

Cognitive impairment in older adults with DM and HBP in a primary care setting

Sergio A. Rodríguez-Castillo¹, Fernando Cortés-Enríquez^{2,3*}, Estefanía González-Alcaraz⁴, Haydé G. Guzmán-Barajas⁵, Elizabeth Sarmiento-Lizárraga⁶, and Danya L. Durán-Humbert^{2,7}

¹Servicio de Consulta Externa, Unidad de Medicina Familiar No. 48, Instituto Mexicano del Seguro Social (IMSS), Guadalajara; ²Departamento de Investigación Clínica, Unidad de Neurociencias de Occidente, Guadalajara; ³Servicio de Neurología, Hospital General Regional 45, IMSS, Guadalajara; ⁴Unidad de Psicología, Clínica "Estefanía González", Guadalajara; ⁵Jefatura de Enseñanza, Unidad de Medicina Familiar No. 51, IMSS, Guadalajara; ⁶Facultad de Medicina, Instituto Tecnológico y de Estudios Superiores de Monterrey, Guadalajara; ⁷Facultad de Medicina, Universidad Autónoma de Guadalajara, Zapopan, Jalisco, Mexico

Abstract

Objective: We conducted a cross-sectional study to identify, characterize, and compare the presence of cognitive impairment in patients with diabetes mellitus (DM) and patients with high blood pressure (HBP) who were seen in primary care. **Methods:** Consecutive patients over the age of 65 with DM or HBP who attended outpatient consultation at the Family Medicine Unit No. 51 of the Mexican Institute of Social Security in Guadalajara were included in the study. The Montreal Cognitive Assessment (MoCA) test was applied to detect the presence of cognitive impairment. **Results:** A total of 177 patients (59.9% men) with DM (59.9%) or HBP (40.1%) were included in the study. It was found that 44.1% of the participants had cognitive impairment. **Conclusions:** The prevalence of cognitive impairment in older adults with DM or HBP is higher than in older adults without these comorbidities. The use of a quick and easy screening test such as the MoCA test in this group of patients could allow for early detection and impact on timely referral, approach, and management.

Keywords: Cognitive impairment. Arterial hypertension. Diabetes mellitus.

Deterioro cognitivo en adultos mayores con DM y HAS en un primer nivel de atención

Resumen

Objetivo: Realizamos un estudio transversal para identificar, caracterizar y comparar la presencia de deterioro cognitivo en pacientes con DM y pacientes con HAS atendidos en el primer nivel de atención. **Métodos:** Se incluyeron pacientes consecutivos mayores de 65 años con DM o HAS que acudieron a consulta externa a la Unidad de Medicina Familiar N° 51 del Instituto Mexicano del Seguro Social de Guadalajara. Se aplicó el MoCA test para detectar la presencia de deterioro cognitivo. **Resultados:** Se incluyeron un total de 177 pacientes (59.9% hombres) con DM (59.9%) o HAS (40.1%). Se encontró que el 44.1% de los participantes presentaba deterioro cognitivo. **Conclusiones:** La prevalencia de deterioro cognitivo en adultos mayores con DM o HAS es mayor que en los adultos mayores sin estos comórbidos. El utilizar una prueba de tamizaje rápida y sencilla como la prueba MoCA en este grupo de pacientes podría permitir una detección temprana y e impactar en una referencia, abordaje y manejo oportunos.

Palabras claves: Deterioro cognitivo. Hipertensión arterial. Diabetes mellitus.

*Correspondence:

Fernando Cortés-Enríquez
E-mail: fercorts08@gmail.com

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Introduction

Clinical context

Cognitive impairment is a clinical syndrome characterized by the loss or decrease of mental functions in different domains such as memory, orientation, calculation, comprehension, judgment, language, visual recognition, behavior, and personality. This concept differs from dementia because it does not affect the functionality of the individuals who experience it^{1,2}. Cognitive impairment increases with age, and it constitutes an important condition, particularly in the population over 65 years of age, with an estimated prevalence of 8%³. As a consequence of the demographic transition we are facing, our country has presented an increase in the frequency of cognitive impairment, becoming a public health problem.

Cognitive impairment is a consequence of neurodegeneration. Neurodegeneration is a multicausal process, and multiple comorbidities have been implicated in its progression⁴⁻⁷. Cognitive impairment in the Mexican population is closely related to highly prevalent chronic degenerative diseases, including diabetes mellitus (DM) and high blood pressure (HBP), which together add up in our country to a prevalence of up to 60.2%^{8,9}.

On the other hand, DM has been associated with an increased risk of cognitive impairment and dementia from 1.5 to almost 3 times when compared with non-diabetic subjects¹⁰, while in patients with HBP, a prevalence of cognitive impairment of 30% has been found, 3 times higher than in the general population¹¹.

Despite these alarming figures, there are few studies that describe the presence of cognitive impairment in patients with diabetes or hypertension in our population^{1,12-15}, so the objective of this study was to identify, characterize, and compare the presence of cognitive impairment in patients with DM and patients with HBP attended at the first level of care.

Methods for detecting cognitive impairment

There are different screening tests to detect cognitive impairment, among the most frequently used are the mini-mental state examination (MMSE) and the Montreal Cognitive Assessment (MoCA).

For this study, we chose the MoCA test because it has a higher sensitivity (82-90%), and specificity (75-89%), and it has been validated in Mexico; as well as because it

has a time of application just a few minutes longer than the MMSE (which has a sensitivity of 80% and specificity of 77.5%)¹⁶.

The MoCA test has the following sections: visuospatial (0-5 points), naming (0-3 points), memory (not scored), attention (0-6 points), language (0-3 points), abstraction (0-2 points), delayed recall (0-5 points), and orientation (0-6 points). The maximum score is 30 points, with a cutoff point for cognitive impairment of < 26^{17,18}.

Additionally, because depression can contribute to or alter cognitive performance, it was decided to screen for this condition in this study. For this, the abbreviated Yesavage geriatric depression scale (GDS) was used, which has a sensitivity of 84% and specificity of 95% for detecting depression. In this scale, scores of 0-4 are considered normal, according to age, education, and complaints; 5-8 indicates mild depression; 9-11 indicates moderate depression; and 12-15 indicates severe depression^{19,20}.

Methods

This was an observational, cross-sectional, and descriptive study, approved by a local Research Ethics Committee with project registration R-2020-1305-083. The sample consisted of 189 consecutive patients who attended the outpatient consultation at the Family Medicine Unit No. 51 of the Mexican Institute of Social Security in Guadalajara. Patients with the following inclusion criteria were selected non-randomly (non-probabilistic convenience sampling): over 65 years of age of both sexes with DM or HBP who agreed to participate in the study, signing the informed consent. As exclusion criteria, the diagnosis of psychiatric diseases (including depression) or behavioral disorders, illiteracy, and presence of comorbidities, as well as patients who had any impairment to communicate, were considered. Patients who did not adequately complete all their assessments were excluded from the study.

Data collection was carried out over a period of 6 months. First, a questionnaire was administered to collect sociodemographic variables of interest: age, gender, education level, marital status, number of prescribed drugs, and other associated comorbidities. The weight and height of the patients were requested to calculate their body mass index (BMI), which for the purposes of this study was considered: underweight < 18.5, normal weight 18.5-24.99, overweight > 25, and obesity > 30. The presence of depression was ruled out with the GDS scale, considering it positive when the patient had a score of 5-15. Subsequently, to assess

the presence of cognitive impairment, the MoCA test was applied, taking 26 as the cutoff point, and defining as a patient with cognitive impairment those who had a score of 0-25 points.

Statistical analysis of the data was performed using the statistical software SPSS, version 20.0 for Windows. Descriptive statistics were used for the variables collected, both central tendency measures and dispersion measures. Due to the non-parametric distribution of the sample, the Chi-square test was used to establish if there was a significant difference in the cognitive impairment profile of patients with DM versus patients with HBP in each of the sections evaluated by the MoCA test, considering a significance level of $p < 0.05$.

Results

Of 189 patients included in the study, 12 were excluded from the study: 11 for having a score greater than 4 on the GDS and 1 for not completing the necessary assessments. Therefore, 177 cases were included in the analysis. The mean age was 74.02 years (range 60-93), and the sociodemographic characteristics are shown in [table 1](#). About 59.9% of the patients had DM while the other 40.1% was given by patients with HBP. About 61.1% did not have other associated comorbidities.

When evaluating the presence or absence of cognitive impairment using the MoCA test, it was found that 44.1% of participants had cognitive impairment, obtaining an average of 22.36 points and a mode of 29 points. About 43% of patients with DM had cognitive impairment, while 44% of patients with HBP had it. Regarding the comparison of the results obtained in the sections of the MoCA test of the group of patients with DM versus patients with HBP, each section was analyzed ([Table 2](#)).

In terms of visuospatial skills, patients with diabetes show worse results, with a score of 0, with a higher frequency of 8.5%; compared to 3.4% with the same rating of patients with hypertension. In the naming section, patients with diabetes have twice as many cases, in terms of the lower score.

In the attention section, patients with diabetes have a mostly negative distribution of cases, the accumulated lower cases (from 0 to 5) to the highest score, which is 6, represent 58.1%. For patients with hypertension, this situation only occurs with 45.1%.

The language dimension behaved as follows, 58.4% of patients with diabetes obtained a maximum rating, while 64.7% of patients with hypertension obtained this score. In the abstraction section, 81.1% of patients with

Table 1. Sociodemographic characteristics of the sample

Variable	Total % (n = 177)
Age (mean ± standard deviation)	74.02 (7.34)
Gender % (n)	
Female	40.1 (71)
Male	59.9 (106)
Educational level % (n)	
Elementary school	73.4 (130)
Secondary	21.5 (38)
High school	4 (7)
Degree	1.1 (2)
Civil status % (n)	
Widowed	52 (92)
Married	26.6 (47)
Divorced	16.4 (29)
Common-law	4.5 (8)
Single	0.005 (1)
BMI % (n)	
Normal	20.9 (37)
Overweight	66.1 (117)
Obesity	13 (23)
Associated comorbidities % (n)	
0	61.6 (109)
1	33.3 (59)
2	5.1 (9)
Number of drugs used % (n)	
0	7.9 (14)
1	12.4 (22)
2	45.8 (81)
3	28.2 (50)
4	7.9 (14)

BMI: body mass index

diabetes obtained a maximum rating, while 84.5% of patients with hypertension also obtained this score. With regard to the distribution of delayed recall, 59.4% of patients with diabetes obtained the maximum approval rating, while this occurred in 66.19% of hypertensive patients.

Finally, in the last section corresponding to orientation, it was found that 7.5% of patients with diabetes obtained a score of 0, a situation that only occurred in 2.8% of patients with hypertension.

Discussion

With the aging population, it is expected that the prevalence of DM, HBP, and cognitive impairment will increase progressively²¹. In Mexico, census data from 1990 and 2020 indicates that the population aged 60 and over has increased from 5 million to 15.1 million, respectively, corresponding to a 6-12% increase in the population. The

Table 2. Comparison of the score obtained in the MoCA in both groups

Domain evaluated (points)	Diabetics (n = 106)	Hypertensive (n = 71)	p
Executive function			
0	15	6	0.772
1	16	11	
2	19	9	
3	15	13	
4	29	23	
5	12	9	
Denomination			
0	3	1	0.734
1	4	1	
2	6	5	
3	93	64	
Attention			
0	16	4	0.105
1	8	2	
2	2	5	
3	8	4	
4	9	10	
5	8	7	
6	55	39	
Language			
0	62	46	0.751
1	7	4	
2	7	5	
3	30	16	
Abstraction			
0	86	60	0.329
1	5	1	
2	15	10	
Deferred recall			
0	63	47	0.733
1	1	0	
2	8	6	
3	11	7	
4	4	2	
5	19	9	
Orientation			
0	8	2	0.588
1	3	4	
2	6	4	
3	1	4	
4	1	1	
5	1	0	
6	86	56	

MoCA: Montreal Cognitive Assessment

doubling or even tripling of the number of cases anticipates that it will also occur in the three pathologies²¹⁻²³. Therefore, studying the interrelationship between these three variables is becoming increasingly important.

The working universe in this study had a male predominance and an average age of 74 years. When analyzing the population, it is found that some of the main characteristics are representative of the Mexican

population in this age group, such as: the predominant marital status is widowhood, a high frequency of overweight and obesity, and low education level²⁴.

The presence of cognitive impairment was also found in 44% of the participants, which constitutes 5.5 times more than what was found in the general Mexican population (ENASEM study). These data coincide with multiple studies that have found an increase in the prevalence of cognitive impairment in patients with DM and HBP compared to the general population²⁵⁻²⁷.

Several hypotheses have been proposed about how both DM and HBP participate in cognitive impairment in patients. Due to the complex nature of DM, numerous explanations have been proposed for how it could cause cognitive impairment. These include the fact that it is an important cardiovascular risk factor, increasing the incidence of strokes. In the non-vascular pathogenesis, we find the effects of dysglycemia in which both hyperglycemia and hypoglycemia are common in diabetic patients; these have deleterious effects on cognition due to the increase in oxidative stress and consequent damage to brain tissue. On the other hand, certain mechanisms have been found in how hyperinsulinemia negatively affects neuronal functioning related to the pathophysiological cascade of beta-amyloid: an increase in tau protein phosphorylation and a decrease in the ability of the insulin-degrading enzyme to eliminate beta-amyloid as the concentration of insulin in the central nervous system increases. Structural correlates of these facts have been described, with cortical and subcortical atrophy, especially affecting the hippocampus and the prefrontal cortex^{21,28-32}.

On the other hand, the pathophysiology of hypertension is related to cognitive impairment in a multivariate way. Emerging evidence suggests that HBP causes remodeling of cerebral blood vessels, causing dysfunction in cerebral perfusion. With the dysfunction of flow autoregulation, it is postulated that the elimination of potentially harmful proteins such as beta-amyloid is limited, which it is worth mentioning has been found in higher concentrations in these patients. In addition, evidence of structural changes in neuroimaging associated with the increase in systolic blood pressure has been found, with a lower cerebral volume in these patients^{11,33}.

Several studies have been conducted to characterize cognitive impairment in patients with DM and HBP. In patients with DM, alterations in all cognitive domains have been found, with the most affected being attention and processing speed^{29,34,35}. On the other hand, in patients with HBP, greater impairment of executive function, processing speed, and semantic memory has been found¹¹.

Despite this, no significant differences were found when comparing the results of the MoCA test sections of diabetic versus hypertensive patients in this study.

The relationship between cognitive impairment, diabetes, and hypertension is not completely understood, but it is becoming clear that cognitive impairment, which was traditionally seen as a primary neurodegenerative disorder, is not dissociated from other chronic degenerative diseases that tend to coexist in the same individual.

A cognitive study, including a neuropsychological test in the first level of care, should be considered in patients with a history of diabetes and hypertension. On the other hand, it is essential to take the above aspects into consideration, as they could affect the patient's ability to adhere to their treatment. Early identification of these patients provides an opportunity to delay or even prevent the progression of cognitive impairment, so the timing of treatment is a major factor in prognosis^{36,37}.

In patients with mild-to-moderate dementia without treatment, there is a 2-point decline per year in the MMSE test, which is reduced to 0.5 points/year when treatment with acetylcholinesterase inhibitors is started. This has a positive long-term impact as it reduces mortality and preserves the ability of patients to perform a greater number of instrumental activities of daily living³⁷.

The importance of early diagnosis will become more important with the use of monoclonal antibodies against amyloid beta, which has only shown effectiveness in the early stages of Alzheimer's disease^{38,39}.

Finally, it is necessary to point out that the following limitations were found in the present study: a more extensive neuropsychological evaluation was not performed, a non-randomized and small convenience sample was used, and the sample was from a single primary care center. In addition, there were confounding factors, such as the use of multiple medications, cardiovascular risk factor and the relative control of the principal pathologies (hypertension and diabetes mellitus).

Future research is needed to assess the impact of cognitive impairment on metabolic control in patients and to develop therapeutic strategies that are tailored to their individual abilities. In addition, the neuropsychological profile of cognitive impairment in patients with hypertension and diabetes should be characterized using larger studies in our population.

Conclusion

The findings of this study reveal that older adults with diabetes or hypertension have a 5.5-fold higher prevalence of cognitive impairment compared to the

population over 65 years of age without these comorbidities. This suggests that it is important to include a cognitive assessment such as the MoCA test as part of the primary care approach for these patients, as cognitive impairment can affect their ability to adhere to treatment and achieve therapeutic goals. Thus cognitive screening should be performed in all people with DM or HBP in order to guide reference to neurology services and to guide adaptations in their activities of daily living management of comorbidities.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

References

- Ríos-Gallardo ÁM, Muñoz-Bernal LF, Aldana-Camacho LV, Santamaría-Iñiguez MF, Villanueva-Bonilla C. Perfil neuropsicológico de un grupo de adultos mayores diagnosticados con deterioro cognitivo leve. *Rev Mex Neuroci*. 2017;18:2-13.
- Gutiérrez-Robledo LM, Arrieta-Cruz I. Demencias en México: la necesidad de un Plan de Acción. *Gac Med Mex*. 2015;151:667-73.
- Mejía-Arango S, Miguel-Jaimes A, Villa A, Ruiz-Arregui L, Gutiérrez-Robledo LM. Deterioro cognoscitivo y factores asociados en adultos mayores en México. *Salud Pública México*. 2007;49:S475-81.
- Cruz-Oliver DM, Malmstrom TK, Roegner M, Tumosa N, Grossberg GT. Cognitive deficit reversal as shown by changes in the Veterans Affairs Saint Louis University mental status (SLUMS) examination scores 7.5 years later. *J Am Med Dir Assoc*. 2014;15:685.e5-10.
- Johnson LA, Hall JR, O'Bryant SE. A depressive endophenotype of mild cognitive impairment and Alzheimer's disease. *PLoS One*. 2013;8:e68848.
- Liu H, Gao S, Hall KS, Unverzagt FW, Lane KA, Callahan CM, et al. Optimal blood pressure for cognitive function: findings from an elderly African-American cohort study. *J Am Geriatr Soc*. 2013;61:875-81.
- Sanford AM. Mild cognitive impairment. *Clin Geriatr Med*. 2017;33:325-37.
- Basto-Abreu A, Barrientos-Gutiérrez T, Rojas-Martínez R, Aguilar-Salinas CA, López-Olmedo N, De la Cruz-Góngora V, et al. Prevalencia de diabetes y descontrol glucémico en México: resultados de la Ensanut 2016. *Salud Pública México*. 2019;62:50.
- Campos-Nonato I, Hernández-Barrera L, Flores-Coria A, Gómez-Álvarez E, Barquera S. Prevalencia, diagnóstico y control de hipertensión arterial en adultos mexicanos en condición de vulnerabilidad. Resultados de la Ensanut 100k. *Salud Publica Mex*. 2019;61:888.
- Mejía-Arango S, Zúñiga-Gil C. Diabetes mellitus as a risk factor for dementia in the Mexican elder population. *Rev Neurol*. 2011;53:397-405.
- Qin J, He Z, Wu L, Wang W, Lin Q, Lin Y, et al. Prevalence of mild cognitive impairment in patients with hypertension: a systematic review and meta-analysis. *Hypertens Res*. 2021;44:1251-60.
- Coronel Chacón ML, Carmona Mejía B, Ponce-Gómez G. Deterioro cognitivo en ancianos diabéticos hospitalizados en medicina interna en un hospital de segundo nivel de atención en México, Distrito Federal. *Rev Enferm Neurol*. 2013;12:5-9.
- María R, Marcia HU, Isaac AC, Luisa SO. Diabetes mellitus y su asociación con demencia y deterioro cognitivo leve en adultos mayores mexicanos de población urbana y rural. *Arch Neuroci*. 2013;18:1-7.
- de León-Arcila R, Milián-Suazo F, Camacho-Calderón N, Arévalo-Cedano RE, Escartín-Chávez M. Risk factors for cognitive and functional impairment in the elderly. *Rev Med Inst Mex Seguro Soc*. 2009;47:277-84.

15. Arjona-Villicaña RD, Esperón-Hernández RI, Herrera-Correa GM, Albertos-Alpuche NE. Association between diabetes mellitus and cognitive decline in older adults. A population based study. *Rev Med Inst Mex Seguro Soc.* 2014;52:416-21.
16. Villaseñor-Cabrera T, Guardia-Olmos J, Jiménez-Maldonado M, Rizo-Curiel G, Peró-Cebollero M. Sensitivity and specificity of the mini-mental state examination in the mexican population. *Qual Quant Int J Methodol.* 2010;44:1105-12.
17. Aguilar-Navarro SG, Mimenza-Alvarado AJ, Palacios-García AA, Samudio-Cruz A, Gutiérrez-Gutiérrez LA, Ávila-Funes JA. Validez y confiabilidad del MoCA (Montreal Cognitive Assessment) para el tamizaje del deterioro cognoscitivo en México. *Rev Colomb Psiquiatr.* 2018;47:237-43.
18. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc.* 2005;53:695-9.
19. Aguilar-Navarro SG, Fuentes-Cantú A, Avila-Funes JA, Garcia-Mayo EJ. Validity and reliability of the screening questionnaire for geriatric depression used in the Mexican health and age study. *Salud Publica Mex.* 2007;49:256-62.
20. Martínez de la Iglesia J, Onís Vilches MC, Dueñas Herrero R, Albert Colomer C, Aguado Taberné C, Luque Luque R. Versión española del cuestionario de Yesavage abreviado (GDS) para el despistaje de depresión en mayores de 65 años: adaptación y validación. *Medifam.* 2002;12:620-30.
21. Cukierman-Yaffe T. Thinking sweet: the relationship between diabetes cognitive dysfunction. *Av Diabetol.* 2010;26:393-6.
22. Instituto Nacional de Estadística y Geografía (INEGI). México: Estadísticas a Propósito Del Día Internacional de Las Personas Adultas Mayores 2021. Available from: https://www.inegi.org.mx/contenidos/saladeprensa/aproposito/2022/eap_adulmay2022.pdf [Last accessed on 2023 Nov 05].
23. Biessels GJ, Whitmer RA. Cognitive dysfunction in diabetes: how to implement emerging guidelines. *Diabetologia.* 2020;63:3-9.
24. Instituto Nacional de Estadística y Geografía (INEGI). México: Estadísticas a Propósito Del Día Internacional De Las Personas De Edad 2019. Available from: https://www.inegi.org.mx/contenidos/saladeprensa/aproposito/2019/edad2019_nal.pdf [Last accessed on 2023 Nov 05].
25. Ryuno H, Kamide K, Gondo Y, Kabayama M, Oguro R, Nakama C, et al. Longitudinal association of hypertension and diabetes mellitus with cognitive functioning in a general 70-year-old population: the SONIC study. *Hypertens Res.* 2017;40:665-70.
26. Hassing LB, Hofer SM, Nilsson SE, Berg S, Pedersen NL, McClearn G, et al. Comorbid type 2 diabetes mellitus and hypertension exacerbates cognitive decline: evidence from a longitudinal study. *Age Ageing.* 2004;33:355-61.
27. Wang X, Ji L, Tang Z, Ding G, Chen X, Lv J, et al. The association of metabolic syndrome and cognitive impairment in Jidong of China: a cross-sectional study. *BMC Endocr Disord.* 2021;21:40.
28. Feinkohl I, Price JF, Strachan MW, Frier BM. The impact of diabetes on cognitive decline: potential vascular, metabolic, and psychosocial risk factors. *Alzheimers Res Ther.* 2015;7:46.
29. Muñoz G, Degen C, Schröder J, Toro P. Diabetes mellitus y su asociación con deterioro cognitivo y demencia. *Rev Méd Clín Las Condes.* 2016;27:266-70.
30. Zilliox LA, Chadrsekaran K, Kwan JY, Russell JW. Diabetes and cognitive impairment. *Curr Diab Rep.* 2016;16:87.
31. Domínguez RO, Pagano MA, Marschoff ER, González SE, Repetto MG, Serra JA. Enfermedad de Alzheimer y deterioro cognitivo asociado a la diabetes mellitus de tipo 2: relaciones e hipótesis. *Neurología.* 2014;29:567-72.
32. Kim TE, Lee DH, Kim YJ, Mok JO, Kim CH, Park JH, et al. The relationship between cognitive performance and insulin resistance in non-diabetic patients with mild cognitive impairment. *Int J Geriatr Psychiatry.* 2015;30:551-7.
33. Jamalnia S, Javanmardifard S, Akbari H, Sadeghi E, Bijani M. Association between cognitive impairment and blood pressure among patients with type II diabetes mellitus in Southern Iran. *Diabetes Metab Syndr Obes.* 2020;13:289-96.
34. Samaras K, Sachdev PS. Diabetes and the elderly brain: sweet memories? *Ther Adv Endocrinol Metab.* 2012;3:189-96.
35. Monette MC, Baird A, Jackson DL. A meta-analysis of cognitive functioning in nondemented adults with type 2 diabetes mellitus. *Can J Diabetes.* 2014;38:401-8.
36. Wattmo C, Wallin AK, Minthon L. Progression of mild Alzheimer's disease: knowledge and prediction models required for future treatment strategies. *Alzheimers Res Ther.* 2013;5:44.
37. Xu H, Garcia-Ptacek S, Jönsson L, Wimo A, Nordström P, Eriksdotter M. Long-term effects of cholinesterase inhibitors on cognitive decline and mortality. *Neurology.* 2021;96:e2220-30.
38. Tousi B, Sabbagh MN. Editorial: a time of transition of Alzheimer's disease in the advent of anti-amyloid monoclonal antibodies. *Neurol Ther.* 2021;10:409-13.
39. Cummings J, Aisen P, Apostolova LG, Atri A, Salloway S, Weiner M. Aducanumab: appropriate use recommendations. *J Prev Alzheimers Dis.* 2021;8:398-410.