https://doi.org/10.46389/rjd-2026-1729
www.rjdnmd.org

Rom J Diabetes Nutr Metab Dis
2026; volume 33, issue 2, pages 168–177

Original Article

Cognitive impairment in diabetes: the impending pandemic

Karun Mammen Philip [1], Smitha Bhat [2] *

[1] Department of Endocrinology, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India
[2] Department of Medicine, Father Muller Medical College, Mangalore, India

* Correspondence to: Smitha Bhat, Department of Medicine, Father Muller Medical College, Mangalore, India. E-mail: doctorsmitha@yahoo.co.in

Received: 9 February 2026 / Accepted: 30 April 2026

Abstract

Type 2 Diabetes Mellitus affects more than 450 million people worldwide. Cognitive impairment is a less recognized chronic complication of diabetes and is referred to as accelerated cognitive aging. The Montreal Cognitive Assessment is a tool to screen for mild cognitive impairment. Our study aimed to determine the factors associated with cognitive impairment in patients with Diabetes Mellitus in a tertiary care center in South India. This was a cross-sectional study done on 109 patients with Type 2 Diabetes Mellitus over a period of 18 months. Montreal Cognitive Assessment scale was administered to subjects in the local language. Cognitive impairment was defined as a score of 25 or less. Data was analyzed using student t-test, chi square test and rank correlation; p-value <0.005 was considered significant. The mean age of subjects was 50.92±10.10 years. Fifty three percent of subjects (58) were male and 46.8% (51) were female. The prevalence of cognitive impairment was 67%. The risk of cognitive impairment increased with the number of episodes of hypoglycemia, the mean duration of diabetes and higher fasting sugars. The duration of formal schooling decreased the risk of cognitive decline. In India the prevalence of cognitive impairment in patients with diabetes is relatively high. Both hypoglycemia and hyperglycemia seem to be associated with an increased risk of cognitive impairment. The risk of impairment is directly proportional to the duration of diabetes and inversely proportional to the duration of formal education. Since therapies to treat dementia once it sets in are not infallible, prevention becomes key. A fine balance between achieving euglycemia and avoiding hypoglycemia must be achieved.

Keywords: type 2 diabetes, cognitive impairment, MoCA scale, cognitive decline, dementia

Introduction

Type 2 Diabetes Mellitus (T2DM) is a global epidemic affecting more than 529 million people worldwide [1]. The prevalence of T2DM is rising in India and is estimated to rise to 134 million by the year 2045 [2]. Chronic complications of T2DM include microvascular complications: diabetic retinopathy, di abetic nephropathy and neuropathy, as well as macrovascular complications: cardiovascular; cerebrovascular and peripheral vascular disease.

Cognitive impairment is increasingly being recognized as a subtle but disabling complication of diabetes – in fact, T2DM is considered to be a state of "accelerated cognitive aging" [3]. The spectrum of cognitive decline in T2DM ranges from Diabetes Associated Cognitive Decrement (DACD) through Minimal Cognitive Impairment (MCI) to frank dementia.

DACD may develop even during the prediabetic stage. In DACD, the patient presents with complaints related to processing speed, executive function or memory [4]. The rate of cognitive aging is almost 50% higher than in individuals without diabetes [5]. In MCI there is an acquired objective cognitive impairment with a documented performance of at least less than 1.5 SD of normative values. Only a single cognitive domain is affected, and activities of daily living are preserved. MCI is considered to be a risk factor for dementia [6].

Once dementia sets in, there is severe acquired objective cognitive impairment which affects multiple domains and inexorably progresses to impair activities of daily living [7].

The risk factors for cognitive decline in T2DM include uncontrolled sugars, glycemic variability and insulin resistance as well as the comorbidities of diabetes – hypertension, dyslipidemia and depression [8, 9].

However, the relative contribution of each of these factors is unknown.

Published Indian literature regarding cognitive impairment in T2DM is relatively scanty. Specifically, cognitive impairment in relation to educational attainment and documented episodes of hypoglycemia has not been studied.

The Montreal Cognitive Assessment (MoCa) is a tool to screen for mild cognitive impairment and takes approximately 10 minutes to administer [7]. A score of 26 or more is considered normal and a score of 25 or less is indicative of cognitive impairment. MoCa is recommended by National Institutes of Health and the Canadian Stroke Network for assessment of cognitive impairment. Our study aimed to use MoCa to assess cognition in patients with T2DM and determine the factors associated with cognitive decline.

Material and methods

Study design and setting

This cross-sectional study was conducted on 119 subjects with Type 2 Diabetes Mellitus (T2DM) who fulfilled the selection criteria and were availing the inpatient and outpatient services of a medical college hospital.

Sample size calculation

The sample size was calculated using the formula:

$$n = Z^2 \times p(1 - p) / e^2$$

Where:

- Z = Confidence level;
- p = Estimated prevalence;
- e = Allowable error.

For an allowable error (e) of 5%, the calculated sample size was 117.

Selection criteria

The selection criteria for the study were defined based on specific inclusion and exclusion parameters.

Inclusion criteria consisted of patients with known cases of Type 2 Diabetes Mellitus (T2DM) who were receiving treatment with oral antidiabetic drugs (OAD), insulin, or a combination of both. In addition, newly diagnosed cases of T2DM, identified according to the American Diabetes Association (ADA) criteria, were also included in the study.

Exclusion criteria included patients who were in an altered sensorium and therefore unable to undergo the Montreal Cognitive Assessment (MoCA). Patients with known conditions associated with dementia, such as Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, Parkinson's disease, and Huntington's disease, were also excluded. Furthermore, individuals with a previous history of head injury or cerebrovascular accidents were not considered for participation. Patients older than 65 years of age were excluded, as were those not conversant in Kannada, Malayalam, or English, since language proficiency was required for assessment. Additionally, alcoholics identified using the CAGE questionnaire were excluded from the study.

Operational definitions

The operational definitions used in this study were as follows:

Diabetes mellitus was defined according to the American Diabetes Association (ADA) criteria. A diagnosis of diabetes was considered if any of the following were present: symptoms of diabetes along with a random blood glucose level ≥11.1 mmol/L (200 mg/dL), fasting plasma glucose ≥7.0 mmol/L (126 mg/dL), two-hour plasma glucose ≥11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test, or HbA1c greater than 6.5%.

Cognitive impairment was assessed using the Montreal Cognitive Assessment (MoCA) scale. In this study, mild cognitive impairment (MCI) was defined as a MoCA score of 25 or less.

Hypoglycemia for the purpose of this study was defined as a random blood sugar level of 70 mg/dL or less measured by a glucometer, and/or the presence of self-reported symptoms such as palpitations, tremors, hunger, or sweating. It also included bystander-reported symptoms such as altered behaviour or confusion suggestive of hypoglycemia.

Data collection procedure

Prior approval was obtained from the Institute Ethics Committee, and written informed consent was obtained from all participants before enrolment in the study. A directed history and physical examination were conducted for each participant and recorded

according to the study proforma. The Montreal Cognitive Assessment (MoCA) was administered to all subjects by one of the authors.

Laboratory investigations

Venous blood samples were collected from the participants and analysed within one hour of collection to minimize variation due to sample aging. Fasting and postprandial blood glucose levels were measured using the hexokinase method, serum sodium was estimated using the indirect ion-selective electrode (ISE) method, and total cholesterol was measured using the cholesterol oxidase method. These parameters were analysed by microturbidimetric assay using the Roche Diagnostics Cobas 6000 clinical chemistry auto-analyzer. HbA1c levels were measured using the high-performance liquid chromatography (HPLC) method with the Turbo Variant II system.

Statistical analysis

The collected data were analysed using SPSS software. Frequencies, percentages, and ratios were calculated. Statistical analysis was performed using the Chi-square test and Student's t-test, and a two-tailed p-value of less than 0.005 was considered statistically significant.

Results

We included 109 patients of T2DM in our study. General characteristics are summarized in Table 1.

The mean subject age was 50.92±10.1. The mean duration of T2DM was 8.47±7.25 years and the mean number of years of formal education was 11.23±2.77 years.

Mean FBS, PPBS and HbA1C were 152.68, 238.96 and 10.6 respectively. 67% of our patients had MCI, and the mean MoCA score was 23.66±5.4.

Though cognition tended to decline with age, this association did not reach statistical significance (Figure 1). Gender was not significantly associated with cognitive decline. (Figure 2). The risk of MCI significantly increased with the duration of diabetes (Figure 3), the fasting sugar (Figure 4), the glycated hemoglobin (Figure 5) and with the number of episodes of hypoglycemia (Figure 6). The degree of post-prandial hyperglycemia did not correlate with cognitive decline (Figure 7); the number of years of formal education was inversely related to MCI (Figure 8).

Discussion

This was a hospital based cross-sectional study to determine the factors associated with cognitive impairment in patients with T2DM. We found that 67% of our subjects had MCI, and the mean MoCa score was 23.66. More women than men had MCI, and subjects with MCI tended to be older, though this result did not achieve statistical significance. MCI was significantly associated with the duration of diabetes and the number of episodes of hypoglycemia and higher blood glucose. The risk of MCI decreased with the number of years of formal education.

The average global prevalence of MCI in T2DM is 45% [10] but it varies widely between countries from a

Table 1: General characteristics of patients.

	Frequency (n)	Percentage (%)
Gender		
Female	51	46.8
Male	58	53.2
Age group (in years)		
<30 years	3	2.8
30–39 years	14	12.8
40–49 years	29	26.6
50–59 years	31	28.4
>60 years	32	29.4
Total	109	100.0

https://doi.org/10.46389/rjd-2026-1729

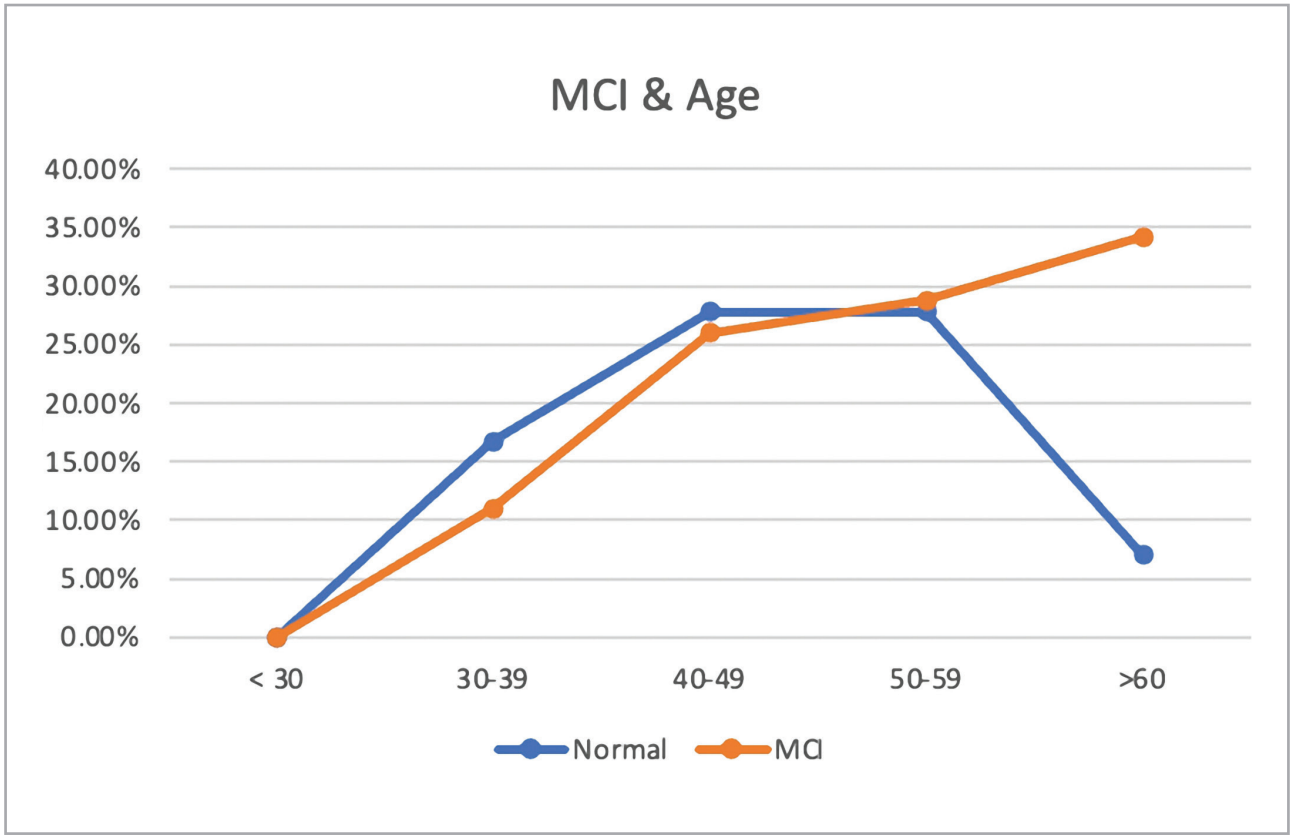

Figure 1: Age and cognitive impairment p=0.08.

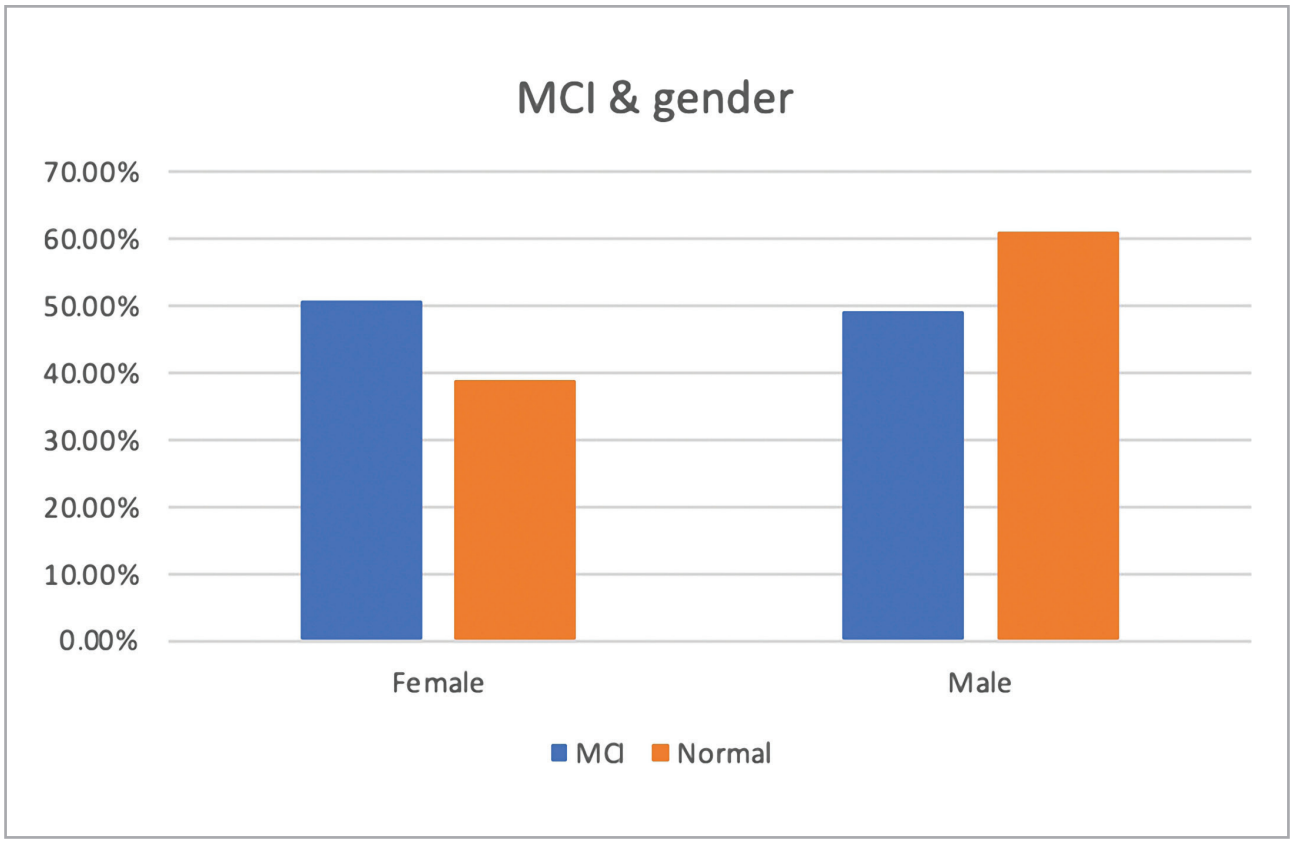

Figure 2: Gender and cognitive impairment.

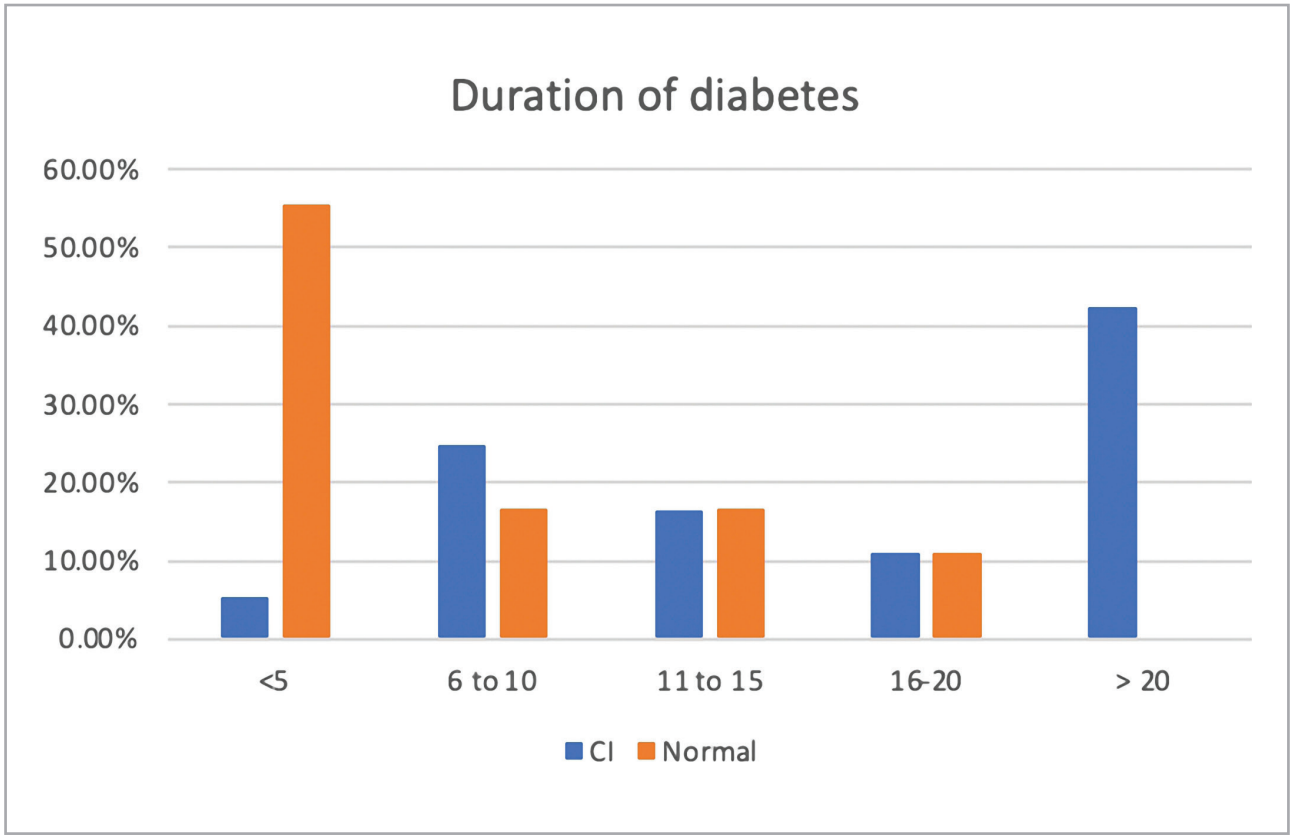

Figure 3: Duration of DM & cognitive impairment p=0.001.

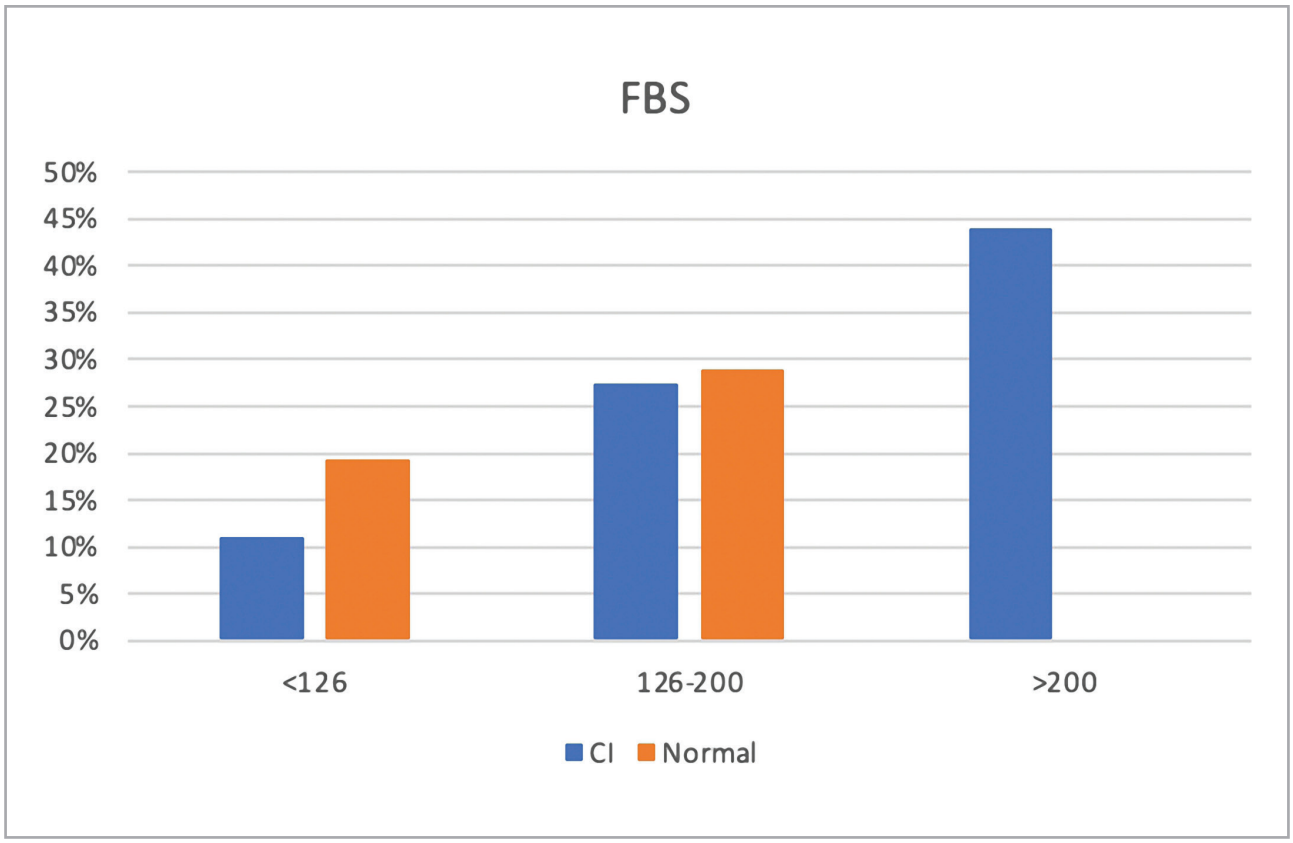

Figure 4: FBS and cognitive impairment p=0.001.

https://doi.org/10.46389/rjd-2026-1729

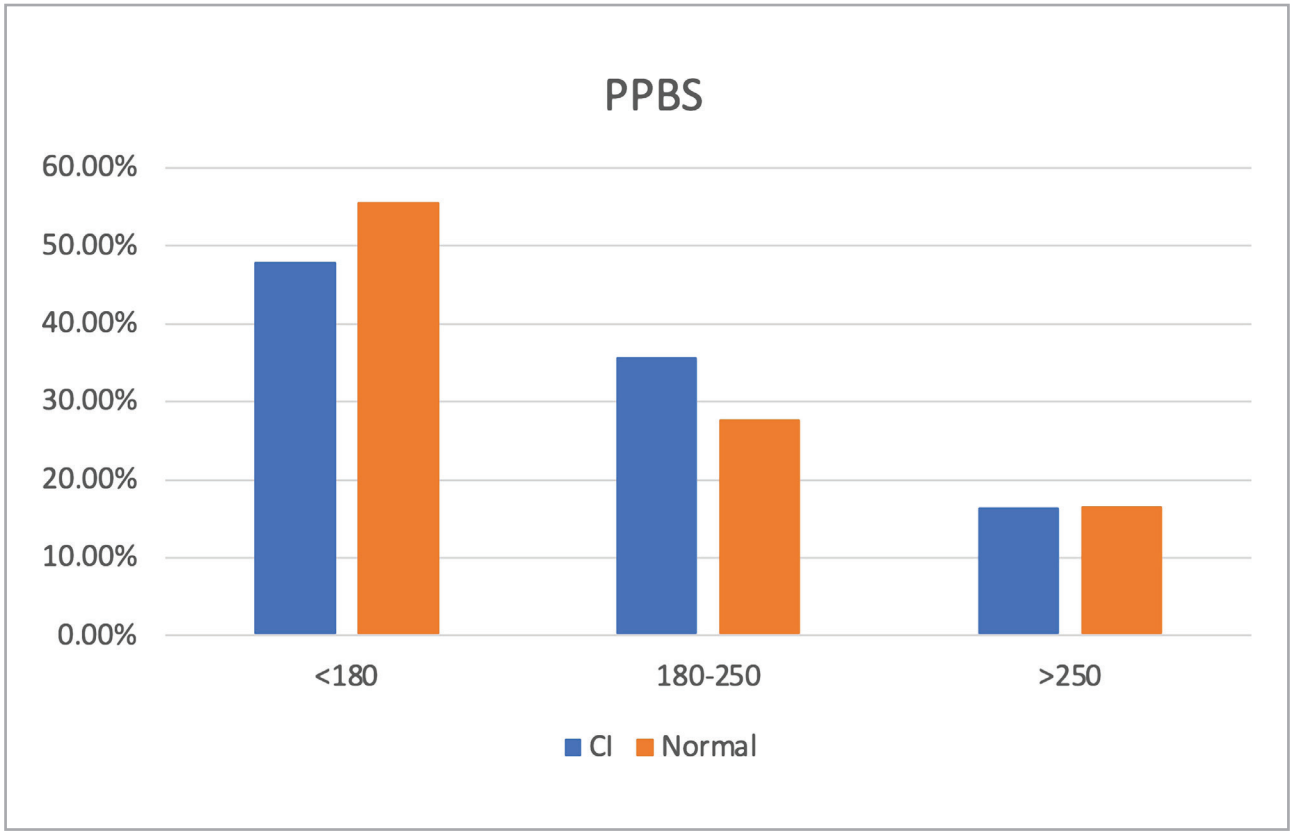

Figure 5: Post prandial sugars and cognitive impairment.

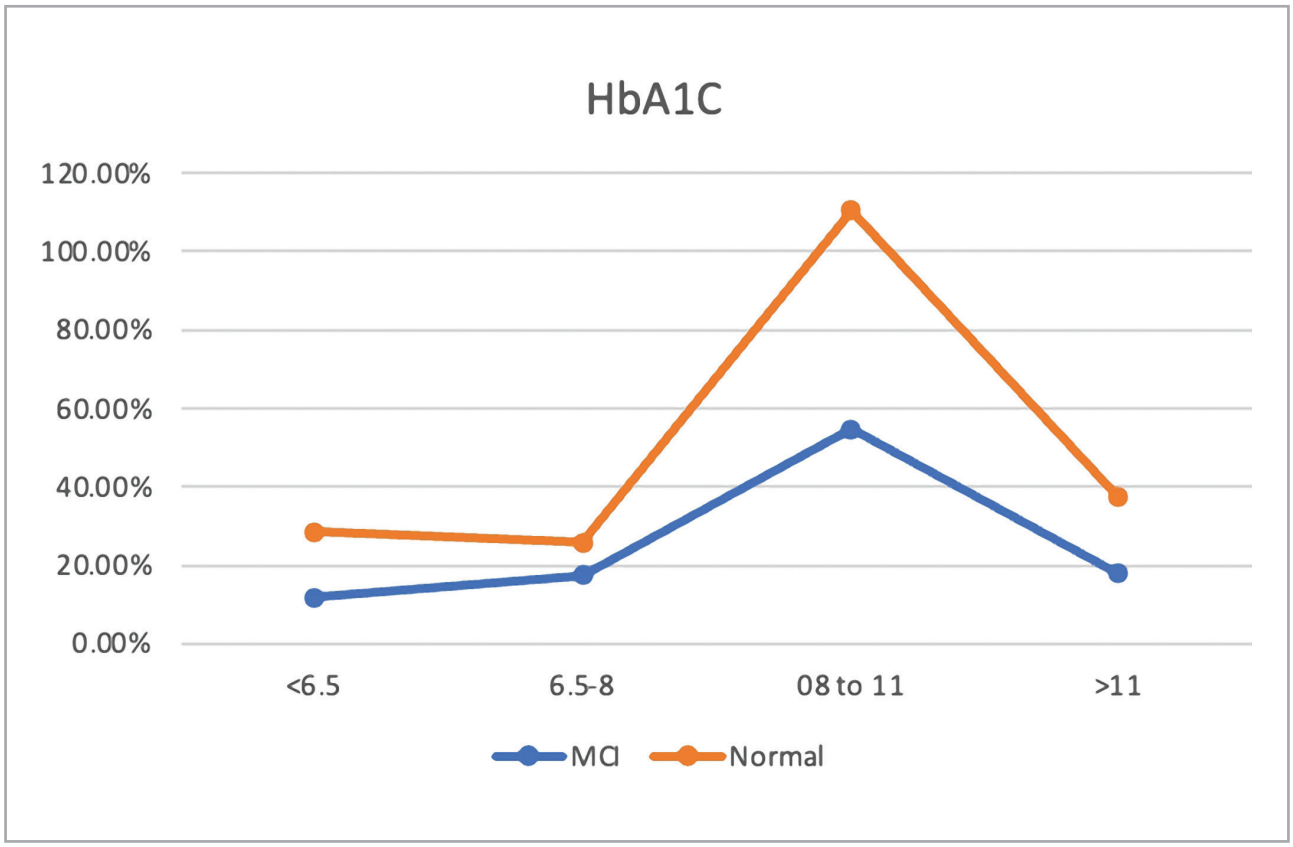

Figure 6: HbA1c and cognitive impairment.

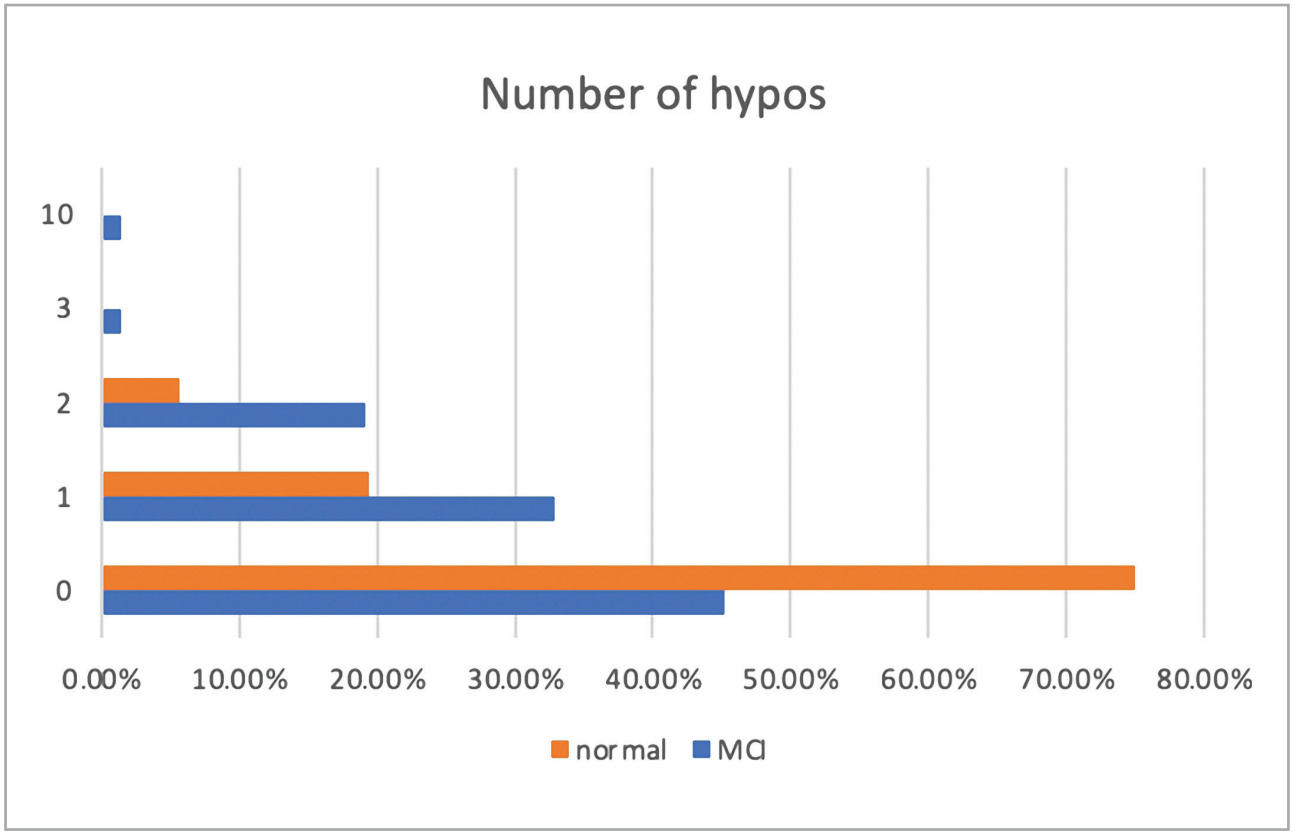

Figure 7: Hypoglycemia and cognitive impairment.

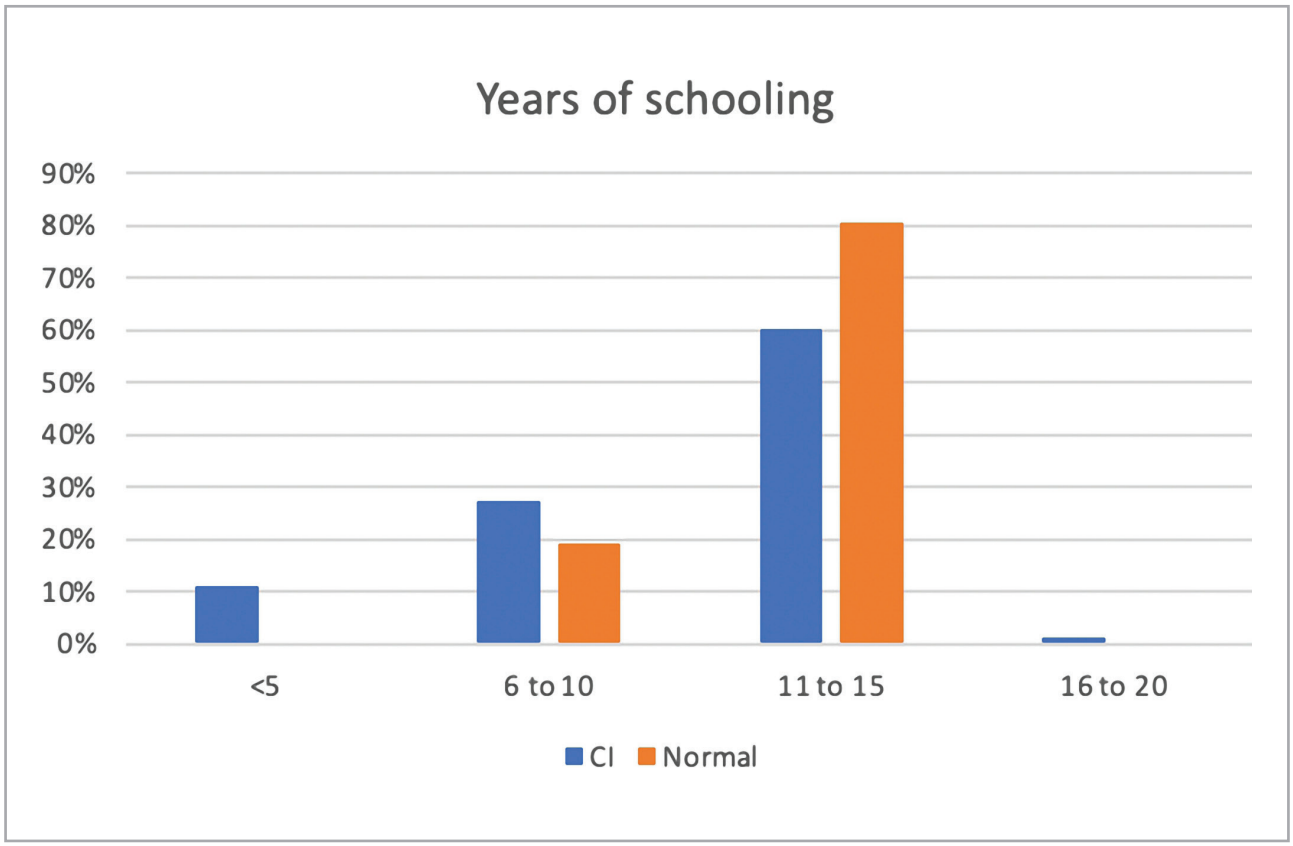

Figure 8: Years of education and cognitive impairment.

https://doi.org/10.46389/rjd-2026-1729

reported 13.5% in China [11] to 67.5% in Pakistan [12]. These differences may be related to the distribution of risk factors like age, diabetes, or the lack of formal education as well as non-uniform criteria for diagnosis of MCI.

Our finding that MCI in patients with diabetes tended to increase with age is in line with published evidence. The prevalence of both diabetes [13] and dementia [14] increase as age progresses. A rapidly ageing global population would mean that the global prevalence of these diseases is rising as well.

Our findings indicate that the risk of MCI increases with hyperglycemia and the duration of diabetes. These results build upon studies from Brazil and India, which all found that duration of diabetes was an independent risk factor for cognitive decline in adults with T2DM [15, 16]. Hyperglycemia (especially fasting hyperglycemia) and the duration of diabetes act synergistically to damage cognition. Putative mechanisms are several [17].

Hyperglycaemia leads to formation of advanced glycation end products (AGE) which enhance the expression of receptors for AGE. These in turn activate pro-inflammatory cytokines and cause neuroinflammation, decline of cognition & impaired memory. Insulin resistance also plays a role, causing post-translational modifications of tau which exacerbate tau pathology. Hyperglycemia has also been found to accelerate oxidative stress, Reactive Oxygen Species (ROS) formation, mitochondrial dysfunction.

As the duration of diabetes increases, there is an increase in neuronal damage secondary to microvascular and macrovascular disease, oxidative stress and insulin resistance. Signal interruption in the neural networks due to diabetes is further exacerbated in long standing T2DM [18]. Since diabetes itself is a risk factor for atherosclerosis, long standing diabetes may result in cognitive decline through its association with cerebrovascular disease and stroke [19]. Long standing hyperglycemia results in increased flux of glucose through the polyol pathway resulting in the formation of advanced glycation end products, thus culminating in oxidative stress and the inexorable progression of neuronal damage [20, 21].

In this study, we found that almost 100% of patients with diabetes for more than 20 years had at least a degree of cognitive impairment.

Our results contradict the findings of several studies including a report on older Korean adults with diabetes [8]. However, in the Korean study, unlike in ours, diabetes was well controlled, and thus perhaps, the cumulative effect of hyperglycemia was minimized.

We found that hypoglycemia was strongly associated with the presence of MCI. Cognitive decline increased with the number of episodes of hypoglycemia.

This data builds upon evidence from previous studies: a meta-analysis of 1.4 million patients showed that patients with hypoglycemic episodes had a higher risk of dementia when compared to those with no such episodes [22]. Again, there are multiple proposed mechanisms for how hypoglycemia might accelerate dementia. Firstly, low blood glucose can result in structural changes in the brain since the brain primarily relies on glucose as a source of energy [23]. Severe hypoglycemia preferentially damages neurons in the hippocampus and cortex which increases the risk of impaired cognition since the hippocampus is the seat of memory [24]. Hypoglycemia may also cause vascular injury and endothelial dysfunction [25]. However microvascular and macrovascular damage is not sufficient to explain the myriad ways in which low blood glucose affects the brain. For example, animal models show that hypoglycemia promotes the accumulation of brain amyloid which is linked with Alzheimer's [26].

Our data suggests a negative association between duration of formal schooling and cognitive decline. This is in line with most published research which shows that education protects against cognitive impairment. Every year of education lowers the risk of dementia by 7% [27] and low education is a risk factor for dementia, [28] though causality remains tenuous.

Several theories have been proposed to elucidate the inverse relationship between formal education and the risk of dementia. A longer duration of schooling could conceivably raise intellectual ability to a higher level, thus increasing cognitive reserve [29]. The protective effect against cognitive impairment may be because a greater neural reserve is less prone to disruption or alternatively because of neural compensation wherein the development of alternate networks counteracts the disruption that leads to dementia [30]. However, other researchers opine that the protective effect of education is in fact because education behaves as a proxy indicator for socioeconomic determinants of brain health [31]. A study published in 1999 supported the "brain battering" hypothesis which suggested, based on autopsy findings, that less educated individuals were more likely to develop vascular dementia. However, this theory is not uniformly accepted as more recent post-mortem imaging studies do not show greater pathology in those less educated [32].

Since this was a cross-sectional study, causality could not be inferred. Neuroimaging was not part of

the study protocol; hence structural abnormalities could not definitively be ruled out, though clinical examination finding were not indicative of the same. Additionally, the generalizability of the results is limited by the fact that it was a single centre study. Nevertheless, our research on patients with diabetes of varying degrees of glycemic control and different comorbidities emphasizes the importance of screening for cognitive impairment in all patients with diabetes. Furthermore, the fact that we used MoCa to assess cognition strengthens our conclusions, as MoCA assesses a broader range of cognitive domains including abstraction and executive function, and thus is more sensitive than MMSE to diagnose MCI in patients with T2DM. However, some authors consider that a MoCA cut-off score of ≤25 yields a high false positive rate and suggest a lower cut-off score of <23 [33]. This lower cut-off suggested for MoCA was based on a meta-analysis of studies comprising patients of widely varying education levels and cultural backgrounds. Since our study was conducted in a relatively homogenous population, we used the cut-off of ≤25, which has been validated by multiple studies [34–36].

The fact that MCI is more common in patients with diabetes and that diabetes accelerates the progression of MCI to dementia results in a vicious circle wherein the twin insults of diabetes and aging further worsen diabetes self-care. At present, there are no infallible treatments for dementia. Hence prevention becomes key [37]. Our results suggesting almost universal cognitive impairment in patients with diabetes for more than 20 years has public health implications. The high prevalence of diabetes would mean a rapidly increasing number of patients with cognitive impairment as the duration of the disease increases. Health resources must be planned and allocated to provide attention to patients whose diabetes self-care abilities are curtailed due to the onset of cognitive impairment.

Conclusion

The fact that both uncontrolled blood sugars and hypoglycemia worsen the risk of dementia means that the management of diabetes with the aim of preventing cognitive damage is akin to walking on a tightrope.

Hence, screening for MCI in diabetes must run in parallel with screening for microvascular and macrovascular complications. Detection of DACD is an excellent opportunity to commence preventive measures in terms of antidiabetic drugs less likely to cause hypoglycemia, prescribing drugs which may benefit cognition, and encouraging performance of cognitive stimulation exercises.

Acknowledgements

This research was done as partial fulfilment of the requirement of completion of postgraduation in internal medicine of Rajiv Gandhi University of Health Sciences Bangalore Karnataka.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Father Muller Medical College, Mangalore (approval ID: FMMC/FMIEC/4502/2017).

References

1. Ong KL, Stafford LK, McLaughlin SA, Boyko EJ, Vollset SE, Smith AE, et al. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet. 2023;402(10397).
2. Pradeepa R, Mohan V. Epidemiology of type 2 diabetes in India. Vol. 69, Indian journal of ophthalmology. 2021.
3. Antal B, McMahon LP, Sultan SF, Lithen A, Wexler DJ, Dickerson B, et al. Type 2 diabetes mellitus accelerates brain aging and cognitive decline: Complementary findings from UK Biobank and meta-analyses. Elife. 2022;11.
4. Dove A, Shang Y, Xu W, Grande G, Laukka EJ, Fratiglioni L, et al. The impact of diabetes on cognitive impairment and its progression to dementia. Alzheimer's and Dementia. 2021;17(11).
5. Levine ME, Harrati A, Crimmins EM. Predictors and implications of accelerated cognitive aging. Biodemography Soc Biol. 2018;64(2).
6. McCrimmon RJ, Ryan CM, Frier BM. Diabetes and cognitive dysfunction. Vol. 379, The Lancet. 2012.
7. Vermeer SE, Den Heijer T, Koudstaal PJ, Oudkerk M, Hofman A, Breteler MMB. Incidence and risk factors of silent brain infarcts in the population-based Rotterdam Scan Study. Stroke. 2003;34(2).
8. Yu JH, Han K, Park S, Cho H, Lee DY, Kim JW, et al. Incidence and risk factors for dementia in type 2 diabetes mellitus: A nationwide population-based study in Korea. Diabetes Metab J. 2020;44(1).
9. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment,

 https://doi.org/10.46389/rjd-2026-1729

MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53(4).
10. Sachdev PS, Lipnicki DM, Kochan NA, Crawford JD, Thalamuthu A, Andrews G, et al. The prevalence of mild cognitive impairment in diverse geographical and ethnocultural regions: The COSMIC Collaboration. PLoS One. 2015;10(11).
11. Gao Y, Xiao Y, Miao R, Zhao J, Cui M, Huang G, et al. The prevalence of mild cognitive impairment with type 2 diabetes mellitus among elderly people in China: A cross-sectional study. Arch Gerontol Geriatr. 2016;62.
12. Atif M, Saleem Q, Scahill S. Depression and mild cognitive impairment (MCI) among elderly patients with type 2 diabetes mellitus in Pakistan: possible determinants. Int J Diabetes Dev Ctries. 2018;38(3).
13. Magliano DJ, Shaw JE, Shortreed SM, Nusselder WJ, Liew D, Barr ELM, et al. Lifetime risk and projected population prevalence of diabetes. Diabetologia. 2008;51(12).
14. 2020 Alzheimer's disease facts and figures. Alzheimer's and Dementia. 2020;16(3).
15. de Almeida Faria ACR, Dall'Agnol JF, Gouveia AM, de Paiva CI, Segalla VC, Baena CP. Risk factors for cognitive decline in type 2 diabetes mellitus patients in Brazil: a prospective observational study. Diabetol Metab Syndr. 2022;14(1).
16. Raina S, Chander V, Raina S, Kumar D, Grover A, Bhardwaj A. Hypertension and diabetes as risk factors for dementia: A secondary post-hoc analysis from north-west India. Ann Indian Acad Neurol. 2015;18(1).
17. Li FR, Yang HL, Zhou R, Zheng JZ, Chen GC, Wu XX, et al. Influence of diabetes duration and glycemic control on dementia: A cohort study. Journals of Gerontology - Series A Biological Sciences and Medical Sciences. 2021;76(11).
18. Ortiz GG, Huerta M, González-Usigli HA, Torres-Sánchez ED, Delgado-Lara DL, Pacheco-Moisés FP, et al. Cognitive disorder and dementia in type 2 diabetes mellitus. World J Diabetes. 2022;13(4).
19. Xing YL, Chen MA, Sun Y, Neradilek MB, Wu XT, Zhang D, et al. Atherosclerosis, its risk factors, and cognitive impairment in older adults. Journal of Geriatric Cardiology. 2020;17(7).
20. Dhananjayan K, Forbes J, Münch G. Advanced Glycation, Diabetes, and Dementia. In: Type 2 Diabetes and Dementia. 2018.
21. Lovestone S, Smithb U. Advanced glycation end products, dementia, and diabetes. Vol. 111, Proceedings of the National Academy of Sciences of the United States of America. 2014.
22. Huang L, Zhu M, Ji J. Association between hypoglycemia and dementia in patients with diabetes: a systematic review and meta-analysis of 1.4 million patients. Vol. 14, Diabetology and Metabolic Syndrome. 2022.
23. Whitmer RA, Gilsanz P, Quesenberry CP, Karter AJ, Lacy ME. Association of Type 1 Diabetes and Hypoglycemic and Hyperglycemic Events and Risk of Dementia. Neurology. 2021;97(3).
24. Languren G, Montiel T, Julio-Amilpas A, Massieu L. Neuronal damage and cognitive impairment associated with hypoglycemia: An integrated view. Vol. 63, Neurochemistry International. 2013.
25. Wright RJ, Newby DE, Stirling D, Ludlam CA, Macdonald IA, Frier BM. Effects of acute insulin-induced hypoglycemia on indices of inflammation: Putative mechanism for aggravating vascular disease in diabetes. Diabetes Care. 2010;33(7).
26. Shi J, Xiang Y, Simpkins JW. Hypoglycemia enhances the expression of mRNA encoding β-amyloid precursor protein in rat primary cortical astroglial cells. Brain Res. 1997;772(1–2).
27. Xu W, Tan L, Wang HF, Tan MS, Tan L, Li JQ, et al. Education and Risk of Dementia: Dose-Response Meta-Analysis of Prospective Cohort Studies. Vol. 53, Molecular Neurobiology. 2016.
28. Sharp ES, Gatz M. Relationship between education and dementia: An updated systematic review. Vol. 25, Alzheimer Disease and Associated Disorders. 2011.
29. Brinch CN, Galloway TA. Schooling in adolescence raises IQ scores. Proc Natl Acad Sci U S A. 2012;109(2).
30. Stern Y. Cognitive reserve and Alzheimer disease. Vol. 20, Alzheimer Disease and Associated Disorders. 2006.
31. Dekhtyar S, Wang HX, Scott K, Goodman A, Ilona K, Herlitz A. A life-course study of cognitive reserve in dementia - From childhood to old age. American Journal of Geriatric Psychiatry. 2015;23(9).
32. Del Ser T, Hachinski V, Merskey H, Munoz DG. An autopsy-verified study of the effect of education on degenerative dementia. Brain. 1999;122(12).
33. Carson N, Leach L, Murphy KJ. A re-examination of Montreal Cognitive Assessment (MoCA) cutoff scores. Int J Geriatr Psychiatry. 2018;33(2).
34. Karim MA, Venkatachalam J. Construct Validity and Psychometric Properties of the Tamil (India) Version of Montreal Cognitive Assessment (T-MoCA) in Elderly. Int J Gerontol. 2022;16(4).
35. McDicken JA, Elliott E, Blayney G, Makin S, Ali M, Larner AJ, et al. Accuracy of the short-form Montreal Cognitive Assessment: Systematic review and validation. Int J Geriatr Psychiatry. 2019;34(10).
36. Luis CA, Keegan AP, Mullan M. Cross validation of the Montreal Cognitive Assessment in community dwelling older adults residing in the Southeastern US. Vol. 24, International Journal of Geriatric Psychiatry. 2009
37. Kawamura T, Umemura T, Hotta N. Cognitive impairment in diabetic patients: Can diabetic control prevent cognitive decline? Vol. 3, Journal of Diabetes Investigation. 2012.