DM patients are multifaceted and interconnected. They involve insulin signalling dysfunction, impaired glucose metabolism, oxidative stress, inflammation, vascular complications, and structural brain changes. Understanding these mechanisms is crucial for developing effective strategies to prevent and manage cognitive decline in diabetic patients. Future research should focus on elucidating the precise molecular pathways involved and identifying potential therapeutic targets to mitigate the cognitive consequences of T2DM.

This study found a significant relationship between HbA1c levels and cognitive function in elderly patients with type 2 diabetes mellitus. The results suggest that poor glycemic control, as indicated by higher HbA1c levels, is associated with a higher likelihood of cognitive impairment in this population.

Despite some limitations, such as the inability to exclude all factors affecting HbA1c levels and not considering the duration of diabetes, this research contributes to the understanding of how diabetes control impacts cognitive function in elderly patients. The findings emphasize the importance of good glucose management in preventing cognitive decline. Further research with larger sample sizes and longitudinal designs is recommended to further elucidate this link and its implications for clinical practice.

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