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Association of Blood Pressure with Mild Cognitive Impairment in Patients with Type 2 Diabetes Mellitus: A Multicenter Cross-Sectional Study

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ABSTRACT

BACKGROUND & OBJECTIVE: Type 2 diabetes mellitus (T2DM) and hypertension frequently coexist and independently elevate the risk of cognitive decline. Although blood pressure (BP) dysregulation is hypothesized to accelerate neurovascular damage, its independent association with mild cognitive impairment (MCI) among individuals with T2DM remains insufficiently characterized in real-world multicenter cohorts.

METHODOLOGY: This multicenter cross-sectional study evaluated 489 adult patients with T2DM recruited from tertiary outpatient clinics. Cognitive performance was measured using the Montreal Cognitive Assessment (MoCA, including MoCA-Basic for low-literacy participants), with MCI defined as a score < 26. Resting blood pressure was measured using standardized protocols. Statistical analyses included Pearson and Spearman correlations, multiple linear and binary logistic regression, independent samples t-tests, ROC analyses, and age-stratified subgroup assessments.

RESULTS: Overall, 79.8% (n = 390) of the participants met the criteria for MCI, with a sample MoCA score of 21.40 ± 5.35. In multivariable models, cognitive performance was independently predicted by:

- **Education**: Higher formal education was protective and associated with higher MoCA scores (B = 0.70, p < 0.001; aOR = 0.93, 95% CI: 0.86–1.00).
- **Age**: Advancing age independently increased the odds of impairment (B = -0.08, p < 0.001; OR = 1.03, 95% CI: 1.00–1.05).
- **Sex**: Female sex was associated with lower cognitive scores and elevated MCI risk (B = -1.71, p < 0.001; OR = 2.02, 95% CI: 1.21–3.37).

In contrast, systolic BP, diastolic BP, pulse pressure, and hypertension status showed no significant independent associations with cognitive scores or MCI risk after multivariable adjustment (all p > 0.05). Blood pressure parameters demonstrated negligible discriminative accuracy for MCI (AUC range: 0.52–0.53), and MoCA scores did not significantly differ between normotensive and hypertensive patients (21.64 vs. 20.94, p = 0.175).

CONCLUSION: Mild cognitive impairment affects nearly four in five diabetic patients in this population. Poorer cognitive performance is primarily driven by demographic and socioeconomic determinants—specifically older age, female sex, and limited education—rather than clinic blood pressure indices. These findings highlight the critical need for routine cognitive screening protocols tailored to high-risk demographic profiles within diabetes management pathways.

KEY WORDS: Mild Cognitive Impairment, Type 2 Diabetes Mellitus, Blood Pressure, Hypertension, MoCA, Cognitive Decline, Cross-Sectional Study

How to cite: *Nasir A, Sajid MS, Abid MA, Haris M, Auns M, Sukhera S. Association of Blood Pressure with Mild Cognitive Impairment in Patients with Type 2 Diabetes Mellitus: A Multicenter Cross-Sectional Study. J Allam Iqbal Med Coll. 2026; 24(3): 50-60*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) and hypertension are among the most prevalent non-communicable diseases of the 21st century, affecting hundreds of millions of people worldwide. These conditions frequently coexist, with hypertension reported in more than 50% of patients with T2DM, thereby increasing their susceptibility to cardiovascular, renal and neurological complications.[1] Diabetes is associated with numerous complications, among which cognitive decline is often overlooked. The diabetic brain is vulnerable to pathological processes such as chronic hyperglycemia, insulin resistance, oxidative stress, neuroinflammation and cerebrovascular disease, all of which may impair neuronal function and synaptic plasticity.[2,3] Mild cognitive impairment (MCI) is characterized by cognitive decline exceeding that expected with normal ageing but not severe enough to substantially interfere with activities of daily living. It has therefore emerged as an important clinical outcome in T2DM and a potential prodromal stage of dementia.[4]

Blood-pressure dysregulation is a characteristic feature of coexisting T2DM and hypertension and may contribute to neurovascular damage through increased arterial stiffness, impaired cerebral blood-flow auto regulation, white-matter hyper intensities and lacunar infarctions.[5-7] Elevated systolic and diastolic blood pressure have independently been associated with

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* Received for Publication: July 18, 2026
* Revision Received: August 25, 2026
* Accepted for Publication: September 10, 2026

cognitive dysfunction in middle-aged and older populations.[8,9] However, the relationship between metabolic and vascular abnormalities and cognitive impairment among patients with T2DM remains insufficiently investigated, particularly in multicenter settings that capture real-world clinical variability.

The Montreal Cognitive Assessment (MoCA) is a brief and validated screening instrument with good sensitivity and specificity for detecting MCI across various clinical settings.[10,11] Its use provides a standardized cognitive outcome measure and facilitates comparisons across participants, studies and research sites.

To address these gaps, this multicenter cross-sectional study was designed to evaluate the association between blood-pressure parameters and MCI among patients with T2DM. The relationship was examined using correlation analysis, multiple linear regression, multivariable logistic regression, independent-samples *t* tests and age-stratified subgroup analyses. The specific objectives of this study were:

1. To describe the distribution of MoCA scores, systolic BP, and diastolic BP in the study sample.
2. To determine the direction and magnitude of Pearson correlations between systolic BP, diastolic BP, and MoCA scores.
3. To identify independent predictors of MoCA scores through multiple linear regression analysis.
4. To compare MoCA scores between normotensive and hypertensive T2DM patients using an independent samples t-test.
5. To explore age-group differences (<50 years vs. ≥50 years) in the relationship between BP and cognitive performance.

To assess the diagnostic accuracy of systolic BP in classifying MCI status using ROC curve analysis.

METHODOLOGY

This observational, multicentre cross-sectional study was conducted in the diabetes and endocrinology outpatient clinics of two tertiary-care hospitals. Ethical approval was obtained from the relevant authorities at Mayo Hospital and Farooq Hospital, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants before enrolment.

Participants were recruited through non-probability convenience sampling. All eligible patients with type 2 diabetes mellitus (T2DM) attending the outpatient clinics during the data-collection period were consecutively approached until the required sample size was achieved. The minimum sample size was calculated using the WHO formula for cross-sectional studies:

n=frac{Z^2P(1-P)}{d^2}

where (Z=1.96) for a 95% confidence level, (P=30.4%), representing the expected prevalence of mild cognitive impairment among patients with T2DM, and (d=6%), representing the margin of error.[12] The calculated minimum sample size was 226 participants.

To account for potential non-response and missing data and to provide sufficient statistical power for age-, sex- and centre-stratified analyses, the sample size was deliberately increased. A total of 489 participants were enrolled, representing an approximately 116% increase over the minimum requirement. This larger sample improved the precision of prevalence estimates, stability of regression models and reliability of subgroup comparisons.

The inclusion criteria were age ≥18 years, diagnosis of T2DM for at least three years, willingness to participate and ability to undergo cognitive assessment. Patients with previously diagnosed dementia, severe psychiatric illness, active neurological disease, recent acute illness, inability to cooperate with MoCA administration, use of medications known to impair cognition or current night-shift employment were excluded.

Before blood-pressure measurement, each participant rested in a seated position for five minutes. Blood pressure was measured using a standardized digital sphygmomanometer, with the participant's feet flat on the floor and the arm supported at heart level. Two readings were obtained five minutes apart and averaged for analysis, in accordance with standard blood-pressure measurement recommendations.[13] For the primary analysis, participants were classified as normotensive when systolic blood pressure (SBP) was <140 mmHg and hypertensive when SBP was ≥140 mmHg, according to the JNC 7 threshold.[13] For descriptive analysis, SBP was further categorized as normal (<120 mmHg), elevated (120–129 mmHg), stage 1 hypertension (130–139 mmHg) or stage 2 hypertension (≥140 mmHg), consistent with the 2017 ACC/AHA classification.[14]

Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA), a validated 30-point screening instrument used to evaluate multiple cognitive domains.[15] A score of <26 was considered indicative of possible MCI according to the conventional MoCA threshold. The assessment was administered by trained research staff using a standardized protocol across both study sites to minimize inter-rater variability.

For participants who were illiterate or had no formal education, the MoCA-Basic was used because it was specifically developed for individuals with limited education and minimizes dependence on reading and writing while retaining assessment of core cognitive domains.[16] As a validated Urdu version of the MoCA-Basic was unavailable during the study, the instrument was translated into Urdu by a bilingual clinical expert, with attention to conceptual and linguistic equivalence. This locally translated version was administered

consistently by trained personnel at both sites. Nevertheless, the absence of formal linguistic validation should be acknowledged as a potential source of measurement bias.

In the study dataset, SBP values were recorded in discrete increments of 110, 120, 130 and 140 mmHg. Participants with SBP of 140 mmHg were classified as hypertensive, whereas those with SBP <140 mmHg were classified as normotensive for the primary analysis.[13]

All statistical analyses were performed using R software (version 4.3.1; R Core Team, Vienna, Austria, 2023) (17). Descriptive statistics were computed for all continuous variables and reported as mean, standard deviation, median, interquartile range, and range. Categorical variables were summarized as frequencies and percentages. The prevalence of mild cognitive impairment (MCI) was defined using a standard MoCA cut-off score of less than 26.

Bivariate associations between blood pressure parameters and MoCA scores were examined using Pearson correlation coefficients, with Spearman rank correlations computed in parallel as a non-parametric check. Differences in continuous variables between participants with and without MCI were assessed using independent samples Welch t-tests, with Mann-Whitney U tests performed as sensitivity analyses. Chi-square tests were used to examine associations between categorical variables and MCI status.

Multiple linear regression was performed to identify independent predictors of MoCA scores, with age, sex, years of education, systolic blood pressure, and pulse pressure entered as predictors. Binary logistic regression was conducted to determine adjusted odds ratios for MCI, reported with 95% confidence intervals. Statistical significance was set at $p < 0.05$ for all analyses. Receiver operating characteristic (ROC) curve analysis was conducted to calculate the area under the curve (AUC) and evaluate the discriminatory accuracy of individual predictors and multivariable models for identifying MCI. The assumption of equal variances for independent samples t-tests was verified using Levene's test, and Cohen's *d* was calculated to report the standardized effect sizes for group differences. Additionally, a formal interaction term was tested to determine whether age strata modified the association between hypertension status and cognitive performance.

RESULTS

A total of 489 participants were included in the analysis, with complete data on every variable. The mean age was 49.41 years (SD 10.91), and ages ranged from 22 to 79 years. The sample was split fairly evenly by sex, with 258 (52.8%) women and 231 (47.2%) men. Formal schooling was limited on the whole. Participants had completed a mean of 5.6 years of education (SD 3.48), and half had 7 years or fewer. Table I sets out the full profile of the sample. Table II shows the frequency distribution of categorical variables.

Table I: Descriptive statistics for the continuous study variables

Variable	Mean (SD)	Median [IQR]	Range
Age (years)	49.41 (10.91)	50 [42 to 56]	22 to 79
MoCA score	21.4 (5.35)	23 [18 to 25]	6 to 30
Education (years)	5.6 (3.48)	7 [1 to 8]	1 to 11
SBP (mmHg)	127.61 (13.51)	125 [115 to 135]	105 to 160
DBP (mmHg)	80.89 (8.26)	80 [75 to 85]	65 to 100

Table II: Frequency distribution of the categorical variables. Blood pressure category and hypertension status describe the same participants under two groupings

Characteristic	n	% of sample
Women	258	52.80%
Men	231	47.20%
MCI present (MoCA < 26)	390	79.80%
No MCI	99	20.20%
Normal BP	111	22.70%
Elevated BP	63	12.90%
Stage 1 hypertension	148	30.30%
Stage 2 hypertension	167	34.20%
Normotensive	322	65.80%
Hypertensive	167	34.20%
Aged under 50	239	48.90%
Aged 50 or over	250	51.10%

MoCA scores averaged 21.4 (SD 5.35) and spanned almost the full range of the instrument, from 6 to 30. The distribution leaned toward the lower end of the scale (Figure 1). Applying the standard cut point of 26, 390 (79.8%) participants screened positive for mild cognitive impairment, so close to four in five people in this sample fell below the threshold. Impairment was therefore the norm rather than the exception, which shapes how the rest of the results should be read. Figure 1 shows distribution of MoCA scores.

Education showed the clearest relationship with cognition. Years of schooling correlated positively and moderately with the MoCA score ($r = 0.54$, $p < 0.001$), so people with more education tended to score higher (Figure 2). Age worked in the opposite direction, with a weaker but still clear negative correlation ($r = -0.19$, $p < 0.001$): older participants scored a little lower on average.

The blood pressure measures told a different story. Systolic pressure, diastolic pressure and pulse pressure each showed a negligible, non-significant correlation with the MoCA score (all $|r| < 0.09$, all $p > 0.05$). Table III reports every coefficient, alongside the Spearman values, which point to the same conclusions

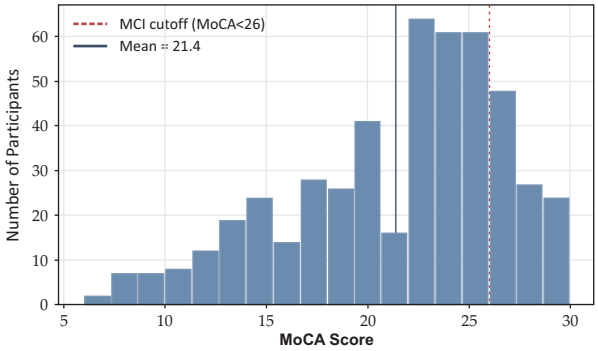

Figure 1: Distribution of MoCA scores across the sample, with the MCI cut point and the sample mean marked.

Table III: Correlation of each continuous variable with the MoCA score

Variable	Pearson r	Spearman rho	p value
Education	0.535	0.478	< 0.001
Age	-0.193	-0.229	< 0.001
SBP	-0.029	-0.067	0.521
DBP	-0.082	-0.054	0.071
Pulse pressure	0.028	-0.011	0.539

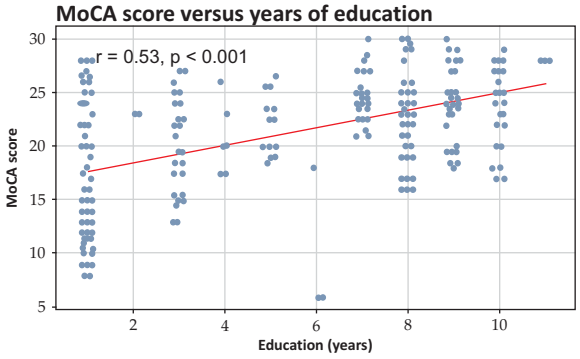

Figure 2: MoCA score plotted against years of education, with the fitted line. Points are lightly jittered on the horizontal axis to reduce overlap.

Splitting the sample by MCI status reinforced the same pattern. Participants with MCI had completed fewer years of education than those without (mean 5.33 versus 6.68 years, $p < 0.001$). They were also somewhat older (mean 49.91 versus 47.44 years, $p = 0.039$ by t test, $p = 0.083$ by Mann-Whitney). Blood pressure did not separate the two groups. Systolic pressure, diastolic pressure and pulse pressure were all but identical whether or not a person was impaired (all $p > 0.28$). Table IV gives the full comparison, and Figure 3 shows the education gap directly.

Table IV: Comparison of continuous variables between participants with and without MCI. The p value column shows the Welch t test and the Mann-Whitney test, in that order.

Variable	MCI, mean (SD)	No MCI, mean (SD)	p value
Age (years)	49.91 (10.99)	47.44 (10.41)	0.039 / 0.083
Education (years)	5.33 (3.44)	6.68 (3.42)	<0.001/<0.001
SBP (mmHg)	127.85 (13.45)	126.67 (13.76)	0.445 / 0.285
DBP (mmHg)	81.01 (8.28)	80.40 (8.20)	0.511/ 0.585
Pulse pressure	46.83 (10.22)	46.26 (9.43)	0.598 / 0.588

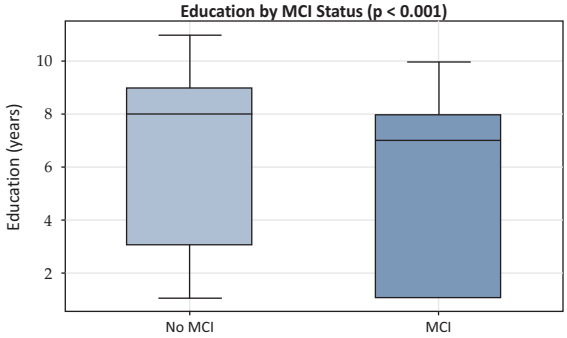

Figure 3: Years of education in the groups with and without MCI.

Sex was linked to impairment. MCI was more common among women than men, and the difference was clear on the chi-square test (chi-square = 11.03, $p < 0.001$; Figure 4). Blood pressure category showed a weaker signal that just cleared the conventional threshold (chi-square = 7.94, $p = 0.047$), though the gradient across the four categories was not orderly (Figure 5). Neither hypertension status as coded here ($p = 0.134$) nor age group ($p = 0.483$) was associated with MCI on its own.

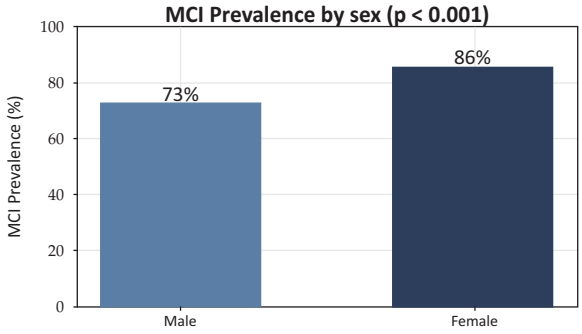

Figure 4: MCI prevalence in men and women.

A multiple linear regression tested whether these relationships held once the variables were considered together. The model regressed the MoCA score on age, sex, education, systolic pressure and pulse pressure. It explained about a third of the variation in cognitive score (R-squared = 0.329, adjusted R-squared = 0.322) and was highly significant overall ($F = 47.4$, $p < 0.001$). Three predictors carried the model. Each additional year of

education raised the MoCA score by 0.70 points ($p < 0.001$). Women scored 1.71 points lower than men on average ($p < 0.001$), and each additional year of age lowered the score by 0.083 points ($p < 0.001$). Neither systolic pressure ($p = 0.108$) nor pulse pressure ($p = 0.614$) contributed once the other factors were in place. Table V reports the full model.

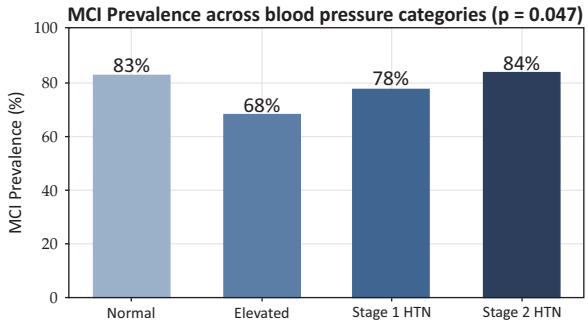

Figure 5: MCI prevalence across the four blood pressure categories.

Table V: Multiple linear regression predicting the MoCA score. Reference category for sex is male.

Predictor	B	SE	p	95% CI
Intercept	26.694	2.447	<0.001	21.89 to 31.50
Age (years)	-0.083	0.019	< 0.001	-0.12 to -0.05
Female sex	-1.707	0.452	< 0.001	-2.59 to -0.82
Education (years)	0.698	0.064	< 0.001	0.57 to 0.82
SBP (mmHg)	-0.039	0.024	0.108	-0.09 to 0.01
Pulse pressure	0.017	0.033	0.614	-0.05 to 0.08

A logistic regression looked at the same question from the other side, modelling the odds of screening positive for MCI from age, sex, education, hypertension status and pulse pressure. The model was significant overall (likelihood ratio $p < 0.001$). Older age raised the odds of impairment slightly, by about 2.5 percent per year (OR 1.03, 95% CI 1.00 to 1.05, $p = 0.028$). Women had roughly double the odds of men (OR 2.02, 95% CI 1.21 to 3.37, $p = 0.007$). Education was protective, with each additional year trimming the odds by about 7.2 percent (OR 0.93, 95% CI 0.86 to 1.000, $p = 0.049$). Hypertension status ($p = 0.179$) and pulse pressure ($p = 0.741$) were not associated with the odds of MCI. Table VI and Figure 6 present the adjusted odds ratios.

Table VI: Multivariable logistic regression for the odds of MCI. Reference categories are male sex and normotensive status.

Predictor	Odds ratio	95% CI	p
Age (years)	1.03	1.00 to 1.05	0.03
Female sex	2.02	1.21 to 3.37	0.01
Education (years)	0.93	0.86 to 1.00	0.05
Hypertension	1.48	0.83 to 2.64	0.18
Pulse pressure	1	0.98 to 1.03	0.74

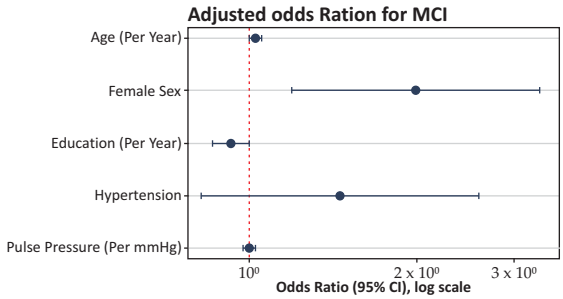

Figure 6: Adjusted odds ratios for MCI with 95 percent confidence intervals, on a log scale. The dashed line marks an odds ratio of one.

Taken together, the picture is consistent across every test. Cognitive performance in this sample was driven by education, age and sex, not by blood pressure. Low education and older age went with poorer scores, women were more likely to screen positive than men, and none of the blood pressure measures held any independent relationship with cognition once those three factors were accounted for.

Receiver operating characteristic analysis asked how well each measure, on its own, separates the participants who screened positive for MCI from those who did not. The area under the curve (AUC) sums this up: 0.5 means no better than a coin toss, 1.0 means perfect separation. None of the measures came close to strong discrimination. Education did best but was still weak, with an AUC of 0.61 (95% CI 0.54 to 0.67). The blood pressure measures were essentially uninformative: systolic pressure reached only 0.53 (95% CI 0.47 to 0.60), diastolic pressure 0.52, and pulse pressure 0.52, each with a confidence interval that crosses 0.5. Age landed in between at 0.56. Figure 7 shows the curves. Table VII shows AUC with 95% CI.

Table VII: AUC with 95 percent confidence interval for each single predictor of MCI, plus the sensitivity and specificity at the Youden optimal cut point.

Measure	**AUC**	**95% CI**	**Sens.**	**Spec.**
Education	0.606	0.54 to 0.67	0.49	0.72
Age	0.556	0.49 to 0.62	0.36	0.76
SBP	0.535	0.47 to 0.60	0.49	0.69
DBP	0.517	0.46 to 0.58	0.4	0.66
Pulse pressure	0.517	0.45 to 0.58	0.32	0.77

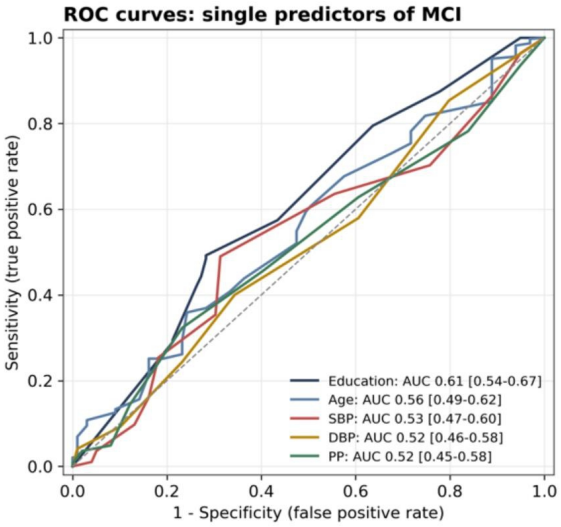

Figure 7: ROC curves for single predictors of MCI.

Combining age, sex, education, hypertension status and pulse pressure in one logistic model lifted discrimination to an AUC of 0.66 (95% CI 0.59 to 0.72), which counts as fair but not clinically useful (Figure 8). The gain over education alone is modest, and it comes almost entirely from age, sex and education rather than from blood pressure.

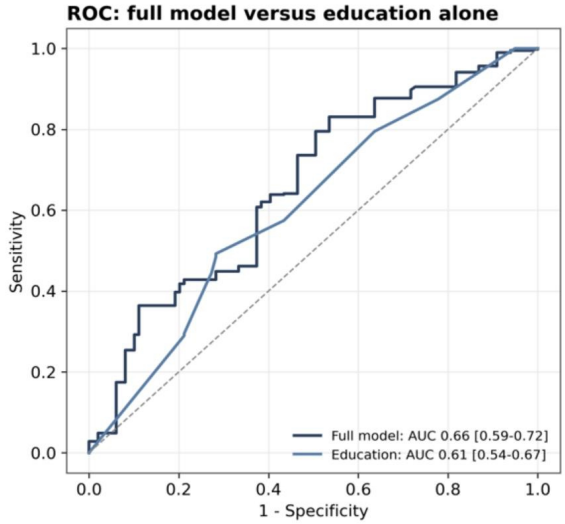

Figure 8: ROC for the full multivariable model against education alone.

An independent samples t test compared the MoCA score between the two blood pressure groups. Normotensive participants scored 21.64 on average (SD 5.31, n = 322) and hypertensive participants 20.94 (SD 5.42, n = 167). The gap of 0.70 points was small and did not reach significance (t = 1.36, p = 0.175; 95% CI for the difference -0.31 to 1.71). Levene's test gave no sign of unequal variances (p = 0.91), and the non- parametric Mann-Whitney test agreed (p = 0.257). The effect size was negligible (Cohen's d = 0.13). In plain terms, hypertensive patients scored a fraction of a point lower, well within what chance would produce. Figure 9 shows the two distributions. Table VIII shows comparison of MoCA scores between both groups.

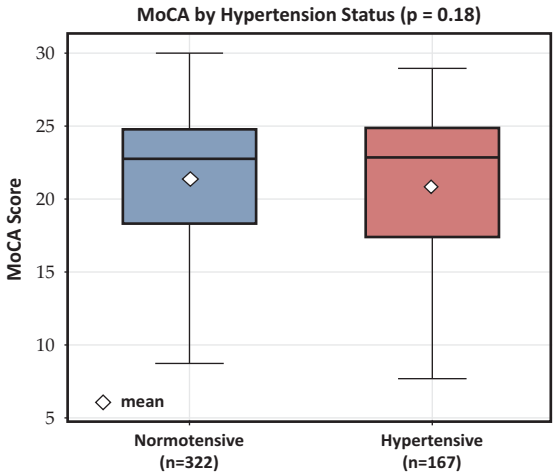

Figure 9: MoCA score by hypertension status. Diamonds mark the group means.

Table VIII: MoCA score compared between normotensive and hypertensive participants.

Statistic	Normotensive	Hypertensive
n	322	167
Mean (SD)	21.64 (5.31)	20.94 (5.42)
Median	23	23
Mean difference	0.70 (95% CI -0.31 to 1.71)	
t test	t = 1.36, p = 0.175	
Mann-Whitney	p = 0.257	
Cohen's d	0.13	

Splitting the sample at age 50 brought out the one clear pattern in these data, which is the pull of age itself. The younger group scored noticeably higher on the MoCA than the older group (22.7 versus 20.2), yet MCI was common in both, affecting 78 percent of the under-50s and 81 percent of those 50 and over. Blood pressure, again, made little difference inside either age band.

Among the under-50s, normotensive participants scored 23.0 and hypertensive participants 22.0, a difference that was not significant (p = 0.155). Among those 50 and over the two groups were almost identical (20.3 versus 20.0, p = 0.731). A formal test for interaction confirmed that age group does not change the (absent) effect of hypertension on MoCA (interaction p = 0.479). Figures 10 and 11 show the scores and the impairment rates side by side. Table IX shows Age subgroup comparisons.

Table IX: Age subgroup comparison. Correlations are Pearson coefficients within each stratum.

Measure	Under 50 (n = 239)	50 and over (n = 250)	p
MoCA, mean (SD)	22.70 (4.58)	20.16 (5.74)	< 0.001
MCI, n (%)	187 (78.2%)	203 (81.2%)	0.48
SBP, mean (SD)	127.4 (14.3)	127.8 (12.7)	
Pulse pressure, mean (SD)	46.0 (9.9)	47.4 (10.1)	
MoCA, normotensive	23.01 (n=162)	20.26 (n=160)	
MoCA, hypertensive	22.05 (n=77)	20.00 (n=90)	
Normo vs HTN, p	0.155	0.731	
MoCA ~ SBP, r	-0.117 (p=0.07)	0.053 (p=0.41)	
MoCA ~ pulse pressure, r	-0.124 (p=0.06)	0.174 (p=0.006)	
MoCA ~ education, r	0.422	0.6	

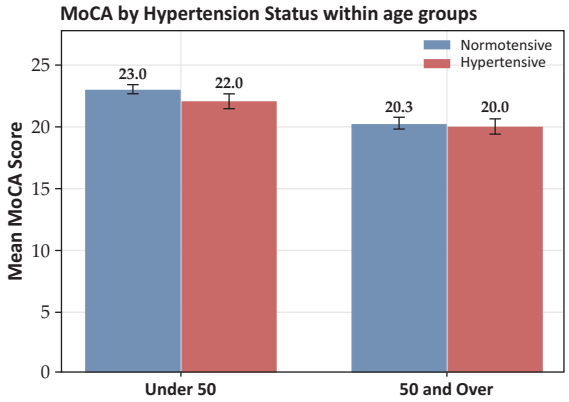

Figure 10: Mean MoCA by hypertension status within each age group. Error bars are standard errors.

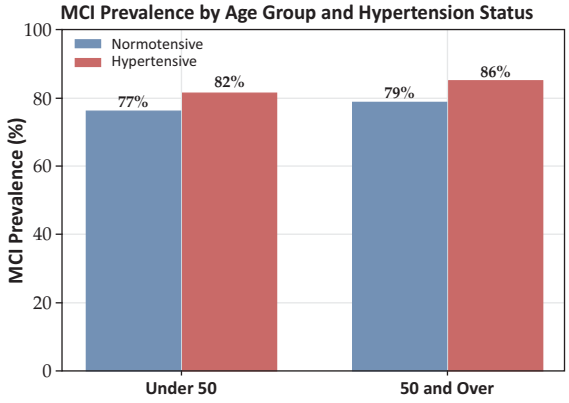

Figure 11: MCI prevalence by age group and hypertension status.

One detail is worth a cautious mention. In the older group, pulse pressure showed a weak positive correlation with the MoCA score (r = 0.17, p = 0.006), the opposite of what a vascular-damage account would predict. The coefficient is small and this is one of several exploratory tests, so it is best treated as a curiosity to revisit rather than a finding to lean on. Education stayed the strongest correlate of cognition in both age bands, and its pull was even stronger in the older group (r = 0.60).

The three analyses point the same way. Blood pressure does not discriminate against cognitive impairment (all AUCs near 0.5), MoCA does not differ between normotensive and hypertensive patients (p = 0.18), and neither pattern shifts when the sample is split by age. Age and education remain the variables that matter for cognition in this dataset.

DISCUSSION

This multicentre cross-sectional study found that blood pressure was not significantly associated with cognitive function in patients with Type 2 Diabetes Mellitus (T2DM) after adjustment for age, sex, and education.[18,19] Instead, older age, female sex, and lower educational attainment were the principal predictors of cognitive impairment. The high proportion of participants screening positive for Mild Cognitive Impairment (MCI) highlights its substantial burden in this population.[20,21]

Overall, 79.8% of participants scored below the MoCA cut-off for MCI, exceeding rates reported previously. Differences in population characteristics, education, diabetes duration, and assessment methods may explain this variation. Nevertheless, our results support evidence that cognitive dysfunction is a common and clinically important complication of T2DM.[22] The low mean educational attainment of 5.6 years may have contributed to this high prevalence.

Education was among the strongest predictors of cognition: additional years of formal education were associated with higher MoCA scores and lower odds of MCI. This protective relationship has also been observed in socioeconomically disadvantaged populations.[23,24] These findings support the cognitive reserve hypothesis, according to which education strengthens the brain's ability to tolerate age- and disease-related changes before clinical impairment becomes apparent.[25,26] Consequently, individuals with greater educational exposure may retain better cognitive function despite comparable underlying

pathology.[27,28] Incorporating health-literacy interventions and cognitively stimulating activities into diabetes care may therefore help preserve cognitive function.

Advancing age was independently associated with higher odds of MCI and lower MoCA scores. Aging-related neuronal loss, vascular alterations, and reduced neuroplasticity may be accelerated by chronic diabetes.[29,30] This agrees with previous studies identifying age as a major predictor of cognitive impairment in diabetes.[31] Hyperglycaemia may further accelerate neurodegeneration through advanced glycation end-product accumulation, oxidative stress, polyol pathway activation, and mitochondrial dysfunction.

Female participants had lower cognitive scores and higher odds of MCI. Postmenopausal hormonal changes, vascular-risk differences, and unequal educational opportunities may contribute to this association.[32,33] Although sex-related differences have been reported previously, findings remain inconsistent across populations.[34] In our population, lower educational attainment among women may have reduced cognitive reserve, suggesting that social factors may be as important as biological mechanisms.

Contrary to our hypothesis, systolic blood pressure, diastolic blood pressure, pulse pressure, and hypertension status were not independently associated with cognition.[35,36] Correlations with MoCA scores were weak, and blood pressure remained non-significant in adjusted linear and logistic regression models.[37–40] Normotensive and hypertensive participants also had identical median MoCA scores, a non-significant difference, and a negligible effect size (Cohen's d = 0.13).

ROC analysis further showed that systolic blood pressure, diastolic blood pressure, and pulse pressure had little ability to identify MCI, with AUC values of approximately 0.52. Education was the strongest individual predictor (AUC = 0.61), while the multivariable model achieved an AUC of 0.66, mainly because of age, sex, and education. Thus, blood pressure alone should not be used as a proxy for cognitive-risk screening in patients with T2DM.

The absence of an association may reflect the multifactorial nature of diabetes-related cognitive impairment, which involves hyperglycaemia, insulin resistance, oxidative stress, inflammation, and microvascular injury.[41,42] Moreover, a single clinic blood pressure measurement may not adequately represent long-term vascular exposure.[43] Blood pressure was measured at one visit according to JNC 7 recommendations.[13] Cumulative blood pressure exposure, ambulatory measurements, and visit-to-visit variability may be more closely associated with cognitive decline than a single measurement.[44] The influence of blood pressure may also have been overshadowed by stronger predictors, particularly age and education.[45,46]

The absence of HbA1c measurements was an additional limitation because chronic hyperglycaemia may contribute substantially to neurovascular injury. Future longitudinal studies should incorporate HbA1c, HOMA-IR, lipid profiles, ambulatory blood pressure, and repeated blood pressure measurements to clarify the respective contributions of metabolic and vascular factors.

MCI remained highly prevalent in both age groups, affecting 78% of participants younger than 50 years and 81% of those aged 50 years or older. Education correlated more strongly with MoCA scores in older participants (r = 0.60) than in younger participants (r = 0.42), supporting the protective role of cognitive reserve. The weak positive correlation between pulse pressure and MoCA scores in older participants (r = 0.17) was counterintuitive and may represent a chance finding. Overall, demographic and educational factors appeared to influence cognition more strongly than blood pressure in this population.

STRENGTHS AND LIMITATIONS

This study has several strengths. It had a relatively large number of participants from multiple centers, thus improving the generalizability of the results. The validated MoCA instrument was used to assess cognitive function and several additional statistical techniques were used to explore the association between blood pressure and cognition. The consistency in results obtained from the correlation analysis, regression models, and group comparisons helps to boost confidence in overall results.

This study has a few drawbacks. First, its cross-sectional design does not allow conclusions about cause and effect. Blood pressure was measured on a single visit following a standardized protocol in accordance with JNC 7 guidelines which may not fully capture long-term blood pressure variability or cumulative vascular exposure. Future studies should consider ambulatory or repeated blood pressure monitoring to better characterize the relationship between chronic blood pressure burden and cognitive decline in patients with Type 2 Diabetes Mellitus. Third, information on diabetes duration, glycemic control, medication use, and other vascular risk factors was not included in the analysis. These factors may also influence cognitive function. Fourth, cognitive assessment relied on the MoCA, which is a screening tool and not a comprehensive neuropsychological evaluation. Finally, although participants were recruited from multiple centers, the findings may not be fully generalized to all populations with Type 2 Diabetes Mellitus. The MoCA-Basic has not been formally validated in Urdu; therefore, an expert-translated version was used for illiterate participants. Additionally, convenience sampling was employed, which may limit the representativeness of the findings to the broader population of patients with Type 2 Diabetes Mellitus. From a clinical standpoint, these results advocate for integrating routine cognitive screening into diabetes care pathways, particularly for older patients, women, and those with limited formal education. The MoCA provides a practical and validated tool for this purpose. Given the

high MCI burden observed — nearly four in five patients — a single negative screen is insufficient; longitudinal monitoring across clinic visits would be more appropriate. Referral pathways to neuropsychology, social support, and caregiver education should be established in diabetes clinics managing high-risk profiles.

CONCLUSION

Mild cognitive impairment was highly prevalent among patients with Type 2 Diabetes Mellitus in this multicenter study. Older age, female sex, and lower educational level were independently associated with poorer cognitive performance. In contrast, blood pressure measurements and hypertension status were not independent predictors of cognitive impairment after adjustment for important confounding factors. These findings suggest that routine cognitive screening should receive greater attention in patients with diabetes, particularly among individuals with advanced age and lower educational attainment. Future prospective studies should evaluate the combined effects of long-term blood pressure exposure, metabolic control, and other vascular risk factors on cognitive decline.

Ethical approval:

Ethical approval was taken from institutional review board of both Akhtar saeed Medical & Dental college and King Edward Medical University with the IRB number M-22/90/-Physiology, Dated 25-08-2022 and IRB number 193/RC/KEMU, Dated 21-03-2024 respectively.

Conflict of Interest:

Authors declare no conflict of interest.

Financial Disclosure:

None

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