

## COGNITIVE DECLINE IN TYPE 2 DIABETES MELLITUS: A COMPREHENSIVE CROSS-SECTIONAL ASSESSMENT

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### Abstract

**Introduction:** Diabetes mellitus (DM) is a metabolic condition with implications affecting various body systems, encompassing the peripheral nervous system, kidneys, eyes, and, notably, the central nervous system. While cognitive impairments have been acknowledged in DM, particularly in types 1 and 2, comprehensive research remains sparse. Episodes of both hypoglycemia and hyperglycemia have been associated with cognitive deficits. The underlying pathophysiological processes, however, remain a subject of ongoing investigation. Moreover, there exists an apparent gap in consensus concerning diagnostic, therapeutic, and preventive approaches for managing cognitive dysfunctions in DM.

**Materials and Methods:** This prospective, randomized comparative study occurred at the Outpatient department, Diabetes Mellitus Clinic, Department of General Medicine, Eeshan Hospital, Hyderabad, Telangana, from March 2022 to February 2023. The cohort consisted of 51 outpatients diagnosed with type-II diabetes mellitus from the diabetic clinic, juxtaposed with 58 age-similar non-diabetic controls. Participants were randomly chosen, adhering to predefined criteria post-obtaining explicit written consent. After demographic data acquisition, participants underwent neurocognitive assessment via the Standardized Mini-Mental State Examination (SMMSE).

**Results:** The participant age averaged  $54.6 \pm 7.24$  years. There were no marked statistical disparities concerning gender allocation ( $p=0.255$ ), educational attainment ( $p=0.087$ ), or place of residence ( $p=0.380$ ) between the diabetic subgroup and control. Contrastingly, type-II diabetic patients exhibited a significantly heightened prevalence of cognitive impairment relative to the control group ( $p=0.047$ ;  $p<0.05$ ). In granular detail, of the diabetic subset, 62 subjects registered SMMSE scores beneath the 26 threshold. In contrast, in the control group, 48 participants recorded scores under the same threshold, delineating them as cognitively challenged.

**Conclusion:** Mild to moderate cognitive deficits manifested more frequently in people with type-II diabetes than non-diabetic people. Crucially, the degree of cognitive deviation correlated with the diabetes duration. This study underscores the merit of promptly integrating the Standardized Mini-Mental State Examination into routine check-ups for type-II diabetes patients to unearth early indicators of cognitive deterioration.

**Key Words:** Diabetes mellitus, cognitive impairment, Standardized Mini-Mental State Examination.

## INTRODUCTION

Diabetes mellitus is one of the most significant global health concerns. It encompasses diverse metabolic disorders typified by persistent hyperglycemia and glucose intolerance. Often analogized to "accelerated aging," diabetes increases vulnerability to degenerative ailments.<sup>1</sup> Beyond its immediate metabolic repercussions, diabetes mellitus (DM) adversely affects the peripheral nervous system and pivotal organs like the kidneys, eyes, and the brain. Intriguingly, the cognitive implications associated with DM have yet to be thoroughly investigated.<sup>2</sup> While type 1 and type 2 DM are recognized for potential cognitive deficits, the intricate pathophysiological connections, especially surrounding hypoglycemia and hyperglycemia, remain inadequately understood.<sup>3</sup> Current scientific literature offers varied interpretations, resulting in an ambiguous understanding of causative relationships. Furthermore, comprehensive guidelines for diagnosing, treating, and preventing DM-induced cognitive impairments are conspicuously absent.<sup>4</sup> However, the discernible cognitive challenges a segment of DM patients faces, which impede their everyday functioning, cannot be overlooked.<sup>5</sup> Given this, there is an exigent need to study and understand cognitive dysfunctions in the diabetic population rigorously.

This study endeavors to demarcate the attributes of cognitive dysfunctions in DM patients, shed light on contributory factors, and scrutinize prevailing theories concerning their onset.

## MATERIALS AND METHODS

- **Study Design:** A prospective, randomized, comparative study.
- **Study Duration:** March 2022 to February 2023
- **Study Location:** Department of General Medicine, Eeshan Hospital, Hyderabad, Telangana
- **Sample Size:** 109 participants (51 diagnosed with Type 2 diabetes, 58 non-diabetic controls)

The research was conducted at the Outpatient department, Diabetes Mellitus Clinic, Eeshan Hospital. The participants included 51 outpatients with type-II diabetes mellitus from the diabetic clinic, juxtaposed with 58 age-similar non-diabetic controls.

#### **Inclusion Criteria:**

- Diagnosis of type-II diabetes mellitus with a minimum duration of 2 years
- Age range: 45-65 years
- Representation from both genders

#### **Exclusion Criteria:**

- Concurrent medical conditions such as stroke, hypertension, liver diseases, chronic renal ailments, or cardiac issues
- Consumption of medications like sedatives, hypnotics, or anti-depressants
- Known psychological or neurological disorders.
- History of substance abuse, including alcoholism and smoking

Participants from both groups, chosen based on the above criteria, provided informed consent. After collecting demographic information, all underwent neuro-cognitive evaluations using the Standardized Mini-Mental State Examination (SMMSE). This tool comprises 12 time-bound questions assessing diverse cognitive domains. For evaluations, a 30-point grading system was employed; a score beneath 26 suggested impairments. Grading 20-25, 10-19, and 0-9 symbolized mild, moderate, and severe cognitive deficits, respectively. Statistical analysis was carried out using the Chi-square test to pinpoint associations.

## **RESULTS**

The aggregate mean age of the participants was  $54.6 \pm 7.24$  years. Upon comparative analysis, both groups displayed no remarkable statistical discrepancies concerning gender distribution ( $p=0.255$ ), educational background ( $p=0.087$ ), or domiciliary settings ( $p=0.380$ ). However, a marked cognitive decline was more evident amongst type-II diabetic individuals than in the control cohort ( $p=0.047$ ;  $p<0.05$ ). Specifically, within the diabetic subset, 62 participants registered SMMSE scores beneath the 26 mark. Simultaneously, 48 participants from the control set scored under the same threshold, designating them as cognitively challenged.

	<b>Case</b>	<b>Control</b>
No cognitive Impairment	19	30
cognitive Impairment	32	28

**Table 1: Comparison of cognitive function between cases and control.**

Out of these 32 cases, 22 had mild cognitive impairment (scores 20-25), 10 had moderate impairment (scores 10-19) and none had severe impairment (scores 0-9).

Characteristics	Case (N)		Control (N)		P Value
	Male	Female	Male	Female	
Gender	25	26	24	34	0.321
	45-55	56-65	45-55	56-65	
Age (years)	30	21	39	19	0.140
	<10th	>10th	<10th	>10th	
Education	25	26	36	23	0.090
	Rural	Urban	Rural	Urban	
Domicile	17	34	24	34	0.410

**Table 2: Patient Demographics**

	Case	Control
20-25 Mild Cognitive impairment	22	18
10-19 Moderate cognitive impairment	10	6
Severe cognitive impairment	0	0

**Table 3: Severity grading of cognitive dysfunction**

Factors affecting cognitive impairment of cases	N
<b>Gender</b>	
Male	11
Female	20
<b>Educational level</b>	
<10th	22
>10th	9
<b>Domicile</b>	
Urban	17
Rural	14
<b>Duration of diabetes</b>	
<5 years	14
>5 years	17

**Table 3: Factors affecting cognitive impairment of cases**

	No cognitive impairment	cognitive impairment
Case	20	31
Control	30	28

**Table 4: Cognitive scores of cases and controls**

	20-25 Mild cognitive impairment	10-19 Moderate cognitive impairment	0-9 Severe cognitive impairment
Case	21	10	0
Control	18	6	0

**Table 5: Severity of cognitive impairment.**

Cognitive impairment appeared significant in females, with a statistical significance of ( $p=0.001$ ;  $p<0.01$ ). Urban dwellers also exhibited heightened cognitive deficits ( $p=0.003$ ;  $p<0.01$ ). Notably, cognitive dysfunction was more prevalent among participants with less formal education ( $p<0.05$ ). The tenure of type-II diabetes mellitus diagnosis was influential; those with diabetes persisting for over five years displayed an increased incidence of cognitive impairment ( $p=0.025$ ;  $p<0.05$ ). Nonetheless, parameters such as age, medication patterns, and glycemic regulation did not exert any statistically significant effect on the outcomes ( $p>0.05$ ).

## DISCUSSION

Mild cognitive impairment (MCI) is steadily gaining acknowledgment as a potential harbinger of graver conditions like dementia. Its evaluation, however, is intricate due to the diverse cognitive domains involved, such as orientation, memory, calculation, language, attention, and construction. While state-of-the-art diagnostic tools like MRI and PET scans offer precision, their exorbitant costs render them unsuitable for regular screenings.<sup>6</sup> The Mini-Mental State Examination (MMSE) stands out as a globally endorsed primary screening tool for cognitive disturbances. Its optimized version, the Standardized Mini-Mental State Examination (SMMSE), boasts superior inter-rater consistency and a swift 10-minute administration duration.<sup>7</sup>

Our findings underscore a potent link between type-II diabetes mellitus and cognitive decline. Intriguingly, our cohort's cognitive dysfunction incidence was elevated by 14% among the type-II diabetic segment, echoing results from multiple international investigations.<sup>8</sup> Our decision to focus on the 45-65 age group was deliberate, considering that the typical onset age for type-II diabetes hovers around 45. Venturing beyond 65 years might intermingle neurodegenerative alterations innate to aging, thereby obscuring the findings. We meticulously weeded out potential participants with histories of smoking, alcoholism, substance abuse, hypertension, or other systemic maladies, cognizant of their roles in enhancing cognitive impairment risks and the subsequent potential for bias.<sup>9</sup>

Consistent with another Indian-centric study, our results spotlighted an inverse relationship between educational accomplishments and cognitive assessment scores. The augmented risk among female participants may mirror some regional sections' comparatively diminished literacy rates. Urban inhabitants constituted a substantial fraction of the cognitively impaired, possibly reflecting the escalating diabetes incidence in urban landscapes.<sup>10</sup> A palpable inverse relationship between cognitive proficiency and diabetes duration echoed the U.S.-based Nurses' Health Study insights. The study did not uncover a clear interrelationship between cognitive deficits and glycemic control. This could be traced back to our reliance on antecedent Fasting Blood Sugar metrics instead of the all-encompassing HbA1C, a constraint rooted in budgetary considerations.<sup>11</sup>

Nevertheless, the study's design carries inherent limitations. The constrained timeline limited our sample size to a mere 50 participants, highlighting the imperative for more expansive research endeavors to validate the increased susceptibility of type-II diabetes patients to cognitive disturbances. Future investigations might benefit from incorporating HbA1C evaluations to understand patient glycemic control better.

### CONCLUSION

A conspicuously augmented prevalence of mild to moderate cognitive dysfunction was observed among type-II diabetes patients vis-à-vis their non-diabetic counterparts. The diabetes diagnosis's duration emerged as a pivotal determinant. Drawing from these insights, it is posited that integrating the Standardized Mini-Mental State Examination into the standard screening regime for type-II diabetic outpatients could be instrumental in the early detection of cognitive anomalies.

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