

Predictors of Cognitive Impairment among Filipino Patients with Type 2 Diabetes Mellitus in a Tertiary Government Hospital

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ABSTRACT

Background. Type 2 Diabetes Mellitus (T2DM) patients are predisposed to cognitive decline and dementia. The co-occurrence of the two diseases translate to a higher medical cost. Identification of factors contributing to cognitive impairment is warranted.

Objective. To determine the predictors of cognitive impairment among Filipino patients with Type 2 Diabetes Mellitus.

Methods. This is a cross-sectional analytical study involving Filipino patients diagnosed with T2DM in the outpatient clinic. A total of 171 patients were included and were screened using AD8-P tool.

Results. A total of 171 adult patients were included and screened for cognitive impairment. 19.3% were cognitively impaired, with mean age of 59.6 years old (vs. 55.5 years old, $p < 0.029$), and two-thirds were female. The mean duration of the patient's diabetes was 11.2 years. After adjusting for confounders and multi-collinearity, the duration of diabetes was significantly associated with cognitive impairment with odds of developing cognitive impairment increasing as the duration reach 10 years above. Those with T2DM for at least ten years were 2.5 times more likely to develop cognitive impairment, holding the age constant. (OR = 2.5, 95% CI – 1.0 to 5.8, $p < 0.043$).

Conclusion. 19.3% of Filipino patients with Type 2 Diabetes Mellitus in a tertiary government hospital are cognitively impaired and this can occur even in less than 65 years old. The ten years or longer duration of T2DM increases the risk of developing cognitive impairment by 2.5%.

Keywords: type 2 diabetes mellitus, cognitive impairment, cognitive dysfunction, dementia, aging, Alzheimer's Disease

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is associated with a 50% increase risk for dementia.¹ In 2014, it was estimated that 3.2 million Filipinos has T2DM. Prevalence rate was 5.9%, occurring among ages 20 to 79 years old, with \$205 as estimated cost per person.² T2DM is also associated with an increased rate of cognitive decline and dementia among elderly people.^{3,4} The median direct medical cost for dementia care in the Philippines was \$238.⁵ The co-occurrence of the two diseases will then translate to a higher medical cost hence identifying predictors of cognitive impairment among patients with T2DM is important.

People with DM showed to have lower performance in mental processing, language, and attention or reasoning.⁶ Poor glycemic control, higher glycosylated hemoglobin (HbA1C) levels, and longer diabetes duration were linked to increased incidence of cognitive impairment.⁷ It predisposed people with DM to treatment-related complications, such as



Finalist – Philippine Neurological Association Research Contest, November 3, 2022 (via Zoom conference).

eISSN 2094-9278 (Online)
Published: August 15, 2024
<https://doi.org/10.47895/amp.vi0.7648>

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acute severe hypo- or hyperglycemic episodes.⁸ Impairment in executive function and memory were also correlated with reduced gray matter density and glucose metabolism in the brain.¹

Determining the relationship between diabetes mellitus and the factors contributing to cognitive impairment may help recognize patients who are at risk of developing cognitive impairment and help promote preventive strategies.⁶

OBJECTIVES

To determine the predictors of cognitive impairment among Filipino patients diagnosed with Type 2 Diabetes Mellitus at a tertiary government hospital from November 2021 to June 2022.

MATERIALS AND METHODS

Study Design

This study is a cross-sectional analytical study involving patients diagnosed with Type 2 Diabetes Mellitus who were seen at the Diabetes Mellitus Clinic at East Avenue Medical Center Out Patient Department.

The case ascertainment and study approach are described in Figure 1. Type 2 Diabetes patients who consented to join the study were recruited. Patients were screened using the AD8-P questionnaire.

Aging and Dementia 8-P, or more known as AD8-P is a Filipino adaptation of the original AD8.⁹ The questionnaire includes eight 'yes' or 'no' questions to be answered by the informant or caregiver (Appendix). The questions comprise changes in terms of memory and thinking abilities over the past years. A score of equal or greater than 3 is considered to have cognitive impairment while less than and equal to 2 is normal. This questionnaire was validated by Dominguez et al. last 2021. It showed a high internal consistency and strong correlation with other cognitive assessment tools such as Montreal Cognitive Assessment (MOCA), Mini Mental Status Examination (MMSE), and CDR (Clinical Dementia Rating); as well as with the Lawton Instrumental Activities of Daily Living (IADL). Due to the fact that AD8-P focuses at the intraindividual decline rather than interindividual performance in comparison to a normative value, it has proven to be more sensitive than MOCA-P and MMSE-P. Additionally, it was discovered that the informant's age and educational background have no bearing on AD8-P score.

Measurements

The following data of included subjects were retrieved and recorded – demographic profile including age, sex, body mass index (BMI). Vascular risk factors include history of smoking (current smoker, previous smoker, or never smoked); history of hypertension and its duration; stroke, psychiatric diseases; patients' latest laboratory tests for the past six months including the HbA1C (glycosylated hemoglobin), FBS (fasting blood sugar), total cholesterol, low density lipoprotein, high density lipoprotein, triglycerides, and estimated glomerular filtration rate (computed based on the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula).

Statistical Analysis

Summary statistics were reported as mean and standard deviation (SD) for continuous data with normal distribution or as the median and interquartile range (IQR) for quantitative variables with skewed distribution and as count and percent for qualitative measures. Prevalence of cognitive impairment of patients diagnosed with Type 2 DM with 95% confidence interval based on AD8-P scores were estimated.

The Shapiro-Wilks test was used to determine if continuous variables deviate from a normal (Gaussian) distribution. Pearson chi-square test or Fisher exact test was used in comparing proportions. Pairwise comparisons were based on Bonferroni-adjusted *p*-values. The independent *t*-test or Mann-Whitney U test was used in comparing the mean between two groups (cognitive impairment vs. normal cognitive function). The median test was used in comparing the median between the two groups. Univariate and multivariate logistic regression analyses were performed to assess the association of duration of diabetes, demographic sex and age, and clinical patient characteristics with cognitive impairment based on the AD8-P scores. Crude and adjusted odds ratio and 95% confidence interval were reported. Statistical significance was based on *p*-value ≤ .05. STATA version 15 (Stata Corp LLC, College Station, TX, US) will be used in data processing and analysis.

Study Population and Sampling Method

Inclusion and Exclusion criteria

Included patients must fulfill the following criteria: (1) Filipino patients diagnosed with Type 2 Diabetes Mellitus; (2) age range of 26-85 years old; (3) no visual or hearing impairment.

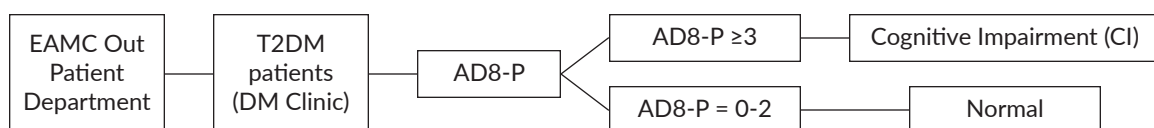


Figure 1. Case Ascertainment and Methodology. EAMC – East Avenue Medical Center.

T2DM – Type 2 Diabetes Mellitus; AD8-P – Aging and Dementia 8-P.

Exclusion criteria include patients who were (1) Diagnosed to have other types of diabetes (Type 1 Diabetes, Gestational Diabetes, Maturity Onset Diabetes of the Young [MODY]); (2) with speech impairment; (3) diagnosed case of psychiatric diseases; and (4) patients who are reluctant to cooperate.

Patients may withdraw their consent to participate at any point in the study, whether verbal or written.

Sample Size

The minimum number of patients for this study is determined using the formula¹⁰:

$$N = 10k/p$$

where: N is the minimum sample size, p is the smallest of the proportions of negative or positive cases in the population and k the number of independent variables. Based on a local study by Blanquisco¹¹, the rate of mild cognitive impairment among elderly Filipino diabetics is 45%. In this study, there are seven hypothesized independent variables considering sociodemographic and clinical factors affecting cognitive impairment. Thus, the minimum sample size is 156.

RESULTS

Two hundred ninety-five patients were initially identified with Type 2 Diabetes Mellitus at the Diabetes Mellitus Clinic. Seventy-three had other types of diabetes, three of which did not correspond to the age range, and one patient had impairment of speech. Two hundred adult patients diagnosed with Type II Diabetes Mellitus ages 26 to 85 were identified at the Diabetes Mellitus clinic for screening and chart review. However, 29 patients withdrew their consent in joining the study, while 18 patients lacked latest laboratory results in their medical charts.

A total of 171 adult patients were included and screened for cognitive impairment (Figure 2). The prevalence of

cognitive impairment was 33 out of 171 or 19.3% (95% CI: 13.9% to 25.7%). Out of 33 patients with cognitive impairment, almost two-thirds of the population are female, have low-educational attainment, three patients (9.1%) have had a previous stroke. The mean duration of the patient’s diabetes was 11.2 years, wherein 19 patients (57.6%) had T2DM for more than 10 years. The average HbA1C was at 8.6%. Moreover, two-thirds of the patients were taking oral anti-hypoglycemic agents, while the rest are insulin-requiring.

Comparison with normal cognitive function showed that patients with cognitive impairment have a mean age of 59.6 years old (vs. 55.5 years old, $p < 0.029$). Also, a higher proportion of patients with cognitive impairment have longer duration of diabetes (11.2 years vs. 6.8 years, $p < .002$). Comparisons also showed that those with cognitive impairment had a longer duration of diabetes (≥ 10 vs. < 5 years, $p < .002$). There were insignificant differences between the two groups for demographic sex, years of education, and clinical characteristics including BMI, fasting blood sugar, HbA1C levels, lipid profile, and eGFR (Table 1).

Assessment of effects of demographic and clinical characteristics in the development of cognitive impairment showed that at the age 66 years and older and the duration of diabetes had crude associations with cognitive impairment based on the AD8-P scores. (Table 2)

Adjusting for confounders and multi-collinearity, the duration of diabetes was significantly associated with cognitive impairment (Table 2). Notably, the odds of developing cognitive impairment increases as the duration reach 10 years above. Those with T2DM for at least ten years were 2.5 times more likely to develop cognitive impairment, holding the age constant. (OR = 2.5, 95% CI – 1.0 to 5.8, $p < 0.043$).

DISCUSSION

This study was the first to use the AD8-P as a tool in assessing cognitive impairment among Filipinos with Type

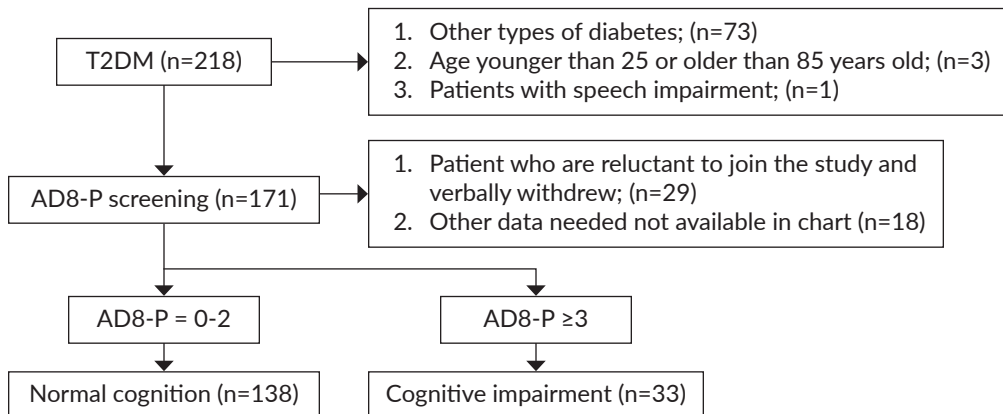


Figure 2. Flowchart of participants.

T2DM – Type 2 Diabetes Mellitus; AD8-P – Aging and Dementia 8-P.

2 Diabetes Mellitus. To date, there is no established best neuropsychological tests to evaluate cognitive impairment in diabetes.¹

The prevalence rate of cognitive impairment among Filipino patients in a tertiary government hospital with T2DM was 19.3%. The prevalence was lower in contrast to the study of Blanquisco et al. which only included Filipino

patients more than 60 years old.¹¹ This study noted that 69.6% of the cognitively impaired patients were less than 65 years old (Table 1).

The prevalence rate using AD8-P was comparable with the study done in Pakistan assessing cognitive impairment among patients with T2DM.¹²

Table 1. Baseline Characteristics of Adult Patients with Type 2 Diabetes by Cognitive Function based on AD8-P scores

Characteristic	All Patients (n=171)	Normal Cognitive Function (n=138)	Cognitive Impairment (n=33)	p-value
Sex				
Male	68 (39.8%)	56 (40.6%)	12 (36.4%)	0.697
Female	103 (60.2%)	82 (59.4%)	21 (63.6%)	
Age in years				
≤44	17 (9.9%)	16 (11.6%)	1 (3.0%)	0.114
45-55	63 (36.8%)	52 (37.7%)	11 (33.3%)	
56-65	61 (35.7%)	50 (36.2%)	11 (33.3%)	
≥66	30 (17.5%)	20 (14.5%)	10 (30.3%)	
Education in years				
≤12	104 (60.8%)	84 (60.9%)	20 (66.7%)	0.978
>12	67 (39.2%)	54 (39.1%)	13 (33.3%)	
Smoking history				
Non-smoker	121 (70.8%)	99 (71.7%)	22 (66.7%)	0.670
Previous smoker	50 (29.2%)	39 (28.3%)	11 (33.3%)	
BMI kg/m²				
	25.8 (4.7)	26.2 (9.6)	26.2 (4.0)	0.997
Duration of diabetes in years				
0-4	78 (45.6%)	67 (48.6%)	11 (33.3%)	0.002 [‡]
5-9	34 (19.9%)	31 (22.5%)	3 (9.1%)	0.083
≥10	59 (34.5%)	40 (29.0%)	19 (57.6%)	0.002 [‡]
HbA1C %				
	8.4 (3.9)	8.8 (2.8)	8.6 (2.4)	0.812
Fasting blood sugar in mg/dl				
	137.4 (92.3)	161.1 (73.8)	156.9 (72.1)	0.769
Total cholesterol in mg/dl				
	170.2 ± 50.0	171.2 ± 49.8	166.0 ± 51.4	0.588
LDL in mg/dl				
	89.9 (59.0)	94.2 (41.8)	92.7 (36.1)	0.846
HDL in mg/dl				
	42.5 ± 11.3	42.5 ± 11.3	42.4 ± 11.7	0.954
Triglycerides in mg/dl				
	130.2 (94.1)	148.4 (86.1)	160.7 (87.1)	0.463
eGFR in mg/dl				
	79.0 (44.0)	79.6 (36.1)	71.5 (32.3)	0.241
Hypertension				
Absent	70 (40.9%)	59 (42.8%)	11 (33.3%)	0.335
Present	101 (59.1%)	79 (57.2%)	22 (66.7%)	
Duration of HTN in years				
<1	2 (2.0%)	1 (1.3%)	1 (4.5%)	0.356
1-5	40 (39.6%)	34 (43.0%)	6 (27.3%)	
6-10	33 (32.7%)	25 (31.6%)	8 (36.4%)	
≥11	26 (25.7%)	19 (24.1%)	7 (31.8%)	
Previous stroke				
No	168 (98.2%)	138 (100.0%)	30 (90.9%)	0.007 [‡]
Yes	3 (1.8%)	0 (0.0%)	3 (9.1%)	
Treatment plan				
Non-insulin requiring	78 (45.6%)	71 (51.4%)	22 (66.7%)	0.125
Insulin-requiring	93 (54.4%)	67 (48.6%)	11 (33.3%)	

AD8-P: Aging and Dementia, HbA1c: glycated hemoglobin, LDL: low-density lipoprotein, HDL: high-density lipoprotein, eGFR: glomerular filtration rate. Data are mean ± SD, median (IQR) or n (%) on 171 adult patients with Type 2 diabetes, 33 with cognitive impairment based on AD8-P scores ≥3.

[†]P <.05, [‡]P <.01 vs. normal cognitive function.

The duration of the diabetes mellitus was correlated with the development of cognitive impairment. Similar with international studies, our results were consistent with their findings that the duration of diabetes was a predictor of cognitive dysfunction. Blood glucose abnormalities and insulin resistance were reported to be linked to cognitive impairment in patients with T2DM.^{7,8,10}

In comparison to a study done by Blanquisco et al.¹¹, low educational attainment was not a predictor of cognitive impairment. Smoking and lipid profile were comparable to both patients with normal cognition and cognitive impairment. This study was not able to assess the recent episodes of hypoglycemia.

Table 2. Results of Simple and Multiple Univariate Logistic Regression on Factors Associated with Cognitive Impairment based on AD8-P

Factors	Dependent variable: cognitive impairment			
	Crude OR (95% CI)	p-value	Adjusted ^a OR (95% CI)	p-value
Sex				
Female	Reference			
Male	0.8 (0.4, 1.8)	0.657		
Age in years				
≤44	Reference			
45-55	3.4 (0.4, 28.3)	0.260	2.8 (0.3, 24.2)	0.343
56-65	3.5 (0.4, 29.4)	0.245	2.8 (0.3, 23.6)	0.364
≥66	8.0 (0.9, 69.2)	0.059	6.1 (0.7, 55.6)	0.107
Education in years				
≤12	Reference			
>12	1.0 (0.5, 2.2)	0.978		
Smoking history				
Non-smoker	Reference			
Previous smoker	1.3 (0.6, 2.9)	0.566		
BMI kg/m²				
	1.0 (0.9, 1.1)	0.997		
Duration of diabetes in years				
0-4	Reference			
5-9	0.6 (0.2, 2.3)	0.441	0.5 (0.1, 2.0)	0.336
≥10	2.9 (1.3, 6.7)	0.013 [†]	2.5 (1.0, 5.8)	0.043 [†]
HbA1C %				
	1.0 (0.9, 1.1)	0.811		
Fasting blood sugar in mg/dl				
	1.0 (1.0, 1.0)	0.769		
Total cholesterol in mg/dl				
	1.0 (1.0, 1.0)	0.586		
LDL in mg/dl				
	1.0 (1.0, 1.0)	0.845		
HDL in mg/dl				
	1.0 (1.0, 1.0)	0.952		
Triglycerides in mg/dl				
	1.0 (1.0, 1.0)	0.461		
eGFR in mg/dl				
	1.0 (1.0, 1.0)	0.239		
Hypertension				
Absent	Reference			
Present	1.5 (0.7, 3.3)	0.325		
Duration of HTN in years				
<1	Reference			
1-5	0.2 (0.0, 3.2)	0.242		
6-10	0.3 (0.0, 5.7)	0.439		
≥11	0.4 (0.0, 6.7)	0.500		
Previous stroke				
No	Reference			
Yes	7x10 ⁹ (too wide)	0.999		
Treatment plan				
Non-insulin requiring	Reference			
Insulin-requiring	0.5 (0.2, 1.2)	0.118		

HbA1c: glycosylated hemoglobin, LDL: low-density lipoprotein, HDL: high-density lipoprotein, eGFR: glomerular filtration rate.

[†]P <.05, [‡]P <.01 vs. reference, ^areduced logistic regression model based on age and duration of diabetes.

Other factors that may also contribute to developing cognitive impairment in patients with T2DM, include increasing age, hypertension, and obesity. These may be due to vascular endothelial dysfunction, inflammation and injury to the blood-brain barrier, development of white matter disease, and demyelination and axonal loss.^{8,11}

A large cohort study by Dove et al., also showed that poorly controlled diabetes was associated with increased risk of cognitive impairment and dementia and may cause adverse outcomes when combined with heart disease and systemic inflammation. They also found out that poorly controlled HbA1c, degree of hyperglycemia rather than the diabetes itself, negatively impacts cognitive health.¹³ These findings were not seen in our study probably due to a smaller sample size.

CONCLUSION

In conclusion, our results showed that 19.3% of Filipino patients with Type 2 Diabetes Mellitus are cognitively impaired and this can occur even in less than 65 years old. The ten years or longer duration of T2DM increases the risk of developing cognitive impairment by 2.5%.

Recommendations

Larger studies may be done to further evaluate the mechanisms and investigate other factors that may be associated with T2DM and cognitive impairment among Filipinos. Cranial imaging will be helpful in ruling out other structural causes of cognitive impairment.

Compliance with Ethical Standards

This study was in accordance with the ethical standards of the Technical Review Board and the Institutional and Ethics Review Board (IERB) of East Avenue Medical Center and with Helsinki Declaration of 1964 and later version. Informed consent was obtained from all patients who were included in the study.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

Funding Source

The study was funded by the authors.

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APPENDIX

AD8-P Dementia Screening Interview

AD8-P (Filipino Version)

AD8 Dementia Screening Interview
by the Dementia Society of the Philippines

	Tandaan, ang "OO, may pagbabago" ay tinutukoy na mayroong pagbabago sa mga nagdaang taon sanhi ng problema sa pag-iisip at sa memorya	OO, May pagbabago	WALA, Walang pagbabago	N/A Hindi alam
1	Problema sa paghusga (halimbawa, problema sa pag-gawa ng desisyon, maling desisyon pampinansiyal)			
2	Nabawasan ang interes sa libangan at aktibidades			
3	Naguulit-ulit ng mga tanong, kuwento o pahayag			
	Nahihirapan matutong gumamit ng mga kasangkapan, gamit pambahay o ibang mga gamit (halimbawa, "cellphone", "remote control", TV, VCD o karaoke)			
5	Pagkalimot sa tamang buwan o taon			
6	Nahihirapan mangasiwa ng komplikadong transaksyong pampinansyal (halimbawa, pagbabadyet ng gastusin, pagbayad ng buwis at ibang mga bayarin tulad ng kuryente at tubig)			
7	Nahihirapan sa pagalala ng mga "appointments" o tipanan			
8	Araw-araw na may problema sa pag-iisip o memorya			
KABUUANG PUNTOS				

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