

High prevalence of cognitive impairment in elderly with diabetes mellitus and associated factors

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Abstract— Cognitive impairment in people with diabetes mellitus (DM) is multifactorial, with evidence that their poor metabolic control is related to impaired cognitive function. **Background/Objectives:** Identify the prevalence of diabetic older with cognitive impairment and characterize the factors associated with this finding. **Methods:** Cross-sectional, quantitative, descriptive and analytical research carried out with 246 diabetic older adults followed up in a specialized center in northeastern Brazil. Sociodemographic and clinical variables related to DM2 and evidence of cognitive decline were assessed using the Mini Mental State Examination (MMSE). **Results:** There was a prevalence of cognitive impairment in 74.4% of the studied sample with an association between cognitive impairment and the variables advanced age ($p = 0.003$) and female gender ($p = 0.025$). There was statistical significance between the presence of self-reported cognitive problems and cognitive impairment at evaluation ($p < 0.001$) and a 1.4 times higher prevalence ratio of cognitive impairment in diabetic underweight than in obese elderly ($p = 0.020$). **Conclusions:** The research reveals the high prevalence of cognitive impairment in older adults with diabetes, especially in women and advanced age. It also corroborates the association already described in the international literature between subjective complaints of memory and nutritional status and cognitive decline.

I. INTRODUCTION

Population indicators at the global level show a demographic trend that two-thirds of 235 countries will experience an increase in population size between 2019 and 2050 and the number of people aged 65 and over is more than double globally [1].

In 2010, based on data from the last census released by the Brazilian Institute of Geography and Statistics (IBGE), it is known that, of 190,755,799 Brazilians, 10.8% (equivalent to 20,590,599 people) are people with 60 years or more. The projection for 2050 is that this older people will reach 64 million, which will correspond to a quarter of the Brazilian population [2]. At this conjuncture, it seems challenging to

explore themes usually experienced in the daily life of the older people and health professionals to discuss public policies that guarantee active and successful aging.

Chronic non-communicable diseases (NCD) common in aging are factors that, isolated or cumulatively, contribute to the increase in the incidence of physical and mental dependence, resulting in impaired quality of life and mortality, with an estimated rate of 4 % for diabetes in the world [3]. Among the most prevalent NCD, diabetes mellitus stands out, whose increased prevalence is associated with rapid urbanization, epidemiological and nutritional transition, physical inactivity, overweight and obesity, population growth and aging and greater survival of people who have diabetes [4].

The cognitive impairment is also among the most important public health problems as a result of population growth. Dementia is a syndrome characterized by persistent decline of at least two functions of the following domains: memory, executive functions, visual-spatial skills, language and behavior, and the interference in social activities or individual professionals, regardless of the level of consciousness changes [5]. Its prevalence has great variability in the literature, since it depends on population characteristics, education level and the screening method used to identify cognitive impairment.

Research has been conducted in order to verify the correlation between diabetes and cognitive decline, but show up in conflicting results, so that some can make this correlation and others do not. The association between small vessel vascular diseases caused by diabetes as responsible for an overall decrease in brain mass that can evolve with atrophy is reported [6].

There is evidence that pathophysiological changes and neuronal and inflammatory stress pathways associate diabetes mellitus and Alzheimer's dementia, being called type 3 diabetes, since it has characteristics of a brain disorder with aspects of diabetes types 1 (insulin deficiency) and 2 (insulin resistance). It is suggested that AD represents a metabolic disease with a deficit in the use of glucose by the brain in the initial course of the disease, leading to cognitive dysfunction [6].

The etiology of cognitive impairment in diabetic individuals is multifactorial, and this disease is associated with a 1.5 to 2.5 risk of dementia [7]. Research shows that poor metabolic control of DM is related to impaired cognitive function in diabetics [8].

In this context, the objective of the present study is to identify the prevalence of elderly diabetics with cognitive impairment and to characterize the factors associated with this finding.

II. MATERIALS AND METHODS

A cross-sectional, quantitative, descriptive and analytical study was carried out at the Integrated Center for Diabetes and Hypertension (CIDH), in Fortaleza, Ceará, Brazil. The CIDH is a reference center for the State of Ceará, specializing in serving people with Diabetes and Hypertension, being a reference for the State of Ceará.

The study included people aged 65 years and over, with type 2 diabetes mellitus, followed up at the CIDH with a diagnosis of this disease for at least a year and who agreed. Patients with type 1 diabetes or secondary diabetes (eg chronic use of corticosteroids) and type 2 diabetes treated with insulin were excluded within six months of the clinical diagnosis of the disease. The data were collected in two stages:

1. At no time beforehand to volunteer for research, we collected demographic data (age and sex), general health data as harmful habits - smoking and alcohol abuse, systemic diseases and comorbidities related to diabetes mellitus, self-reported cognitive problems, body mass index, with specific stratification for the older adult group [9] and time of disease in years. For the educational level variable, the study time in years was evaluated to facilitate the stratification of groups according to the cut-off point specific to the Brazilian reality with regard to cognitive assessment. The general health data collected through face-to-face clinical evaluation were: Systemic Arterial Hypertension, Coronary Artery Disease, Cerebral Stroke, Obliterating Arteriopathy of the lower limbs, Peripheral Neuropathy, corresponding to sensory-motor polyneuropathy in the lower limbs, assessed using the test such as 10g monofilament, Presence of Foot Wound, Amputation, Congestive Heart Failure, and, for acute complications, those that were ongoing six months before the evaluation: Hypoglycemia, Ketotic decompensation, Hyperosmolality and Infectious episodes.

2. In the second stage of the research, the Mini-Mental State Examination (MMSE) was applied personally to all patients mentioned above for cognitive assessment. MMSE is an important indicator of the cognitive status of the elderly [10]. The domains of cognitive function were evaluated using questions organized in seven categories, as suggested in a previous study: orientation to time (0-5 points), space orientation (0-5 points), immediate memory (0-3 points), attention and calculation (0-5 points), memory recovery (0-3 points), language (0-8 points) and visual constructive capacity (0-1 point). The score ranges from 0 (zero) to 30 points, with a minimum score of 0 (zero) points indicating the highest degree of cognitive impairment [11]. Therefore, higher scores suggest better cognitive ability. All questions were asked in the order listed and received an

immediate score. The scores assigned to each task successfully completed have been added. The analysis of cognitive impairment considered five levels of education: illiterate, one to four years of study, five to eight years of study and nine to eleven years of study and twelve or more years of study, with a MMSE score of 20, 25, 27, 28 and 29, respectively, for cognitive deficit outcome, as suggested in a previous study [12].

For calculation, applying the MMSE was considered the total number of older people in 2012 (N = 242,430) of the city of Fortaleza, a figure taken from DATASUS Report (2012) [13]. It is considered a minimum sample size population to estimate the proportion of elderly diabetics with expected maximum proportion of 20%, a significance level of 5% (95% confidence interval) and maximum permissible error of 5%.

For this purpose, the finite formula for the population was considered, obtaining as a sample size a total of 246 elderly people. The CIDH has a total of 1978 elderly people aged 65 and over with at least one year diagnosed with diabetes. The patients' medical records were selected by non-probabilistic sampling due to their original numbering, with one out of every eight medical records selected. Results were organized and consolidated using the Statistical Package for the Social Sciences Program, Co. Chicago IL USA (SPSS) for Windows (version 20.0).

Statistical measures were used that allowed the interpretation of the data, seeking to answer the research

objectives, being calculated absolute and relative frequencies for qualitative variables, as well as mean, median, standard deviation, quartiles, minimum and maximum for quantitative. The bivariate analyzes were performed using the Chi-square or Fisher's exact tests for comparisons involving qualitative characteristics. In this step, the magnitude of the associations was expressed through gross prevalence ratios with a 95% confidence interval and a 5% significance level.

The research was approved by the Research Ethics Committee under opinion no. 1,666,717, as dictated by the Resolution No. 466/12 of the National Health Council, of December 12, 2012.

III. RESULTS

Of the total of older diabetic people evaluated in research with the Mini-Mental State Examination, 74.4% (183) had cognitive impairment. The study showed that older people aged 75 years or more had a 1.26-fold higher prevalence rate of expressing cognitive impairment at the assessment than older people aged 65 to 74 years ($p = 0.003$). Concerning the sex, it was found that older had a prevalence ratio of 1.19 times greater cognitive impairment present for evaluation older ($p = 0.025$). There was no statistical significance between harmful habits - smoking and alcohol consumption - and cognitive impairment (Table 1).

Table 1. Risk factors for cognitive impairment according to sociodemographic variables among older people with diabetes mellitus. Fortaleza - Brazil, 2019.

Variables	Total	Cognitive impairment				PR (IC95%)	P value
		Yes		No			
		n	%	n	%		
Age Range							0,003 ¹
75 years and older	85	73	85,9	12	14,1	1,26 (1,1 - 1,44)	
Sex							0,025 ¹
Female	139	111	79,9	28	20,1	1,19 (1,02 - 1,39)	
Smoking							0,315 ¹
No	226	170	75,2	56	24,8	1,16 (0,83 - 1,61)	
Drinking							0,178 ¹
No	215	163	75,8	52	24,2	1,18 (0,9 - 1,54)	

¹Chi-squared test.

In the analysis of clinical variables related to type 2 diabetes mellitus, it was found that there is a statistically significant association between self-reported cognitive problems and positive screening for cognitive impairment with a prevalence ratio 1.42 times higher in the elderly who reported having memory problems who denied having cognition problems ($p < 0.001$). The assessment of nutritional status, using the body mass index with specific classification ranges for the elderly population, revealed that elderly diabetics with a BMI below 22 and a BMI between 22 and 27 had prevalence ratios of 1.40 and 1.02 times greater than having cognitive impairment than elderly diabetics with a BMI greater than 27 ($p = 0.020$). For the other clinical variables evaluated in the study, there was no statistical significance with the outcome cognitive impairment. There was no statistically significant difference between the other variables related to diabetes complications and cognitive impairment (Table 2).

Table 2. Risk factors for cognitive impairment according to clinical variables among elderly people with diabetes mellitus. Fortaleza - Brazil, 2019.

Variables	Total	Cognitive impairment				PR (IC95%)	P value
		Yes		No			
		n	%	n	%		
Arterial hypertension							0,608 ¹
Yes	208	156	75,0	52	25,0	1,06 (0,85 - 1,31)	
Coronary insufficiency							0,323 ¹
Yes	74	58	78,4	16	21,6	1,08 (0,93 - 1,26)	
Cardiac insufficiency							0,987 ¹
Yes	31	23	74,2	8	25,8	1 (0,8 - 1,25)	
Stroke							0,231 ¹
Yes	30	25	83,3	5	16,7	1,14 (0,95 - 1,36)	
Peripheral Neuropathy							0,260 ¹
Yes	94	74	78,7	20	21,3	1,09 (0,94 - 1,27)	
Foot ulcer							0,104 ¹
Yes	25	22	88,0	3	12,0	1,2 (1,02 - 1,42)	
Amputation							0,368 ²
Yes	15	13	86,7	2	13,3	1,17 (0,95 - 1,45)	
Self-reported cognitive problem							<0,001 ¹
Yes	46	45	97,8	1	2,2	1,42 (1,28 - 1,58)	
Hypoglycemia within 6 months prior to the consultation							0,358 ¹
Yes	52	36	69,2	16	30,8	0,92 (0,75 - 1,12)	
Ketotic decompensation							0,343 ²
Yes	6	6	100,0	0	0,0	1,36	

						(1,26 - 1,47)	
Hyperosmolarity							0,788 ²
Yes	19	15	78,9	4	21,1	1,07 (0,84 - 1,36)	
BMI							0,020 ²
BMI < 22kg/m ²	17	17	100,0	0	0,0	1,40 (1,26 - 1,55)	
22 < BMI < 27 kg/m ²	74	54	73,0	20	27,0	1,02 (0,86 - 1,21)	

¹Chi-squared test; ²Fisher's Exact test.

Concerning the clinical treatment instituted for the elderly diabetics in the study, there was no significant difference between adherence to dietary measures ($p = 0.227$), use of oral antidiabetics ($p = 0.756$) and insulin ($p = 0.061$) and cognitive decline (Table 3).

Table 3. Risk factors for cognitive impairment according to clinical treatment among elderly people with diabetes mellitus. Fortaleza - Brazil, 2019.

Variables	Total	Cognitive impairment				PR (IC95%)	P value
		Yes		No			
		n	%	n	%		
Diet							0,227 ¹
Yes	170	130	76,5	40	23,5	1,11 (0,93 - 1,32)	
Insulin							0,756 ¹
Yes	133	100	75,2	33	24,8	1,02 (0,88 - 1,19)	
Oral antidiabetic drugs							0,061 ¹
Yes	199	143	71,9	56	28,1	0,84 (0,73 - 0,98)	

¹Chi-squared test.

IV. DISCUSSION

Cognitive impairment is increasingly recognized as an important comorbidity of diabetes mellitus. It can be classified into different stages with different cognitive characteristics and varied prognosis, including by the affected age group. The deficit in the cognitive functioning of the person affected by type 2 diabetes can be divided into three different stages, according to severity: cognitive decrease associated with diabetes, mild cognitive impairment and dementia [14].

This research was not intended to diagnose dementia in the elderly evaluated diabetics, since it used only screening tool for cognitive impairment. However, aimed to assess factors

associated with complications related to diabetes mellitus and cognitive impairment.

The prevalence of cognitive impairment in the elderly with diabetes was high (74.4%) and this association was found either by Cichosz, Jensen & Hejlesen (2020) [15]. Dysglycemia is associated with poorer executive function and processing speed [16]. The risk of Alzheimer's dementia in diabetics is higher than in the general population, and the pathophysiological mechanism of this relationship is still controversial in the world literature [17].

The significant association between age and cognitive impairment, with a 1.26-fold higher prevalence rate of cognitive impairment for older diabetic patients, is a finding corroborated with the international literature that

demonstrates an association between advancing age and cognitive impairment [14]. Consequently, with increasing age, there is a higher prevalence of chronic diseases that are responsible for causing a significant decrease in the quality of life of the elderly. Many of these chronic diseases are related to diabetes and facilitate cognitive decline in this age group. Cognitive dysfunction can be related to diabetes itself due to the longer duration of microvascular lesions caused by the disease, as well as it can also be associated with other chronic diseases [16-18].

There was a higher prevalence of cognitive impairment in elderly diabetic women when compared to men, which is a controversial finding in the literature, given that studies do not consider females as a risk factor for cognitive decline in diabetes mellitus. Diabetes can increase the risk of dementia in both sexes and at all ages, with a higher risk rate in diabetic women aged 65 and over [19].

In the analysis of diabetes-related comorbidities, there was a statistical significance between the presence of self-reported cognitive problems and cognitive dysfunction at evaluation ($p < 0.001$). This finding is justified considering that Diabetes is a chronic disease that induces changes in vascular structure and function, altering the metabolism of beta-amyloid and Tau proteins. At the same time, cognitive impairment influences the systemic glucose metabolism, contributing to behavioral and memory changes, exercising two-way interaction between DM and dementia [20]. Kaup et al. (2015) [21] demonstrated that subjective memory complaints are associated with cognitive decline approximately two decades after the beginning of self-reported reports in elderly women, alluding to the hypothesis that it may be an early symptom of neurodegenerative diseases such as Alzheimer's dementia.

The research showed a 1.4 times higher prevalence rate of cognitive impairment in the older adult with low weight than in the obese ($p = 0.020$). It is known that fragility is a state of vulnerability resulting from the cumulative decline in various systems throughout life. It results from muscular and nervous functions, pulmonary reserve and executive capacity, diabetes mellitus being an important disease that contributes to the deterioration of homeostasis and functional capacity, especially if associated with malnutrition [19]. Cognitive fragility is an emerging concept defined by the presence of cognitive impairment and physical fragility. In diabetic older people, it is associated with increased mortality compared to isolated evidence of physical frailty or cognitive impairment [22]. Authors mention a statistically significant association between diabetes mellitus and cognitive impairment and physical frailty, being prognostic factors for mortality [23].

In the same understanding, it is demonstrated in a study that the majority of patients with frailty and sarcopenia present cognitive impairment with no significant difference between groups with and without diabetes, hypertension and dyslipidemia [24].

There was no significant association between cognitive impairment and macro and microvascular complications related to diabetes mellitus in the present study. However, the literature demonstrates that, even in a non-specific way, microvascular lesions are associated with a higher risk of cognitive decline. Researchers like Biessels and Despa (2018) [14] point out that this fact happens because there is a vascular accumulation of toxic lipids that, in turn, increase reactive oxygen species, impairing vasodilation and consequent reduction of blood flow to the brain. They also mention that one of the pathologies associated with the microvascular involvement of DM is the white matter disease of vascular origin, causing long-term vascular lesions and even areas of cerebral ischemia, thus contributing to constant cognitive loss.

Likewise, there was no statistical significance between episodes of hypoglycemia, ketotic decompensation and hyperosmolarity in the six months prior to the clinical evaluation of the older adult and cognitive impairment. Cognitive dysfunction together with chronic complications of DM influences functional disability and hypoglycemia, leading to a worse prognosis and reduced life expectancy [8].

Cognitive decline is also influenced by diet in the older people, contributing to the development and evolution of chronic diseases. Patients with DM2 who ate more vitamins and minerals had higher MMSE values when compared to older people with a diet rich in carbohydrates and proteins, because those foods are richer in antioxidant substances that reduce cognitive decline [25-28]. However, in this research there was no significant association between adherence to dietary measures and cognitive decline, as well as with the use of insulin or ADO.

The study's limitation is the failure to identify a previous diagnosis of dementia among diabetic elderly people who expressed cognitive impairment during the evaluation.

V. CONCLUSIONS

This study reveals a high prevalence of cognitive impairment in older patients with diabetes mellitus, especially in women and at older ages. It also corroborates the association already described in the international literature between subjective complaints of memory and nutritional status and cognitive decline.

We emphasize the importance of investing in longitudinal follow-up in elderly diabetics in order to track and detect early complications related to the disease in order to contribute to healthy aging and successful this particular portion of the population. There is an urgent need to effectively implement care for the elderly, respecting their particularities and diseases faced with advancing age.

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