

Factors associated with dementia in elderly

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Abstract *We analyzed the factors associated with dementia in the elderly attended at a memory outpatient clinic of the University of Southern Santa Catarina (UNISUL). This is a cross-sectional study with data analysis of medical records from January 2013 to April 2016. The outcome was the clinical diagnosis of dementia. The control variables were: serum vitamin D level at the time of diagnosis, gender, skin color, schooling, age, type 2 diabetes, hypertension, and depression. We performed a crude and adjusted analysis with logistic regression. The sample consisted of 287 elderly, with the predominance of age between 60 and 69 years (48.78%), female (79.09%) and white (92.33%). The mean number of years of study was 6.95 years (SD ± 4.95) and mean vitamin D was 26.09 ng/mL (SD ± 9,20). The prevalence of elderly with dementia was 16.72%. Depression was the most prevalent (42.50%) among the morbidities, followed by hypertension (31.71%). The following were independently associated with dementia: vitamin D (OR = 0.92, 95%CI, 0.88;0.97), depression (OR = 4.09, 95%CI, 1.87;8.94), hypertension (OR = 2.65, 95%CI, 1.15;6.08) and individuals aged 80 years and over (OR = 3.97 95%CI, 1.59;9.91). Dementia prevalence was high and diagnosed dementia was associated with lower levels of vitamin D. Vitamin D is a modifiable factor, opening up essential perspectives for public health policies.*

Key words *Elderly, Dementia, Memory outpatient clinic*

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Introduction

The Brazilian's population aging is accelerating. The population aged 60 years and over, equivalent to 10% of the total population in 2010, is estimated to reach 13.7% of the population by 2020 and 23.8% by 2040, or almost a quarter of nationals will consist of elderly¹. These transformations in the age pyramid result from the changes in the balance between birth and mortality, as well as in the morbidity profile of the population, characterizing the demographic and epidemiological transition.

With increased life expectancy, chronic non-communicable diseases (DCNT) stand out as a significant public health challenge, mainly due to the high morbidity they cause. These diseases can result in severe degrees of disability that affect both the life and well-being of the individuals and the country's economy. In 2002, CNCDs accounted for almost 60% of all deaths². Approximately 80% of the elderly have at least one chronic disease, of which 50% with two or more pathologies³.

Among the aging-related CNCDs are dementias, which stand out as the leading causes of functional impairment and the quality of life of the elderly⁴. According to the World Health Organization (WHO) in 2012, more than 35 million people in the world had some level of dementia, which can triple by 2050 to more than 115 million people, and the highest prevalence of dementia will fall on low- and middle-income countries, with about 60% of dementia cases⁵.

According to WHO⁶, the time lived with dementia accounts for 11.9% of the years of living with disabilities due to noncommunicable diseases, with an estimated global cost of US\$ 604 billion in 2010.

Cognitive losses due to dementia are more prevalent in females⁷, among low schooling individuals⁸ who do not engage in physical activity⁹, people with low economic status¹⁰, advanced age¹¹ and frailty¹². Other risk factors associated with dementia are hypertension¹³, diabetes mellitus¹⁴, depression¹⁵ and low levels of vitamin D¹⁶, and the latter is a modifiable factor.

In recent years, associations between vitamin D and dementia have attracted increasing interest^{16,17}. Studies indicate that vitamin D deficiency is more prevalent in patients with dementia¹⁸. A meta-analysis has shown that demented individuals have a lower level of vitamin D (25-hydroxyvitamin D (25 (OH) D)) compared with the control group healthy age-matched pa-

tients¹⁹. Lower 25 (OH) D may be only a marker or potential risk factor for developing dementia, as indicated by recent studies¹⁸⁻²¹.

In the study by Baumgart *et al.*²², the importance of studies aimed at analyzing modifiable risk factors for dementia is emphasized, since these are amenable to intervention, highlighting the practice of healthy behaviors.

Thus, this study aims to analyze the factors associated with dementia in the elderly followed by a Memory Outpatient Clinic of the University of Southern Santa Catarina.

Methods

This is a cross-sectional study conducted in the city of Palhoça, Santa Catarina. According to IBGE²³, the city of Palhoça consists of approximately 137,334 inhabitants. Of these, individuals aged 60 and over correspond to 30,513 inhabitants (8.79%). Data were analyzed from the records of the elderly monitored by the Memory Outpatient Clinic of the University of Southern Santa Catarina (Unisul).

A total of 406 medical records were identified from January 2013 to April 2016, of which 119 were excluded since the medical records did not show the serum vitamin D dose. The final sample of the study consisted of 287 elderly. Inclusion criteria were individuals aged 60 years and over, with a clinical diagnosis of the cognitive status and who had serum 25-hydroxyvitamin D 25 (OH) D at the time of diagnosis as part of standardized routine tests for the investigation of dementia and its causes. Exclusion criteria were individuals who had recently taken or were taking vitamin D replacement during the study period, patients with delirium or other acute diseases at the time of collection of the tests or the diagnostic process for dementia.

Regarding the dependent variable, dementia was analyzed from the clinical diagnosis, which was composed of anamnesis, physical and neurological examination, complementary exams and cognitive evaluation^{24,25}. The cognitive evaluation tests for screening and diagnostic support used were the Montreal Cognitive Assessment (MoCA) and the Clinical Dementia Rating (CDR), both validated for Brazil.

The independent variables were serum levels of vitamin D (25 (OH) D) in ng/mL, age (60-69, 70-79 and 80 years and over), gender (male and female), skin color (white, black and brown), schooling (full study years), and concerning

health conditions (diabetes mellitus, hypertension and depression), data were obtained from the clinical diagnosis and were dichotomized in “no” and “yes”.

Statistical analysis was performed using the Stata/SE 13.0 program. The descriptive statistics with absolute and relative frequency were performed by calculating the measures of central tendency and dispersion for the continuous variables, and of frequency for the categorical variables. Concerning the identification of the dementia-associated factors, bivariate analyzes were initially performed between each exposure variable and the dependent variable, and Pearson's chi-square test (χ^2) was used, with a significance level of 5%. Odds ratios (unadjusted OR) were also obtained between dichotomous variables and their respective 95% confidence intervals (95% CI).

Multivariate logistic regression was performed using all variables of bivariate analysis to identify variables that remained significantly related to the occurrence of dementia ($p < 0.05$) and with biological plausibility. The maximum likelihood ratio test was used to verify the significance of the final model.

The Human Research Ethics Committee (CEPSH) of the Federal University of Santa Catarina (UFSC) approved this study, with co-participation of the University of Southern Santa Catarina. All participants – and in case of vulnerability, the legal guardian – signed an informed consent form.

Results

The sample consisted of 287 older adults, aged 60-69 years (48.78%), female (79.09%) and white (92.33%). The prevalence of elderly with dementia was 16.72%. Among the elderly with dementia, the mean vitamin D levels were 21.90 (SD \pm 8.10), and elderly without dementia averaged 26.93 ng/mL (SD \pm 8.80).

Among morbidities, depression was the most prevalent (42.50%), followed by hypertension (31.71%) and diabetes mellitus (20.21%). The mean number of study years was 6.95 (SD \pm 4.95) and mean vitamin D was 26.09 ng/mL (SD \pm 9.20) (Table 1).

In the bivariate analysis, increased vitamin D had a protective effect vis-à-vis dementia (OR = 0.93, 95%CI 0.89;0.97); concerning morbidities, the elderly diagnosed with depression were 166% more likely to have the outcome (OR = 2.66

95%CI 1.40;5.05). Subjects aged 80 years and over were 354% more likely to have dementia compared to those aged 60-69 years (OR = 4.54 95%CI 2.05;10.04) (Table 2).

In the adjusted analysis, vitamin D remained independently associated with dementia – each unit of vitamin D (ng/mL) reduces by 8% the probability of the outcome (OR = 0.92, 95%CI 0.88;0.97) –; elderly patients diagnosed with depression (OR = 4.09, 95%CI 1.87, 8.94) and hypertension (OR = 2.68 95%CI 1.15;6.08) were more likely to have dementia (309%, and 168%, respectively) when compared with elderly without the disease. Regarding age, older individuals aged 80 years and over were 297% more likely to be diagnosed with dementia when compared to those aged 60-69 years (OR = 3.97, 95% CI 1.59;9.91) (Table 2). The final model was considered adjusted ($p = 0.39$) from the maximum likelihood ratio test.

Discussion

At the time of this review, this was the first Brazilian study that evaluated the factors associated with dementia in the elderly in a memory outpatient setting. The prevalence of dementia found in this study was 16.72%, higher than that of Nitrini et al. who evaluated studies on the prevalence of dementia in Latin American countries and found a prevalence of 7.1%. This difference was due to the specificity of a population attended at a memory outpatient clinic that receives people with suspected cognitive problems²⁶ referred from primary care.

In Brazil, few studies evaluate dementia in the elderly population, and the existing ones show significant differences concerning prevalence and incidence. In a recent systematic review²⁷, the prevalence of dementia among Brazilian elderly ranged from 5.1% to 19%, but most studies evaluated the cognitive status by questionnaires such as the Mini-Mental State Examination (MMSE), and not from the diagnosis (gold standard) as in this study.

We found that the prevalence of having a diagnosis of dementia fell 8% with each vitamin D (ng/mL) unit increase, and recent studies have shown these associations^{16,17,20,21}. In a cohort study with French elderly monitored for 12 years, elderly patients with insufficient vitamin D (< 20 ng/mL) and vitamin D deficiency (< 20 ng/mL) were approximately three times more likely to have dementia²⁸.

Table 1. Description of the sample of elderly participants of the Memory Outpatient Clinic (UNISUL), Palhoça (SC), Brazil, 2013-2016 (n = 287).

Variables	n (%) Mean (SD*)
Dementia	
No	239 (83.28)
Yes	48 (16.72)
Gender	
Male	60 (20.91)
Female	227 (79.09)
Age (years)	
60-69	140 (48.78)
70-79	101 (35.19)
80+	46 (16.03)
Skin color	
White	265 (92.33)
Non-White	22 (7.67)
Depression	
No	165 (57.49)
Yes	122 (42.51)
Hypertension	
No	196 (68.29)
Yes	91 (31.71)
Diabetes	
No	229 (79.79)
Yes	58 (20.21)
Vitamin D	26.09 (± 9.20)
Schooling	6.95 (± 4.95)

*SD (Standard Deviation).

The results of this study corroborate other experimental studies that suggested that hypovitaminosis D could mediate the neurodegenerative processes involved in dementias^{16,29,30}. Case-control studies indicated that individuals with dementia had lower circulating levels of vitamin D^{31,32}. Also, several longitudinal studies found an association between low vitamin D levels and accelerated cognitive decline^{30,33-36}.

However, there are conflicting results, such as those found in two longitudinal studies conducted in Sweden and the United States. No association was found between vitamin D levels and the cognitive status of the elderly in these studies. However, in the study carried out in Sweden³⁷, the sample consisted only of men and the prevalence of hypovitaminosis D was low; of these, 15.5% had insufficiency and 1.7% deficiency. In the U.S. study³⁸, while no associations were found between vitamin D and dementia, low vitamin D concentrations were found to be associated with

worse executive function, processing speed and visual and perceptive abilities.

It is known that vitamin D plays a vital role in brain development and maturation of vitamin D receptors (VDRs) present in various areas of the brain, including those related to learning and memory functions. Besides, vitamin D is involved in several brain health pathways, including neurotransmission, neuroprotection, modulation of immune response, inhibition of pro-inflammatory agents and regulation of oxidative stress^{16,30,39}.

Studies were conducted to verify the effect of vitamin D supplementation on cognitive function. However, Annweiler et al.⁴⁰ observed that an improved cognitive function was found after the addition of 800 IU/day of vitamin D in elderly with cognitive decline. The daily consumption of 800 IU of vitamin D resulted in lower Alzheimer's risk after seven years of follow-up⁴¹. This neuroprotective effect was further confirmed by an experimental study that reported cognitive improvement⁴². The benefits of supplementation were noticeable after four weeks⁴³ and appeared to be particularly strong for executive function and processing speed⁴⁴.

Regarding morbidities, approximately 50% of the elderly of the sample had a diagnosis of depression. Barcelos-Ferreira et al.⁴⁵ reviewed the scientific literature on depression in community elderly in Brazil and identified a prevalence of 7% for depression and 26% for depressive symptoms. A study conducted with community elderly in Canada found a prevalence of depression ranging between 1.3% and 18.8% in women and between 0.9% and 7.9% in men⁴⁶.

Depressive elderly were 4.09 times more likely to have dementia. A recent 14-year longitudinal study showed that depressive male elders were more likely to have dementia (OR = 1.5 95%CI 1.2;2.0)⁴⁷. Norton et al. estimated that 5-11% of Alzheimer's disease cases could be attributed to depression, and this means that the prevalence of dementia in the population would be reduced by the same amount if depression can be prevented or adequately treated⁴⁸.

On the other hand, in a study conducted by Mirza et al. In 2014, 4,393 elderly people were followed for up to 13.7 years for incident dementia and found that about 13% developed dementia and that depression increased the risk of dementia by approximately 20% for 2 and 5 years, but the same study suggests that depressive symptoms at advanced ages are part of the initial symptoms of dementia and not an independent

Table 2. Crude and adjusted analysis of variables associated with dementia in elderly participants of the Memory Outpatient Clinic (UNISUL), Palhoça (SC), Brazil, 2013-2016.

Variables	Crude Analysis			Adjusted Analysis	
	%	OR (CI95%)*	p-value	OR (CI95%)*	p-value
Vitamin D		0.93(0.89;0.97)	0.001	0.92(0.88;0.97)	0.001
Gender					
Male	20.00	1.00		1.00	
Female	15.85	0.75(0.36;1.55)	0.446	0.42(0.17;1.02)	0.060
Age (years)					
60-69	11.43	1.00		1.00	
70-79	14.85	1.35(0.63;2.88)	0.435	1.61(0.72;3.62)	0.247
80+	36.95	4.54(2.05;10.04)	<0.001	3.97(1.59;9.91)	0.003
Skin color					
White	17.35	1.00		1.00	
Black/Brown	9.10	0.47(0.11;2.10)	0.318	0.54(0.11;2.58)	0.439
Schooling		0.95(0.88;1.02)	0.138	0.95(0.88;1.03)	0.260
Depression					
No	10.90	1.00		1.00	
Yes	24.60	2.66(1.40;5.05)	0.003	4.09(1.87;8.94)	<0.001
Hypertension					
No	15.81	1.00		1.00	
Yes	18.68	1.22(0.64;2.34)	0.545	2.68(1.16;6.18)	0.020
Diabetes					
No	14.85	1.00		1.00	
Yes	24.14	1.82(0.90;3.68)	0.090	2.12(0.91;4.95)	0.080

Obs.: Pearson's ($p = 0.39$) *Crude OR: odds ratio; CI95%: 95% Confidence Interval.

risk factor for depression⁴⁹. There is evidence that depression can lead to loss of volume of the hippocampus, mainly when symptoms are persistent, thus contributing to the onset of dementia⁵⁰.

Concerning hypertension, after the adjusted analysis, the elderly with hypertension were 168% more likely to have dementia, corroborating a study conducted in people over 80 years in China, which found that the hypertensive elderly were 193% more likely to evidence mild cognitive disorder and evolve towards dementia⁵¹.

Interestingly, in people 60 years of age or older, systolic blood pressure (SBP) was inversely associated with all-cause dementia⁵². This is paradoxical because it is generally recognized as a risk factor for cognitive decline and dementia⁵³⁻⁵⁵. However, the association between blood pressure and the brain is complex and depends on factors such as age, chronicity, and use of antihypertensive medication⁵².

Antihypertensive therapies may reduce cognitive decline and the incidence of dementia. Most observational studies have suggested a potential

preventive effect of antihypertensive therapies on cognitive decline and dementia, particularly calcium channel blockers and renin-angiotensin system blockers⁵⁶.

No association was found between diabetes mellitus and dementia in this study, possibly because of the sample size. However, in a meta-analysis, the relative risk of dementia in patients with diabetes was estimated at 1.46. Based on six studies gathering a total of 5,706 people with diabetes and 36,191 without diabetes, the analyzed relative risk for vascular dementia was 2.48, i.e., there was a considerably increased risk for this type of dementia⁵⁷.

The prevalence of women in the study was 79.09%, and this is associated with feminization in old age, women represent 55.5% of the Brazilian elderly population and 61% of the elderly population over 80 years of age²³. This female overrepresentation results from the longer life expectancy of women who, on average, live eight years longer than men⁵⁸.

The age group 80 years and older were 297% more likely to have dementia when compared to

the 60-69 age group. Several studies^{26,27,59} have shown this relationship in which older individuals are more likely to have dementia. Regarding the gender variable, there was no association with the outcome, but many studies^{26,27} indicate that female subjects are more likely to have the outcome.

Dementia has a significant impact on the costs of society and the family. When investigating 41 households of dementia carriers residing in Rio de Janeiro, Veras *et al.* (2008) found that the projection of costs associated with the care of elderly with dementia reached approximately of two-thirds of the household income, with a 75% increase when the elderly were in the early stages of the disease and 80% when other chronic diseases were considered⁶⁰.

In 1998, Meek *et al.* stated that concerning total costs to society, dementia was the third most expensive disease in the U.S., after cancer and coronary heart disease⁶¹. Also, Brookmeyer *et al.*⁶² mentioned that the impact of healthcare-related costs for the treatment of dementia would be huge, burdening the U.S. economy with up to US\$ 36 billion per year.

Recent estimates have shown that the costs associated with dementia in the UK top 17 billion euros per year, which are estimated to reach 50 billion euros by 2038, with an incidence of 1.4 million new cases per year⁶³. Dementia care social cost spirals dramatically with disease's severity, and institutionalization is the main reason⁶⁴.

Limitations of this study were the lack of control regarding which season of the year vitamin D dosage tests were performed, assuming that there was a random distribution throughout the studied period. Because it is a cross-sectional study, it is not possible to infer causality. The population studied does not allow generalization of the results for the population as a whole, since it is a specialized outpatient clinic.

Conclusion

Dementias have a multifactorial origin and are a public health problem with high impact on health expenditure. In this study, dementia-associated factors were vitamin D, depression, hypertension, and age above 80 years. Knowing and understanding these factors assists in the medical clinic, diagnosis, and treatment of demented elderly.

The results of this study may positively influence public health policies where virtually costless lifestyle changes such as increased sun exposure may result in better health conditions for the elderly, both for possible protection against dementia and prevention of hypovitaminosis D among dementia carriers, avoiding major health problems. Further prospective, randomized and intervention studies with larger samples will ensure continuity of this work.

Collaborations

CS Santos: study design, statistical analysis, manuscript writing. AJ Xavier: writing of excerpts of the manuscript, planning of the analyzes and revision of its final version. TA Bessa: theoretical contribution, revision of the final version of the manuscript.

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