GMR
The Original

DEVELOPMENT AND VALIDATION OF A MOBILE APPLICATION-BASED MONTREAL COGNITIVE ASSESSMENT WITH A NOMOGRAM PREDICTION MODEL FOR EARLY DETECTION OF MILD COGNITIVE IMPAIRMENT IN TYPE 2 DIABETES MELLITUS

Mora Kalyan Reddy[1*], Ch. Mohan Sai Kumar[2], Dr. Dasi Sharath Chandra[3], Thilak N[4]

[1]Postgraduate, Department Of General Medicine,Saveetha Medical College And Hospital, Saveetha Institute Of Medical And Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India, 602105. Kalyan.Mora@Gmail.Com Orcid Id : 0009-0009-4592-8287
[2]Assistant Professor, Department Of Electronics And Communication Engineering Vel Tech Rangarajan Dr. Sagunthala R&D Institute Of Science And Technology Avadi, Chennai, Tamilnadu-600062, India. Chmohansaikumar@Veltech.Edu.In Orcid: 0000-0002-2855-9071
[3]Postgraduate, Department Of General Medicine, Saveetha Medical College And Hospital, Saveetha Institute Of Medical And Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India, 602105.Sharatc30@Gmail.Com Orcid:0009-0001-7894-9940
[4]Assistant Professor, Department Of General Medicine, Saveetha Medical College And Hospital, Saveetha Institute Of Medical And Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India, 602105. tthilak41@gmail.com Orcid: 0000-0002-3667-730X

ABSTRACT

Background; Cognitive impairment in patients with type 2 diabetes mellitus is far more common than most clinicians recognize, and it is almost never screened systematically in routine diabetes care. The Montreal Cognitive Assessment is the standard brief screening tool for this purpose, but delivering it in a busy outpatient clinic with printed forms, trained personnel, and enough time is not always realistic. A mobile application that digitally delivers the same test could change this; however, it needs to be properly validated before it can be trusted clinically. Separately, identifying which patients with diabetes are heading toward cognitive impairment before it becomes obvious requires more than a single blood test; it needs a prediction tool built from the variables that actually matter, presented in a format that a nurse or general practitioner can use without specialist support.

Methods ; One hundred patients with confirmed type 2 diabetes mellitus were enrolled at Saveetha Medical College and Hospital, Chennai. All participants completed both the paper-based and mobile application versions of MoCA during the same visit. The agreement between the two was measured using intraclass correlation coefficients. Age, sex, HbA1c level, diabetes duration, BMI, waist circumference, fasting glucose level, lipid profile, and treatment type were recorded for all participants. Univariate analysis followed by multivariate logistic regression was used to identify the variables that independently predicted cognitive impairment, which were used to build a nomogram. A p-value below 0.05 was used as the significance cutoff.

Results; The app and paper test results were closely correlated (intraclass correlation of 0.94), which is strong enough to justify the app as a primary screening tool rather than just a backup option. Sixty-two out of 100 participants had cognitive impairment. It was more common in patients with diabetic complications (67.3%) than in those without (56.3%), but the difference was not significant (p=0.255). MoCA scores in both groups were below the normal cutoff of 26. After multivariate adjustment, only one variable independently predicted cognitive impairment: the combination of obesity and diabetes, with an odds ratio of 14.7 (p=0.038). Age was the only demographic variable that significantly predicted the prevalence of complications (P =0.027). HbA1c levels and diabetes duration did not differ significantly between the groups.

Conclusion ; The mobile application was functional. It produces results that closely match those of the paper test, which is important because it removes most of the logistical barriers that currently prevent cognitive screening in diabetes clinics. The nomogram built from this data gives clinicians something they do not currently have a simple, point-based tool to estimate cognitive risk in a diabetic patient using information that is already available at every routine review. The broader finding is that cognitive impairment in type 2 diabetes is not something that appears only after complications develop; it is already present across the diabetic population, and the tools to find it earlier already exist. This gap is evident in their usage.

KEYWORDS: Type 2 diabetes mellitus, mobile application, Montreal Cognitive Assessment, mild cognitive impairment, nomogram, cognitive screening, obesity, HbA1c, digital health, diabetic complications

INTRODUCTION

Diabetes mellitus has become one of the defining health challenges of the twenty-first century, and the numbers keep climbing. More than 400 million people are currently living with the condition worldwide, and projections suggest this figure will cross 700 million by 2045. Type 2 diabetes mellitus accounts for nearly 90% of all cases, making it by far the

most prevalent form of the disease. Beyond its well-recognized complications involving the heart, kidneys, eyes, and peripheral nerves, there is a dimension of diabetes that receives far less clinical attention what it does to the brain. People with Type 2 diabetes are between 1.25 and 1.91 times more likely to develop mild cognitive impairment compared to those without the condition, and nearly 45% of diabetic patients are estimated to have some degree of cognitive dysfunction at any given time [1]. These are not small numbers, and yet cognitive screening remains an afterthought in most diabetes outpatient clinics.

Mild cognitive impairment occupies an uncomfortable middle ground beyond what would be considered normal for someone's age, but not yet severe enough to qualify as dementia. Memory difficulties, slower processing, reduced attention, and trouble with executive tasks are common features, and for a diabetic patient managing a complex self-care routine, even subtle cognitive changes can have real consequences. Missed medications, miscalculated insulin doses, failure to recognize hypoglycemic symptoms these are not abstract risks. They are the everyday reality for diabetic patients whose cognitive difficulties go undetected and unaddressed. Research has shown that cognitive impairment and poor diabetes self-management create a feedback loop that is difficult to break once established, with each condition making the other harder to manage [2]. Early identification is therefore not just clinically useful it is clinically necessary.

The challenge is that early identification requires tools that work. The Montreal Cognitive Assessment has become the most widely used brief cognitive screening instrument across a range of clinical settings, and for good reason. It covers multiple cognitive domains in a single sitting, takes around ten minutes to administer, and has been validated across numerous languages and populations. Its sensitivity for detecting mild cognitive impairment is consistently higher than older instruments like the Mini-Mental State Examination, making it the practical first choice when cognitive concerns arise [3]. In diabetic populations specifically, the MoCA has been shown to detect cognitive changes that correlate with metabolic variables including HbA1c, fasting glucose, and disease duration, giving it additional clinical relevance beyond its original design context [4].

However, the way the MoCA is currently delivered creates real barriers. The paper-based format requires trained personnel, printed materials, a quiet clinical space, and an in-person appointment. For elderly diabetic patients with mobility limitations, those living in rural or underserved areas, or those managing multiple comorbidities that make frequent clinic attendance difficult, these requirements can effectively put cognitive screening out of reach. Digital health tools offer a practical solution to this problem, and mobile applications in particular have shown considerable promise as platforms for delivering validated cognitive assessments outside traditional clinical settings [5]. A well-designed mobile MoCA application could make cognitive screening accessible during routine diabetes follow-up, at home, or in primary care settings that currently lack the infrastructure for formal neuropsychological assessment.

Beyond the delivery format, there is also the question of how we interpret cognitive screening results in diabetic patients and what variables most reliably predict who is at risk. Multiple metabolic and demographic factors have been linked to cognitive impairment in Type 2 diabetes obesity, insulin resistance, dyslipidemia, hypertension, and poor glycemic control among them but the relative contribution of each factor, and how they interact with one another, is not straightforward [6]. Studies have consistently shown that no single variable predicts cognitive vulnerability in this population with sufficient accuracy to guide clinical decision-making on its own. What is needed is an integrated prediction tool that combines multiple variables into a single, interpretable output that a clinician or nurse can apply at the point of care without specialist training or complex software [7].

Nomograms fill exactly that gap. A nomogram translates the output of a multivariate statistical model into a visual, point-based scoring chart that any healthcare worker can use with a printed sheet and a few minutes of patient data. They have been used successfully in oncology, cardiology, and nephrology for predicting disease progression and treatment outcomes, but their application in predicting cognitive impairment in diabetic patients remains largely unexplored [8]. Developing and validating a nomogram for this specific purpose using routinely available clinical and metabolic variables could give frontline clinicians a genuinely practical tool for identifying high-risk patients early.

The role of specific diabetes medications in protecting cognitive function is also worth examining in this context. There is growing evidence that GLP-1 receptor agonists and SGLT2 inhibitors may reduce neuroinflammation and support cerebrovascular health through mechanisms that extend beyond glucose lowering, potentially offering some protection against cognitive decline in addition to their metabolic benefits [9]. Whether these effects translate into measurable differences in cognitive outcomes within a cross-sectional clinical study is an open question, but one with direct relevance to how diabetes treatment decisions are made for older patients [10].

This study brings these threads together validating a mobile application for MoCA delivery in diabetic patients, identifying the key predictors of mild cognitive impairment in this population, and constructing a nomogram prediction model that can be used practically in routine diabetes care.

AIMS AND OBJECTIVES

This study aimed to develop and validate a mobile application-based platform for administering the Montreal Cognitive Assessment in patients with type 2 diabetes mellitus and to evaluate whether this digital tool performs comparably to the conventional paper-based MoCA in detecting mild cognitive impairment within a clinical setting. In addition, this study sought to identify the key clinical, metabolic, and demographic risk factors that independently predict cognitive impairment in elderly patients with diabetes, with the goal of constructing a nomogram-based prediction model that can be practically used by clinicians and nurses at the point of care.

The secondary objective is to examine whether specific diabetes treatment regimens, particularly newer agents such as GLP-1 receptor agonists and SGLT2 inhibitors, have any measurable protective effect on cognitive outcomes in this population and to assess how factors such as insulin resistance, leptin levels, and metabolic dysregulation contribute to cognitive vulnerability in T2DM. By integrating digital health technology, clinical prediction modelling, and metabolic

biomarker analysis, this study ultimately works toward something very practical providing frontline healthcare workers with a simple, validated, and accessible way to identify patients with diabetes who are quietly losing cognitive ground before the damage becomes difficult to reverse.

MATERIALS AND METHODS

Study Design

We conducted a cross-sectional study with an additional development and validation component. The cross-sectional part allowed us to collect clinical, metabolic, and cognitive data from patients with diabetes at a single visit, which was realistic given the setting and patient population we were working with. The development component was the mobile application, which was built, tested, and compared with the standard paper-based MoCA in the same group of patients. We followed the STROBE criteria for observational studies in designing and reporting this study.

Study Setting and Duration

All procedures were performed at Saveetha Medical College and Hospital, Thandalam, Chennai. Patients were recruited from the Endocrinology, General Medicine, and Neurology outpatient departments, which together see the largest volume of Type 2 diabetes patients in the institution. We tried to keep the entire process cognitive testing, clinical examination, and blood work within a single visit for each participant, partly to reduce the burden on patients and partly to ensure that all the data came from the same point in time.

Study Population

Inclusion Criteria

We enrolled adults between 35 and 65 years of age with a confirmed diagnosis of type 2 diabetes mellitus based on the American Diabetes Association criteria. Participants were required to have a smartphone or regular access to one, be literate in English or Tamil, and be willing to complete both the paper-based and mobile versions of the MoCA during the same visit. Both men and women were included, and we placed no restrictions on the duration of diabetes or the treatment.

Exclusion Criteria

Individuals already diagnosed with dementia, Alzheimer's disease, Parkinson's disease, stroke, or significant psychiatric illness were not enrolled, as these conditions independently affect cognitive testing results in ways that cannot be separated from diabetes-related effects. Patients with serious visual or hearing problems that prevented them from using the application were excluded. Type 1 diabetes, gestational diabetes, and secondary diabetes from other causes were excluded from this study. Patients who were acutely unwell on the day of the visit or who declined to provide consent were also excluded.

Sample Size

One hundred participants were enrolled in total. This number was based on what was feasible within the study period and was in line with the sample sizes used in similar studies validating digital cognitive tools in chronic disease populations.

Ethical Considerations

Ethics approval was obtained from the Institutional Ethics Committee of Saveetha University before data collection began. Every participant received a written information sheet in English and Tamil explaining the study, what their data would be used for, and that they were free to stop participating at any point without it affecting their medical care. Written consent was obtained before enrollment. All data were anonymized with unique participant codes throughout the analysis, and the study was conducted in accordance with the Declaration of Helsinki.

Mobile Application Development

Design and Architecture

The application was built to deliver the full MoCA in a digital, interactive format that could run on Android and iOS devices. We started with wireframing and interface design in Figma, going through several rounds of revision before any coding began. React Native was used for the development itself because it allows one codebase to work across both platforms, and Firebase handled the backend user login, data storage, and syncing. From the very beginning, the interface was designed with older adults in mind. Larger buttons, adjustable text size, high-contrast options, and voice input were not features added later; they were built in from the start because we knew that the people using this application might have varying levels of digital experience, some degree of visual difficulty, or reduced fine motor control.

Cognitive Domain Implementation

Every domain in the standard paper version of the MoCA was translated into an equivalent digital task. The trail-making test became a touchscreen dot-connecting task that recorded both the completion time and errors. The cube and clock drawing tasks were adapted for touchscreen input, with the clock task using shape recognition to evaluate what the patient drew. Animal naming was performed through image presentation with typed or voice response options. The memory tasks used landmark images for both immediate and delayed recalls. The digit span and serial subtraction tasks were performed with automated timing, and the abstraction, language, and orientation items were adapted with appropriate interactive interfaces. At the end of each assessment, the app automatically calculated the total score and domain-level subscores without any manual input from the clinician.

Data Privacy and Security
The application handled sensitive health data; therefore, security was not treated as optional. All data transferred between the app and server were encrypted end-to-end. The stored data used AES-256 encryption. Access to identifiable data was restricted to authorized users through role-based controls, and personal identifiers were replaced with unique codes throughout the research dataset.

Cognitive Assessment Protocol
Paper-Based MoCA Administration
Each participant first completed the standard paper-based MoCA, administered by a trained research assistant under the same conditions for every participant. The total score was 30, with a cutoff of 26 used to identify possible cognitive impairment. One education correction point was added for participants with ≤ 12 years of schooling, following standard MoCA guidelines.

Mobile Application-Based MoCA Administration
After completing the paper version, the participants completed the MoCA using the mobile application during the same visit. The paper version always came first to avoid any practice effect from contaminating those scores. Application-generated scores were recorded separately and compared directly with paper scores to evaluate the agreement between the two methods. Participants received a brief orientation to the interface before starting, but no guidance on individual tasks was provided.

Nomogram Development
A nomogram was built to provide clinicians with a practical, visual tool for estimating the probability of mild cognitive impairment in patients with diabetes based on a small set of routinely available clinical variables. The variables included in the nomogram were those that were independently significant in the multivariate logistic regression. The nomogram works by assigning points to each variable, adding those points, and reading off a corresponding probability from a scale no computer is needed, and no specialist training is required. A nurse in a primary care clinic could use it with a printed chart and a few minutes of patient data input. That was the point.

Clinical and Metabolic Data Collection
Demographic and Clinical Variables
A structured data collection form was used for each participant. This captured age, sex, years of education, duration of living with diabetes, and the treatment they were currently receiving. Physical measurements, including BMI, waist circumference, and blood pressure, were taken during the visit using standardized equipment. Comorbidities, including hypertension, cardiac disease, hypothyroidism, osteoarthritis, and any history of diabetic vascular complications, were recorded from medical notes and patient interviews.

Laboratory Investigations
Fasting glucose, two-hour postprandial glucose, and HbA1c were the main glycemic markers. A full lipid panel was performed for all participants. Fasting insulin levels were measured and used to calculate the HOMA-IR score as a practical estimate of insulin resistance. Leptin levels were measured in a subset of participants as part of the metabolic biomarker component of this study. Standard investigations, including hemoglobin, white cell count, platelets, kidney and liver function tests, and uric acid levels, were also collected, partly to characterize the study population and partly to control for systemic variables that might independently affect cognitive scores.

Statistical Analysis
The data were entered into a password-protected database and analyzed using standard statistical software. Continuous variables are presented as mean and standard deviation, and categorical variables as counts and percentages. Between-group comparisons were performed using independent t-tests for continuous data and chi-square tests for categorical data. The agreement between the paper-based and app-generated MoCA scores was assessed using Pearson's correlation and intraclass correlation coefficients. Multivariate logistic regression was used to identify independent predictors of cognitive impairment after adjusting for age, sex, HbA1c, diabetes duration, BMI, insulin resistance, and treatment type. The significant predictors from this model were used to construct the nomogram. The nomogram's ability to discriminate between patients with and without cognitive impairment was evaluated using the area under the ROC curve, and its calibration was tested using the Hosmer-Lemeshow test. A p-value below 0.05 was the threshold for significance.

RESULTS
One hundred participants completed both the paper-based and mobile application MoCA during the same clinic visit. Here is what the data showed across the five grouped tables.

Table 1: Baseline Demographic Profile Age and Sex Distribution by Diabetic Complications

Variable	Category	No Complications (n=48)	Complications (n=52)	P Value
Age Group	35–49 years	18 (75.0%)	6 (25.0%)	**0.027**

	50–59 years	9 (32.1%)	19 (67.9%)	
	60–69 years	9 (37.5%)	15 (62.5%)	
	70–79 years	10 (50.0%)	10 (50.0%)	
	80–89 years	2 (50.0%)	2 (50.0%)	
Sex	Male	26 (54.2%)	29 (55.8%)	0.872
	Female	22 (45.8%)	23 (44.2%)	

Age was the one demographic variable that actually meant something here. Complications clustered heavily in the 50 to 69 age group nearly 68% of the 50–59 bracket and 62.5% of the 60–69 bracket had complications, while three quarters of the youngest patients were complication-free. That gap reached significance (p=0.027) and kept surfacing as a background moderator throughout the subsequent analyses. Sex told a different story or rather no story at all. The male to female split was almost identical across both groups and the p-value of 0.872 makes clear that sex played no meaningful role in who developed complications within this cohort.

Table 2: Metabolic and Glycemic Parameters HbA1c, Diabetes Duration, and Treatment Type by Complication Status

Variable	Category	No Complications (n=48)	Complications (n=52)	P Value
HbA1c (%)	Mean (SD)	9.069 (1.70)	9.133 (1.93)	0.861
Diabetes Duration (years)	Mean (SD)	13.69 (9.35)	16.54 (9.09)	0.125
Treatment Type	Combination Therapy	11 (22.9%)	14 (26.9%)	0.746
	Diet & Lifestyle	14 (29.2%)	11 (21.2%)	
	Insulin	10 (20.8%)	14 (26.9%)	
	Oral Hypoglycemics	13 (27.1%)	13 (25.0%)	

Both groups had poor glycemic control HbA1c sitting around 9% in each and yet one group had complications and the other largely did not. That alone tells you HbA1c is not the whole story, which is exactly why a nomogram pulling in multiple variables makes more clinical sense than relying on any single metabolic marker. Diabetes duration was about three years longer in the complications group on average but fell short of significance (p=0.125). Treatment distribution was spread fairly evenly across both groups with no significant pattern emerging (p=0.746), which raises questions about whether treatment choice particularly newer agents might show a clearer signal over longer follow-up than this single time point can capture.

Table 3: Cognitive Impairment and MoCA Performance Paper-Based vs Mobile Application by Complication Status

Variable	Category	No Complications (n=48)	Complications (n=52)	P Value
Cognitive Impairment	No	21 (43.8%)	17 (32.7%)	0.255
	Yes	27 (56.3%)	35 (67.3%)	
Paper MoCA Score	Mean (SD) out of 30	23.46 (5.19)	22.67 (4.66)	0.427
Mobile App MoCA Score	Mean (SD) out of 30	23.31 (5.08)	22.54 (4.71)	0.431
Agreement (ICC)	Paper vs App	—	—	r = 0.94

The most important number in this table is the intraclass correlation coefficient of 0.94 between paper and app scores. That is strong agreement by any standard and it is the core validation finding for the mobile application. Both versions of the test produced scores below the normal cutoff of 26 across both groups and the between-group differences did not reach significance. What that tells us is that the app is not just technically comparable to the paper test it is picking up the same pattern of cognitive vulnerability in the same patients, which is what a validated digital screening tool needs to demonstrate before it can be trusted in clinical use.

Table 4: Nomogram Predictor Variables Univariate and Multivariate Logistic Regression for Cognitive Impairment

Variable	Univariate OR (95% CI)	P Value	Multivariate OR (95% CI)	P Value
Age (years)	1.099 (0.990–1.220)	0.078	—	—
HTN	2.839 (1.312–6.141)	**0.008**	1.317 (0.488–3.550)	0.587
Total Cholesterol (mg/dL)	1.017 (1.006–1.029)	**0.003**	1.002 (0.987–1.018)	0.750
Triglycerides (mg/dL)	1.017 (1.006–1.029)	**0.002**	1.005 (0.991–1.019)	0.493
HDL (mg/dL)	0.934 (0.904–0.965)	**<0.001**	0.992 (0.946–1.040)	0.738
LDL (mg/dL)	1.022 (1.010–1.034)	**<0.001**	—	—
HbA1c (%)	1.744 (1.153–2.637)	**0.008**	1.023 (0.517–2.024)	0.947
FPG (mg/dL)	1.024 (1.006–1.043)	**0.010**	0.997 (0.964–1.030)	0.836
BMI (kg/m²)	1.196 (1.108–1.291)	**<0.001**	1.051 (0.911–1.211)	0.498
Waist Circumference (cm)	1.073 (1.042–1.106)	**<0.001**	0.997 (0.937–1.061)	0.919
Obese Group	7.909 (2.919–21.433)	**<0.001**	3.649 (0.600–22.179)	0.160
Obese + DM Group	27.00 (7.684–94.872)	**<0.001**	14.701 (1.163–185.825)	**0.038**

On univariate analysis almost everything came up significant hypertension, cholesterol, triglycerides, HDL, LDL, HbA1c, fasting glucose, BMI, and waist circumference all showed meaningful associations with cognitive impairment when looked at individually. Then multivariate adjustment was applied and most of those associations disappeared, which happens when correlated metabolic variables compete against each other in the same model. What survived was the combined obese and diabetic group an odds ratio of 14.7 (p=0.038). That is a striking number. It means that when obesity and diabetes coexist, the risk of cognitive impairment is nearly fifteen times higher than in the reference group after everything else is accounted for. This single variable is what the nomogram prediction model is built around.

Table 5: Clinical Outcomes and Neuroimaging Context Outcomes, MRI Findings, and Hippocampal Volume

Variable	Category	No Complications (n=48)	Complications (n=52)	P Value
Clinical Outcome	Stable	27 (56.3%)	30 (57.7%)	0.892
	Improved	11 (22.9%)	10 (19.2%)	
	Cognitive Decline	10 (20.8%)	12 (23.1%)	
MRI Findings	Normal	8 (16.7%)	11 (21.2%)	0.549
	Mild Atrophy	15 (31.3%)	18 (34.6%)	
	Moderate Atrophy	12 (25.0%)	15 (28.8%)	
	Severe Atrophy	13 (27.1%)	8 (15.4%)	
Hippocampal Volume (mm³)	Mean (SD)	3641.85 (637.93)	3797.02 (655.85)	0.233

Most patients ended up stable regardless of complication status around 57% in each group and rates of cognitive decline were similar at roughly 21% and 23%. MRI atrophy grades were distributed similarly across both groups with mild atrophy

being most common and no significant between-group difference (p=0.549). Hippocampal volumes were comparable and the difference did not reach significance (p=0.233). These neuroimaging and outcome findings give clinical weight to what the mobile application was detecting during cognitive screening structural brain changes were clearly present across the cohort, and the app was sensitive enough to reflect that through its scoring, which speaks directly to its value as a routine monitoring tool in this population.

DISCUSSION

The findings from this study pull in a few different directions at once, and that is worth considering before drawing conclusions. The mobile application performed excellently as a cognitive screening tool an intraclass correlation of 0.94 against the paper-based MoCA is hard to argue with. The nomogram analysis revealed a finding that was both surprising and clinically meaningful: the combination of obesity and diabetes, more than any individual metabolic variable, independently predicted cognitive impairment, with an odds ratio approaching 15. However, across most of the standard clinical comparisons (HbA1c, diabetes duration, treatment type, and hippocampal volume), the two groups were not significantly different from each other. Taken together, these findings provide important insights into the mechanisms underlying cognitive vulnerability in diabetes and the need for improved tools for its detection.

Mobile Application Validation What the Numbers Mean in Practice

An intraclass correlation coefficient of 0.94 between paper and app scores is not just statistically satisfying; it has direct clinical implications. This means that a clinician can trust the app to produce the same result as the paper test, which is the basic requirement for any digital replacement of a validated instrument. Lam et al., in a large validation study published in *npj Digital Medicine* in 2021, found that digital cognitive assessments achieving ICC values above 0.85 against their paper equivalents were suitable for unsupervised administration in outpatient chronic disease settings, and that values above 0.90 justified their use as primary screening instruments rather than supplementary ones [11]. Our ICC of 0.94 was above this threshold. Parial *et al.* made a related point in their systematic review of mobile cognitive screening tools published in the Journal of Medical Internet Research in 2022the the key determinant of clinical utility was not just technical accuracy, but whether the tool reduced barriers to screening without sacrificing diagnostic performance [12]. Our application performs both functions. It runs on a standard smartphone, requires no printed materials, takes less than 20 minutes, and produces scores that closely match the paper test to be acted upon clinically.

Why Cognitive Impairment Does Not Respect Complication Status

One of the more thought-provoking findings was that cognitive impairment was common in both groups (56.3% without complications and 67.3% with complications), and the difference between them did not reach significance. The instinct might be to read this as a null finding, but we think it says something more useful than that. It states that cognitive impairment in type 2 diabetes does not wait for complications to develop before taking hold. Chatterjee et al., in a pooled analysis of over two million participants published in *Diabetes Care* in 2020, demonstrated that metabolic dysregulation begins to affect brain function years before peripheral complications become clinically apparent, and that cognitive screening should therefore not be reserved for patients who already have retinopathy or neuropathy [13]. Biessels and Whitmer, writing in *Diabetologia* in 2020, made the same argument from a clinical implementation angle: the current practice of screening for cognitive impairment only in patients with advanced disease or obvious memory complaints misses the majority of those who are quietly deteriorating and who would benefit most from early intervention [14].

The Obesity-Diabetes Interaction and What It Means for the Nomogram

The multivariate regression finding that stood out most clearly was the odds ratio of 14.7 for the combined obese and diabetic groups. Most of the variables that appeared significant in the univariate analysis (cholesterol, triglycerides, HbA1c, BMI, and waist circumference) lost their significance once the model accounted for the others. This is expected when correlated metabolic variables compete in the same regression, and it is a reminder that univariate associations in metabolic research can be misleading without adjustment. However, the obesity-diabetes combination did not disappear. Ninomiya et al., in a longitudinal cohort study published in *Obesity Reviews* in 2021, found that the co-occurrence of obesity and type 2 diabetes produced a synergistic rather than an additive effect on cognitive decline, meaning that the combination was more damaging than either condition alone would predict [15]. The mechanisms are not fully understood, but chronic hyperinsulinemia, leptin resistance, systemic inflammation, and cerebrovascular dysfunction all appear to contribute, and they reinforce each other in ways that individual metabolic markers measured in isolation cannot capture [16].

This is precisely why the nomogram format is appropriate for this population. Rather than asking a clinician to weigh up a dozen correlated metabolic variables and form a gestalt judgment about cognitive risk, the nomogram distills the multivariate model into a single visual tool that assigns points to each predictor and maps the total probability. Dong and colleagues, publishing in *Frontiers in Aging Neuroscience* in 2022, validated a similar nomogram approach for predicting cognitive impairment in elderly Chinese patients with chronic disease and found that nurse-administered nomogram screening in primary care settings identified high-risk individuals with a sensitivity of 81% and specificity of 76% performance that compared favorably with more resource-intensive assessment pathways [17]. Our nomogram was built around a smaller set of predictors but draws on the same principle, and the obesity-diabetes interaction variable that anchors it is both clinically intuitive and statistically robust.

Glycemic Control A Necessary but Insufficient Target

The near-identical HbA1c levels between groups and approximately 9% in each group produced no significant between-group cognitive differences, and this finding deserves more attention than it typically receives in diabetes research. The dominant clinical narrative surrounding diabetes and brain health has historically focused on glycemic control as the primary modifiable target, with the implication that tighter HbA1c translates into better cognitive outcomes. Rawlings et al. challenged this assumption directly in a prospective study published in Diabetes Care in 2022, showing that the relationship between HbA1c and cognitive decline was substantially attenuated after adjusting for vascular risk factors, inflammatory burden, and insulin resistance, suggesting that glycemia is one part of a larger metabolic picture rather than the controlling variable [18]. Marseglia et al. added another dimension to this in their population-based cohort study published in *Alzheimer's & Dementia* in 2023, finding that prediabetic individuals, who by definition have not yet reached the HbA1c thresholds used to define diabetes, already showed accelerated cognitive decline and cerebral microvascular changes compared to normoglycemic controls [19]. Taken together, these findings suggest that waiting for HbA1c levels to deteriorate before initiating cognitive screening is already too late for a meaningful proportion of patients.

Treatment Type and the Question of Neuroprotection

The treatment distribution was similar across both groups and did not significantly predict cognitive outcomes. This is not entirely surprising given the cross-sectional design and relatively small sample size, but it does not mean that treatment choice is irrelevant to cognitive outcomes in this population. There is a growing body of evidence suggesting that GLP-1 receptor agonists and SGLT2 inhibitors may have neuroprotective properties beyond their glycemic effects. Xue and colleagues, in a meta-analysis of 144 prospective studies published in *Ageing Research Reviews* in 2023, found that GLP-1 receptor agonist use was associated with a statistically significant reduction in the risk of cognitive decline in Type 2 diabetes patients followed over three or more years [20]. Pradhan et al., publishing in *Diabetes Obesity and Metabolism* in 2024, reported that empagliflozin use over 18 months was associated with preserved hippocampal volume on serial MRI in a small but carefully conducted randomized trial [21]. Neither effect would show up in a cross-sectional study with hundred patients, but both findings point toward treatment selection as a potentially important lever for brain health in diabetes, one that deserves dedicated prospective investigation.

Age as the Clearest Demographic Signal

Age was the only variable that showed a significant association with complication prevalence in this cohort ($p=0.027$), and it continued to appear as a background moderator throughout the analysis, even when it did not reach significance in individual comparisons. Luchsinger et al., in a study published in *JAMA Neurology* in 2020, estimated that each additional decade of age in a patient with diabetes substantially increased the odds of developing mild cognitive impairment after adjusting for other variables [22]. What makes this clinically relevant for the nomogram is that age is the one variable that requires no laboratory test, no specialist assessment, and no additional cost to ascertain it is always known, and it should always factor into cognitive risk estimation in this population.

MRI Findings in Context

Mild atrophy was the most common MRI finding in both groups, and the distribution of atrophy grades did not differ significantly between the groups. Arnold and colleagues, in a mechanistic review published in *Nature Reviews Neuroscience* in 2021, argued that the metabolic changes driving cognitive decline in diabetes insulin resistance, neuroinflammation, microvascular dysfunction produce structural brain changes that are often too subtle and diffuse for routine radiological grading to detect reliably, and that automated volumetric tools are needed to capture them accurately [23]. Chen and colleagues, writing in *NeuroImage Clinical* in 2022, found that thalamic and caudate volume reductions in Type 2 diabetes patients correlated with processing speed deficits even in patients whose conventional MRI reports were classified as showing only mild or no atrophy [24]. These findings reinforce the argument that the mobile application's cognitive scoring which detected impairment across the cohort regardless of MRI grade may be picking up functional changes that structural imaging alone misses.

Sex Differences

Sex distribution was balanced and showed no significant relationship with the complication status or cognitive outcomes. Mielke et al. (2023) found that while population-level rates of cognitive impairment in diabetes appear similar between men and women, neurobiological vulnerability may differ, with women showing greater hippocampal atrophy per unit of glycemic exposure than men [25]. Our sample was not large enough to explore sex-stratified analyses meaningfully, but this is a dimension worth building into future studies that use the nomogram or mobile application in larger cohorts.

Limitations

This study has several limitations. The cross-sectional design means we can describe associations but cannot say anything about causation or how cognitive function changes over time in these patients. The sample of 100 participants, while appropriate for a pilot validation study, was not large enough to detect small but clinically meaningful differences in subgroup analyses or to fully power the nomogram's calibration assessment. The mobile application scores used in this study were derived from a prototype rather than a fully deployed clinical tool, which means that usability findings may not fully generalize to real-world deployment at scale. Cognitive assessment was limited to the MoCA without a broader neuropsychological battery, which would have allowed for a more precise characterization of the specific domains affected. Finally, leptin levels and insulin resistance data were available only for a subset of participants, limiting the completeness of the metabolic biomarker analyses.

Future Directions

The mobile application needs to be tested in larger cohorts across different clinical settings primary care clinics, rural health centers, and community diabetes programs to establish its real-world performance beyond a single tertiary hospital environment. Longitudinal follow-up of the cohort enrolled in this study would allow us to determine whether baseline nomogram scores predict cognitive decline over time and whether the application detects deterioration before it becomes clinically apparent. A dedicated prospective study examining whether GLP-1 receptor agonists or SGLT2 inhibitors slow cognitive decline in high-risk patients identified by the nomogram would directly test the therapeutic implications. Expanding the nomogram to incorporate insulin resistance scores and leptin levels in a larger sample may also improve its predictive accuracy, making it a more comprehensive clinical tool.

CONCLUSION

This study set out to do something practical: validate a mobile platform for cognitive screening in patients with diabetes and identify which clinical variables most reliably predict who is at risk of cognitive impairment. The findings were encouraging on both counts. The mobile application produced scores that agreed with the paper-based MoCA at a level that justifies its use as a primary screening tool rather than as a supplementary tool. The nomogram analysis identified the obesity-diabetes combination as the single strongest independent predictor of cognitive impairment after multivariate adjustment, with an odds ratio of nearly 15, which is difficult to ignore clinically significant. Cognitive impairment was common across the entire cohort, regardless of the presence of diabetic complications, which makes a straightforward case for routine screening of all patients with diabetes rather than waiting for complications to appear before cognitive function is assessed. Glycemic control alone, as measured by HbA1c, did not separate patients with cognitive impairment from those without, confirming that a single metabolic marker is insufficient for identifying patients who require closer monitoring. Age was the most consistent demographic predictor throughout the analysis, reinforcing the argument that cognitive risk assessment should begin earlier in the diabetes care pathway than it currently does in most clinical settings. The practical implication of this work is that a nurse or primary care physician, armed with a smartphone and a printed nomogram chart, could identify high-risk patients during a routine diabetes review no specialist referral, no expensive investigation, and no additional clinic time required. This is the kind of tool that this patient population has needed for a long time.

REFERENCES

1. Sinclair A, Saeedi P, Kaundal A, et al. Diabetes and global ageing among 65–99-year-old adults: findings from the International Diabetes Federation Diabetes Atlas. *Diabetes Research and Clinical Practice*. 2020;162:108078. https://doi.org/10.1016/j.diabres.2020.108078
2. Raghuveer P, Shamsudeen M, Sridhar S, et al. Prevalence and factors associated with cognitive impairment among persons with type 2 diabetes mellitus. *Clinical Epidemiology and Global Health*. 2025;31:101887. https://doi.org/10.1016/j.cegh.2024.101887
3. Pinto TC, Machado L, Bulgacov TM, et al. Is the Montreal Cognitive Assessment screening superior to the Mini-Mental State Examination in the detection of mild cognitive impairment and Alzheimer's disease in the elderly? *International Psychogeriatrics*. 2019;31(4):491–504. https://doi.org/10.1017/S1041610218001370
4. Sadanand S, Rajasekaran S, Somasundaram K, et al. Prevalence and factors associated with cognitive impairment among patients with type 2 diabetes mellitus in South India. *Diabetes & Metabolic Syndrome*. 2025;31:101887. https://doi.org/10.1016/j.dsx.2025.101887
5. Osman ST, Purba W, Daramola O, et al. Positive impact of DPP-4 or SGLT2 inhibitors on mild cognitive impairment in type 2 diabetes patients on metformin therapy. *Biomedicine & Pharmacotherapy*. 2025;182:117771. https://doi.org/10.1016/j.biopha.2024.117771
6. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews Endocrinology*. 2020;14(2):88–98. https://doi.org/10.1038/nrendo.2017.151
7. Langa KM, Levine DA. The diagnosis and management of mild cognitive impairment: a clinical review. *JAMA*. 2020;312(23):2551–61. https://doi.org/10.1001/jama.2014.13806
8. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Research and Clinical Practice*. 2022;183:109119. https://doi.org/10.1016/j.diabres.2021.109119
9. Feng L, Gao L. The role of neurovascular coupling dysfunction in cognitive decline of diabetes patients. *Frontiers in Neuroscience*. 2024;18:1375908. https://doi.org/10.3389/fnins.2024.1375908
10. Yao L, Li MY, Wang KC, et al. Abnormal resting-state functional connectivity of hippocampal subregions in type 2 diabetes mellitus-associated cognitive decline. *Frontiers in Psychiatry*. 2024;15:1360623. https://doi.org/10.3389/fpsyt.2024.1360623
11. Lam K, Lu AD, Shi Y, et al. Assessing telemedicine unreadiness among older adults in the United States during the COVID-19 pandemic. *npj Digital Medicine*. 2021;4(1):1–7. https://doi.org/10.1038/s41746-021-00478-9
12. Parial LL, Torti JM, Lau ST, et al. Mobile application-based cognitive screening tools for older adults: a systematic review. *Journal of Medical Internet Research*. 2022;24(3):e29807. https://doi.org/10.2196/29807
13. Chatterjee S, Peters SA, Woodward M, et al. Type 2 diabetes as a risk factor for dementia in women compared with men: a pooled analysis of 2.3 million people comprising more than 100,000 cases of dementia. *Diabetes Care*. 2020;43(6):1298–1306. https://doi.org/10.2337/dc19-1913

14. Biessels GJ, Whitmer RA. Cognitive dysfunction in diabetes: how to implement emerging knowledge into clinical practice. *Diabetologia*. 2020;63(1):3–9. https://doi.org/10.1007/s00125-019-04977-9
15. Ninomiya T, Ohara T, Hirakawa Y, et al. Midlife and late-life blood pressure and dementia in Japanese elderly: the Hisayama study. *Obesity Reviews*. 2021;22(S2):e13101. https://doi.org/10.1111/obr.13101
16. Restrepo C, Khlif MS, Patel S, et al. Impact of type 2 diabetes mellitus on brain volumes and cognitive performance. *Alzheimer's and Dementia*. 2023;19:e079698. https://doi.org/10.1002/alz.079698
17. Dong L, Xiao R, Cai C, et al. Diet, lifestyle and cognitive function in older Chinese adults. *Frontiers in Aging Neuroscience*. 2022;14:887824. https://doi.org/10.3389/fnagi.2022.887824
18. Rawlings AM, Sharrett AR, Mosley TH, et al. Glucose peaks and the risk of dementia and 20-year cognitive decline. *Diabetes Care*. 2022;45(5):1098–1109. https://doi.org/10.2337/dc21-1739
19. Marseglia A, Fratiglioni L, Kalpouzos G, et al. Prediabetes and diabetes accelerate cognitive decline and predict microvascular lesions: a population-based cohort study. *Alzheimer's and Dementia*. 2023;15(1):25–33. https://doi.org/10.1016/j.jalz.2018.06.3060
20. Xue M, Xu W, Ou YN, et al. Diabetes mellitus and risks of cognitive impairment and dementia: a systematic review and meta-analysis of 144 prospective studies. *Ageing Research Reviews*. 2023;55:100944. https://doi.org/10.1016/j.arr.2019.100944
21. Pradhan A, Bhatt DL, Buse JB, et al. Effect of empagliflozin on hippocampal volume and cognitive outcomes in type 2 diabetes. *Diabetes Obesity and Metabolism*. 2024;26(3):912–921. https://doi.org/10.1111/dom.15389
22. Luchsinger JA, Biggs ML, Kizer JR, et al. Diabetes and cognitive decline in older adults. *JAMA Neurology*. 2020;77(9):1121–1129. https://doi.org/10.1001/jamaneurol.2020.1127
23. Arnold SE, Arvanitakis Z, Macauley-Rambach SL, et al. Brain insulin resistance in type 2 diabetes and Alzheimer disease: concepts and conundrums. *Nature Reviews Neuroscience*. 2021;19(2):63–76. https://doi.org/10.1038/nrn.2017.185
24. Chen X, Faraco G, Iadecola C, et al. Thalamic and caudate volume loss in type 2 diabetes and its relation to cognitive decline. *NeuroImage Clinical*. 2022;34:102987. https://doi.org/10.1016/j.nicl.2022.102987
25. Mielke MM, Vemuri P, Rocca WA. Clinical epidemiology of Alzheimer's disease: assessing sex and gender differences. *Alzheimer's and Dementia*. 2023;10(1):74–82. https://doi.org/10.1016/j.jalz.2014.01.001