Section: Physiology

Original Research Article

GENDER-WISE ASSESSMENT OF COGNITIVE FUNCTION IN PREDIABETES AND TYPE 2 DIABETES MELLITUS USING EVENT-RELATED POTENTIALS

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Received : 08/05/2026
Received in revised form : 26/06/2026
Accepted : 10/07/2026

Keywords:
Prediabetes; Type 2 diabetes mellitus; Cognitive function; Event-related potentials; P300.

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DOI: 10.47009/jamp.2026.8.4.87

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (4); 505-509

ABSTRACT

Background: Prediabetes and type 2 diabetes mellitus (T2DM) are associated with cognitive dysfunction, which may develop before the onset of overt diabetes. Event-related potentials (ERP), particularly the P300 component, provide an objective assessment of cognitive processing, while the Mini-Mental State Examination (MMSE) serves as a clinical screening tool. The abjective is to assess cognitive function among male and female patients with prediabetes and T2DM using ERP-P300 parameters and MMSE scores and to determine the influence of gender on cognitive performance. **Materials and Methods:** This hospital-based cross-sectional study was conducted in the Department of Physiology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, India. Participants aged 25–50 years were categorized into four groups: healthy controls (n=30), prediabetes (n=14), T2DM of <5 years duration (n=14), and T2DM of 5–10 years duration (n=31). Cognitive function was evaluated using MMSE and auditory oddball ERP-P300 recordings. Gender-wise comparisons of MMSE scores, P300 latency, and P300 amplitude were performed using appropriate statistical tests, with $p<0.05$ considered significant. **Result:** No significant gender differences were observed in MMSE scores (p=0.241–0.948), P300 latency (p=0.362–0.877), or amplitude (p=0.348–0.636). Among controls, prediabetic subjects, and patients with T2DM of varying disease duration, cognitive performance and electrophysiological indices were comparable between males and females. **Conclusion:** Gender did not significantly influence MMSE scores, P300 latency, or P300 amplitude among healthy controls, prediabetic individuals, or patients with T2DM. These findings suggest that diabetes-related cognitive dysfunction occurs independently of gender.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a rapidly growing global health problem, affecting more than 537 million adults worldwide, with projections indicating a substantial increase over the coming decades. India contributes significantly to this burden and is recognized as one of the countries with the highest prevalence of diabetes. Beyond its well-established metabolic and vascular complications, T2DM has increasingly been associated with cognitive impairment and an elevated risk of dementia.1-4 Cognitive deficits in diabetes commonly involve attention, executive function, learning, memory, and processing speed, adversely affecting quality of life and disease self-management.[1-4]

The pathogenesis of diabetes-related cognitive dysfunction is multifactorial and involves chronic hyperglycemia, insulin resistance, oxidative stress, neuroinflammation, endothelial dysfunction, and cerebral microvascular disease.[3-5] These mechanisms may contribute to neuronal injury, impaired synaptic plasticity, and accelerated neurodegeneration. Recent evidence suggests that cognitive decline may begin even before the onset of overt diabetes. Individuals with prediabetes have been shown to exhibit subtle cognitive deficits, structural brain changes, and an increased risk of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

future cognitive impairment, emphasizing the importance of early detection and intervention.[6,7]

The Mini-Mental State Examination (MMSE) is one of the most widely used screening tools for cognitive assessment.[8] However, subtle alterations in cognitive processing may not be detected by conventional neuropsychological tests alone. Event-related potentials (ERPs), particularly the P300 component, provide an objective neurophysiological measure of cognitive processing.[9,10] P300 latency reflects the speed of stimulus evaluation and information processing, whereas P300 amplitude reflects attentional resource allocation and working memory updating. Several studies have demonstrated prolonged P300 latency and reduced P300 amplitude among individuals with T2DM, indicating impaired cortical information processing.[11]

Although diabetes-related cognitive dysfunction has been extensively investigated, the influence of gender remains unclear. Some studies have reported sex-related differences in cognitive performance, potentially attributable to hormonal, genetic, educational, and sociocultural factors, whereas others have found no significant gender effect after adjusting for metabolic variables.[12,13] Furthermore, data regarding gender differences in cognitive function among individuals with prediabetes and T2DM in the Indian population remain limited.

Therefore, the present study was undertaken to assess cognitive function among male and female patients with prediabetes and T2DM using MMSE and ERP-P300 parameters and to determine whether gender significantly influences cognitive performance in these populations.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the Neurophysiology Laboratory, Department of Physiology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, Manipur, India. Participants were recruited from the Endocrinology Outpatient Department of JNIMS. The study included healthy controls, prediabetic individuals, and patients with type 2 diabetes mellitus (T2DM) aged 25–50 years of either sex. The study was approved by the Institutional Ethics Committee of JNIMS, Imphal (Approval No. 113(6) PGT 2018). Written informed consent was obtained from all participants. The Prediabetes and Type 2 Diabetes Mellitus subjects were recruited from the Endocrine (Medicine) OPD who were diagnosed based on criteria from American Diabetes Association (ADA), along with general history and clinical examination. Healthy controls were recruited from JNIMS staff members, based on clinical examination and general history. Subjects with history of intake of drugs like Methyldopa, reserpine, phenytoin, Antipsychotic, Anti- depressant, any history of drug abuse (nicotine, alcohol, opium etc.), any systemic illness that might affect the nervous system (uraemia, hepatic-encephalopathy, multiple sclerosis, thyroid disorders, anaemia, meningitis etc.), any known diabetic complication such as retinopathy, nephropathy and peripheral neuropathy and psychological disturbances were excluded from the study. The Mini- mental State examination (MMSE) was done using Folstein test consisting of 30 point questionnaire, in the Department of Physiology. Fasting plasma glucose (FPG) and 2 hour plasma glucose (2h-PG) were measured by glucose peroxidase method using Vitro's instrument. All the tests were done in the hospital laboratory of JNIMS. The Evoked potential (EP) recordings from the scalp of the subjects was done using Neuron spectrum-5(combo), Neurosoft, Russia. The EP was recorded with the disk electrode from standard scalp location of the 10-20 International system. The active electrodes was placed at FZ, CZ, PZ, grounding electrode at FPZ, reference electrodes at A1 and A2, after cleaning the scalp or skin site with alcohol followed by Nuprep skin preparation gel and EEG paste. The skin- electrode contact impedance was kept below 5KΩ. The recording settings used were: Hi cut pass 35Hz, Low cut pass 0.5Hz, Preset count 30, Target or infrequent Stimulus 1 (Auditory1) at stimulus rate of 0.3 Hz and 20% occurrence. Non-Target or frequent Stimulus 2 (Auditory2) at stimulus rate of 0.3 Hz and 80% occurrence. Auditory stimulus 1 – Time frequency 2 KHz, stimulus intensity 85dB nHL. Auditory stimulus 2 – Time frequency 1 KHz, stimulus intensity 85dB nHL. Response time recording range 0-500ms. ERP recordings were performed in response to auditory oddball paradigm where frequent and rare stimuli was given. The subject has to press a button on the response pad with the thumb of their dominant hand on hearing of Auditory 1(target) stimulus, delivered by headphones. During the recording session, subjects were instructed to fix his/her eyes on a particular spot on the wall in front in order to avoid electrooculographic artifacts due to eye movement. Data for two trails was obtained, stored, analysed and averaged by the software. Peak latencies and baseline to peak amplitudes of P300 were evaluated.

Statistical Analysis: The data obtained were analyzed using Statistical Package for the Social Sciences (SPSS) version 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Normality of data distribution was assessed using the Shapiro–Wilk test. Gender-wise comparisons of MMSE scores, P300 latency, and P300 amplitude within each study group were performed using the Independent Samples t-test. Because the T2DM <5 years group contained only three male participants, Mann–Whitney U test results were additionally reported to confirm the findings obtained from the Independent Samples t-test. A p-value <0.05 was considered statistically significant.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

RESULTS

The results are based on the study conducted in the Department of Physiology and Endocrine (Medicine) Department, JNIMS, Imphal. A total of 89 subjects were included in the study. The subjects were categorized into 4 groups: controls (n=30), prediabetes (n=14), T2DM <5 years (n=14), and T2DM 5–10 years (n=31). The mean age of the control group was 37.5 ± 6.73 years, prediabetes was 40.71 ± 6.57 years, T2DM (< 5 years) was 41.64 ± 6.92 years and T2DM (5–10 years) was 42.68 ± 5.36 years.

Preliminary gender-wise analysis revealed no statistically significant differences in MMSE scores, P300 latency, or P300 amplitude between male and female participants within any study group [Table 1]. All p-values were greater than 0.05, indicating absence of statistically significant gender differences.

Table 1: Preliminary Gender-wise Comparison of Cognitive Parameters

Group	P300 Latency (p-value)	P300 Amplitude (p-value)	MMSE (p-value)
Control	0.523	0.415	0.241
Prediabetic	0.693	0.348	0.449
T2DM <5 years	0.877	0.433	0.948
T2DM 5–10 years	0.362	0.636	0.883

Table 2: Gender-wise Comparison of Cognitive Parameters among Controls (n=30)

Variable	Male Mean ± SD (n=22)	Female Mean ± SD (n=8)	p-value
MMSE	29.45 ± 0.86	29.75 ± 0.46	0.241
P300 Latency (ms)	289.64 ± 26.27	282.13 ± 28.13	0.523
P300 Amplitude (µV)	11.28 ± 4.34	13.00 ± 5.10	0.415

Among healthy controls, MMSE scores, P300 latency, and P300 amplitude were comparable between males and females, with no statistically significant differences observed [Table 2].

Table 3: Gender-wise Comparison of Cognitive Parameters among Prediabetes (n=14)

Variable	Male Mean ± SD (n=7)	Female Mean ± SD (n=7)	p-value
MMSE	27.29 ± 2.56	26.43 ± 1.27	0.449
P300 Latency (ms)	309.14 ± 37.16	301.86 ± 29.76	0.693
P300 Amplitude (µV)	6.75 ± 4.29	9.37 ± 5.64	0.348

No statistically significant gender differences were observed among prediabetic participants for MMSE, P300 latency, or P300 amplitude [Table 3].

Table 4: Gender-wise Comparison of Cognitive Parameters among T2DM<5 years (n=14)

Variable	Male Mean ± SD (n=3)	Female Mean ± SD (n=11)	p-value
MMSE	26.33 ± 1.15	26.27 ± 1.95	0.948
P300 Latency (ms)	300.33 ± 29.50	303.45 ± 23.00	0.877
P300 Amplitude (µV)	12.24 ± 7.88	7.79 ± 4.25	0.433

Similarly, participants with T2DM <5 years duration showed no significant gender-related differences in any cognitive parameter [Table 4].

Because of the small sample size among male participants in the T2DM <5 years group, a Mann–Whitney U test was performed. No significant gender differences were observed for MMSE score (U = 17.0, p = 1.000), P300 latency (U = 14.0, p = 0.769), or P300 amplitude (U = 22.0, p = 0.436) [Table 5].

Table 5: Mann–Whitney U Test Results

Variable	U statistic	p-value
MMSE	17.0	1.000
P300 Latency (ms)	14.0	0.769
P300 Amplitude (µV)	22.0	0.436

Table 6: Gender-wise Comparison of Cognitive Parameters among T2DM (5–10 years) (n=31)

Variable	Male Mean ± SD (n=13)	Female Mean ± SD (n=18)	p-value
MMSE	27.23 ± 3.37	27.39 ± 2.15	0.883
P300 Latency (ms)	281.00 ± 28.77	293.94 ± 48.71	0.362
P300 Amplitude (µV)	6.31 ± 3.01	7.06 ± 5.71	0.636

No significant gender differences were identified among participants with diabetes duration of 5–10 years [Table 6].

Across all study groups, MMSE scores, P300 latency, and P300 amplitude were comparable between male and female participants. These findings suggest that gender does not significantly influence cognitive performance assessed by either MMSE or ERP-P300 among healthy controls, individuals with prediabetes, and patients with T2DM.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

DISCUSSION

The present study evaluated gender-related differences in cognitive function among healthy controls, prediabetes, and T2DM using MMSE scores and ERP-P300 parameters. The principal finding was the absence of statistically significant differences between male and female participants with respect to MMSE scores, P300 latency, and P300 amplitude across all study groups. These findings suggest that gender does not significantly influence cognitive performance or electrophysiological markers of cognitive processing in individuals with prediabetes and T2DM.

Diabetes mellitus has consistently been associated with cognitive dysfunction. Meta-analytic evidence has demonstrated impairments in executive function, processing speed, attention, and memory among individuals with T2DM compared with normoglycemic controls.2 Similarly, structural neuroimaging studies have reported cerebral atrophy, white matter abnormalities, and reduced hippocampal volume among diabetic individuals.[14] These alterations are believed to arise from chronic hyperglycemia, insulin resistance, vascular dysfunction, oxidative stress, and neuroinflammatory processes.[3-5,13]

An important observation of the present study is that no significant gender-related differences were detected within the control, prediabetes, or T2DM groups. This finding is consistent with the concept that metabolic abnormalities associated with dysglycemia exert a stronger influence on cognitive function than biological sex alone. Although sex hormones have been implicated in cognitive aging and neuroprotection, diabetes-related metabolic disturbances may affect neural networks similarly in both males and females.

Our findings are in agreement with studies that have reported minimal or no independent effect of sex on diabetes-associated cognitive decline after accounting for glycemic status and vascular risk factors. Rawlings et al. reported that diabetes in midlife was associated with long-term cognitive decline irrespective of sex.[12] Similarly, Biessels and Despa emphasized that metabolic and vascular mechanisms rather than gender-specific factors play a central role in diabetes-related neurocognitive impairment.[13] Large epidemiological investigations have also suggested that the severity of hyperglycemia, disease duration, and associated cardiovascular risk factors are stronger predictors of cognitive decline than gender.[15]

The present study also demonstrated comparable ERP-P300 parameters between males and females. ERP-P300 is considered a sensitive electrophysiological marker of attention, stimulus evaluation, and working memory.9,10 Previous investigations have shown prolonged P300 latency and reduced P300 amplitude among diabetic individuals, reflecting impaired cortical information processing.[11] However, studies specifically examining gender differences in ERP-P300 responses among individuals with dysglycemia remain limited. The absence of significant gender differences in the present study suggests that the neurophysiological consequences of hyperglycemia and insulin resistance may affect cortical processing similarly in both sexes.

Interestingly, no gender differences were observed even among prediabetic participants. Recent systematic reviews have demonstrated that cognitive dysfunction and structural brain changes may be detectable during the prediabetic stage.[16,17] The present findings suggest that these early neurocognitive alterations are unlikely to differ substantially between males and females, although larger longitudinal studies are required to confirm this observation.

The clinical implications of the present findings are noteworthy. Since cognitive dysfunction appears to occur similarly in both sexes, screening and preventive strategies for diabetes-related cognitive impairment may be applied uniformly to male and female patients. Furthermore, ERP-P300 may serve as a useful objective adjunct to conventional cognitive screening methods for identifying early cognitive dysfunction in individuals with prediabetes and T2DM.

The present study has several limitations. First, its cross-sectional design precludes causal inference. Second, the sample size was relatively small, particularly in the T2DM group of less than five years duration, where only three male participants were included. Consequently, the study may have been underpowered to detect subtle gender-related differences, increasing the possibility of Type II error. Third, educational status, socioeconomic factors, glycemic control, and lifestyle variables were not evaluated and may have influenced cognitive performance. Future longitudinal studies with larger and more balanced samples are warranted to further clarify the interaction between gender, dysglycemia, and cognitive function.

CONCLUSION

The present study demonstrated that gender does not significantly influence cognitive performance, as assessed by MMSE scores and ERP-P300 parameters, among healthy controls, prediabetic individuals, and patients with type 2 diabetes mellitus. The absence of significant gender-related differences across all study groups suggests that diabetes-associated cognitive dysfunction is primarily driven by metabolic and disease-related factors rather than biological sex. Furthermore, the comparable P300 latency and amplitude observed in males and females indicate similar neurophysiological effects of dysglycemia on cognitive processing. These findings suggest that cognitive screening strategies may be applied

ISSN (O): 2687-5365; ISSN (P): 2753-6556

similarly in both sexes among individuals with prediabetes and T2DM. ERP-P300 may serve as a valuable objective tool for the early detection of subtle cognitive impairment. Further large-scale longitudinal studies are warranted to clarify the complex relationship between glycemic status, disease progression, and cognitive function.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556