DOI: 10.1590/1413-81232022277.19932021EN

Association between zinc deficiency and cognitive decline in community-dwelling older adults

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Abstract *This is a cross-sectional study evaluating the association between zinc deficiency and cognitive decline in 591 community-dwelling older adults living in the cities of Campinas, Limeira, and Piracicaba-SP. Cognitive status was evaluated using the Cognitive Abilities Screening Instrument-CASI-S, considering a decline for scores <23 for those aged 60-69 and <20 for those aged ≥70 years. Among the evaluated cognitive domains, older adults with zinc deficiency had significantly lower mean scores on the memory test (p=0.018). For zinc deficiency, values below 70 μg/dL were considered for women and 74 μg/dL for men. The prevalence of zinc deficiency was 3.9%, and cognitive deficit was 9.4%, being significantly higher in those with zinc deficiency compared with those with normal serum zinc concentrations. In adjusted multiple logistic regression analysis, the factors that remained associated with cognitive decline were zinc deficiency (OR=3.80; 95%CI=1.30-11.12), low schooling level (OR=3.12; 95%CI=1.49-6.50), lack of a partner (OR=1.88; 95%CI=1.04-3.42), risk of malnutrition (OR=3.98; 95%CI=2.36-6.71), and a history of encephalic vascular accident (OR=2.70; 95%CI=1.04-6.98). Zinc deficiency was associated with the presence of cognitive decline in older adults. Actions in primary health care are necessary to prevent the deficiency of this nutrient.*
Key words *Zinc, Cognition, Older adults*

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Introduction

The older adult population is the population segment with the highest growth rate. According to data and projections from the Brazilian Institute of Geography and Statistics (IBGE), Brazil may have growth rates higher than 4% per year in the period from 2012 to 2022[1]. According to IBGE estimates, the older population could reach 41.5 million in 2030 and 73.5 million in 2060[1].

Older adults compose a group very susceptible to change in nutritional consumption due to several factors. Among these factors, we can highlight the use of several medications, which may cause changes in taste and olfactory sensitivities; dental problems (poorly adjusted prostheses, gingival problems, and edentulism), which may be associated with difficulty chewing and swallowing; difficulty in locomotion, depression, and isolation that can lead the older adult to opt for a diet based on dairy products and farinaceous foods (cheap and easy-to-make foods); among others, mainly compromising the intake of vitamins and minerals[2].

Zinc is among the minerals whose consumption or bioavailability may drop in this population, influenced by reduced absorption, increased number of diseases that alter the use of zinc and increased use of drugs that reduce its bioavailability in the body[3,4]. It is one of the most prevalent and essential elements involved in brain function and plays an important role in physiological processes, such as in the regulation of neurotransmission, endocrine, and neurogenesis pathways[5,6]. Changes in zinc homeostasis can lead to the pathogenesis of cognition-related diseases, with implications for learning, memory, and emotion and mood control, which can cause disorders such as depression and anxiety, as well as neurodegeneration and dementia, such as that observed in Alzheimer's disease[5-7].

The exact role of zinc in cognitive function is still partially unclear. Most studies addressing the role of zinc in central nervous system function used animal samples, which have shown that zinc deficiency can result in reduced brain activity, impairing activity, memory, and attention. However, the evidence in humans is less clear, remaining poorly understood[8].

Currently, some international studies have shown that cognitive decline may be associated with low serum levels of this micronutrient[3,9,10]. A study with older adults without cognitive decline in the city of Valencia, Spain, showed a positive association of serum zinc with cognitive function assessed by performance in the Mini Mental State Examination (MMSE)[9]. A review study also describes that a decrease in serum zinc level has been associated with cognitive function insufficiency[10]. However, the literature poorly describes the association between zinc and specific dimensions of cognitive function, such as orientation, memory and attention, evocation and language in older individuals.

In this context, nutrition plays a fundamental role since the maintenance of zinc homeostasis and prevention of its deficiency seem essential in maintaining the cognitive capacity of older individuals. However, studies on the relationship between serum zinc levels and cognitive decline are still scarce[10,11], and in Brazil this association has yet to be studied. This lack of knowledge is worrisome, considering that the older population is an important risk group for nutritional deficiencies. Further studies evaluating the prevalence of cognitive decline in older adults and its correlation with other variables, such as zinc deficiency, are needed to improve prevention or treatment methods since this condition interferes in the quality of life of this population.

Thus, our study aims to identify the prevalence of serum zinc deficiency and evaluate its association with cognitive decline and its domains in older adults residents of the municipalities of Campinas, Limeira, and Piracicaba.

Materials and methods

Sample selection

This study is part of the project "*Avaliação da prevalência de deficiência de micronutrientes em idosos residentes em cidades da região de Campinas-São Paulo*", with a cross-sectional design, whose data collection occurred from September 2018 to December 2019 in three municipalities of São Paulo belonging to the administrative region of Campinas: Campinas, Limeira, and Piracicaba.

The sample was estimated based on the total number of inhabitants of the municipalities aged 60 years and over, published in population estimates for the year 2018, considering a 70% prevalence of older adults with deficiency of at least one of the nutrients evaluated, with 10% sampling error and 95% confidence level. With this, the total expected sample was 600 older people.

The inclusion criteria for subjects to participate in the study were: age equal to or greater than 60 years, being a resident of one of the mu-

nicipalities: Campinas, Limeira, or Piracicaba, be registered in the Family Health Strategy and have the ability to understand the study procedures and the terms of the consent form. Exclusion criteria were: use of dietary supplements based on vitamins and/or minerals, being under follow-up by the home care program or undergoing chemotherapy. The research protocol was approved by the Research Ethics Committee of the University of Campinas in September 2018 under CAAE number 95607018.8.0000.5404 and opinion number 2.878.652.

More detailed information about the study population, sample calculation, collection of variables are described in a previously published study[12].

In total, data were collected from 611 participants of the research. For our study, 20 individuals who did not have complete data on serum zinc and cognition were excluded, totaling a final sample of 591 older adults.

Data collection

Volunteers were recruited by the health team of the Basic Health Units (UBS) indicated by the respective Health Departments of each municipality. In each health unit selected, registered older adults were invited to participate in the research and instructed to attend the health unit after fasting for at least 8 hours on the scheduled date. An interview was applied to fill out a structured questionnaire with closed questions prepared by the researchers themselves that consisted of personal data, socioeconomic conditions, health, lifestyle and cognitive topics. Data collection was performed by a team of undergraduate and graduate students in the healthcare area, previously trained by the research coordinators.

In addition, fasting blood samples were collected to assess the nutritional status of some vitamins and minerals. Biological material was collected by nurses from the health unit itself or hired for the study, according to the availability of the site and the previous agreement with the municipalities.

For this study, we considered the dosage of serum zinc, which was collected in TRACE polyethylene tubes, white cap, without additives. The tubes containing collected blood were stored in a thermal box with ice and sent immediately after the end of the collection to the same private laboratory contracted for the research (Pasteur®). Since this laboratory did not perform the zinc dosage, it performed the sample centrifugation, separation, and freezing of the serum and sent it daily to a reference laboratory, which performed the analyses as soon as the samples were received. The method of analysis was atomic absorption spectrophotometry (flame) - In house mode.

Variables of the study

For the evaluation of cognitive status, the Cognitive Abilities Screening Instrument - short form (CASI-S) was used. The CASI-S is the reduced form of the CASI-C test, with similar sensitivity and specificity to the complete test, and includes tests for 4 cognitive domains: memory (0-3 points), orientation (0-11 points), executive function (0-10 points) and evocation (0-9 points), obtaining a maximum score of 33 points, where lower scores in the CASI-S questionnaire are related to worse cognitive performance. The cutoff point for the presence of cognitive decline adopted followed the study that translated and validated the instrument in Brazil: <23 points for those aged 60 to 69 years and <20 points for those aged 70 years or more[13].

For the analysis of serum zinc, the reference value 70 µg/dL was used for women and 74 µg/dL for men, as recommended by the International Zinc Nutrition Consultative Group (IZiNCG)[14] and indicated in the study by Hennigar *et al.*[15]. Individuals who presented lower serum zinc values than the reference were considered to have deficiency of this micronutrient. These values, although proposed for the adult population, were used due to the lack of specific cutoff points for older adults.

Independent variables were also included in the analyses, those being:

- Sociodemographic: gender (male and female), age group (between 60-69 years, 70-79 years, and ≥80 years), schooling in years of study (0-4 years and ≥5 years), marital status (with a partner, including married and living together; without a partner, including singles and widowers);

- Clinical variables, represented by self-reported diseases (diabetes, hypertension, cardiovascular diseases, cancer, encephalic vascular accident (EVA), lung diseases, osteoarticular diseases – arthritis, arthrosis, rheumatism – and osteoporosis);

- Lifestyle variables: To evaluate smoking, older adults were asked about never having smoked (characterized as "no"), smoking currently (characterized as "yes") or being a former smoker. Regarding alcoholism, older adults

were questioned about alcohol consumption and characterized in two categories: non-alcoholics or alcoholics/ex-alcoholics. For the classification of physical activity practice, the individuals who reported performing at least 150 minutes of aerobic physical activity of moderate intensity or 75 minutes of vigorous intensity throughout the week[16] were considered as "active" and the others, not active or insufficiently active, were grouped into a single category;

- Indicators of nutritional status: body mass index (BMI, categorized by ≤22.0 kg/m² for underweight, >22.0 and <27 kg/m² for eutrophic weight and ≥27 kg/m² for overweight); and nutritional risk (identified by the Mini Nutritional Assessment (MNA), considering at risk of malnutrition individuals who score between 17 and 23.5 points and considered as malnourished individuals who presented scores below 17)[17].

Statistical analysis

For statistical analysis of the study variables, mean and standard deviation were calculated for the continuous variables and proportions for categorical variables. Adhesion to the normal distribution of the data was evaluated using the Shapiro Wilk test. To test the difference in the serum zinc mean in relation to the presence of cognitive decline, the t-student test was used. Pearson's x^2 test was adopted to test the differences between the other categorical variables.

The score of each of the different domains (evocation; temporal orientation; verbal fluency; memory) of the CASI-S questionnaire was compared with the zinc deficiency using the Mann-Whitney test since the variables did not adhere to the normal distribution. The odds ratio (OR) of the presence of cognitive decline (study-dependent variable) in relation to serum zinc deficiency (independent variable of interest) was estimated using a multiple logistic regression model. All variables that presented $p<0.20$ in the bivariate analyses between each variable and cognitive decline were included as independent variables, and only those that remained significant were maintained in the final model.

The statistical significance level used was $p<0.05$. The analyses were performed using Stata® software version 14.

Results

Table 1 shows the score obtained by the participants in the total score of the Cognitive Abilities Screening Instrument (CASI-S) and its domains separately according to the presence of zinc deficiency. The mean total score among the participants of the study with adequate serum zinc was 27.2, whereas those with zinc deficiency had a significantly lower mean score, 25.4 ($p=0.022$). Only the memory test score showed a significant difference in the mean score between the domains ($p=0.018$).

The mean serum zinc concentration was 93.4 µg/dL in the study participants, and the prevalence of zinc deficiency in the sample was 3.9%, with no significant difference between genders (5.4% in men and 3.1% in women).

Of the 591 study participants, 68.9% were female, with a mean age of 69 years, and 57.5% had low schooling (up to 4 years of schooling), 60% of the sample reported having a partner (Table 2). Regarding the clinical variables, 27.2% of the older adults reported having a history of diabetes, 61.7% of hypertension, 23.9% of cardiovascular diseases, 7.3% of cancer, 6.3% of EVA, 7.9% of pulmonary diseases, 46.2% of osteoarticular diseases (arthritis, arthrosis, rheumatism), and 17.8% reported a history of osteoporosis. Only the history of EVA showed a significant difference from the other clinical variables ($p=0.045$).

In the lifestyle variables, 59.6% reported not being a smoker and 61.8% reported not being an alcoholic, whereas 54.8% of the sample was insufficiently active or inactive regarding physical activity. Regarding nutritional status, 60.2% were classified as overweight and 80.2% of the sample did not present nutritional risk identified by MNA (Table 2).

Table 2 shows the characteristics of the participants according to the presence of cognitive decline. The total prevalence of cognitive decline was 9.4%. The older adults with zinc deficiency had a prevalence of cognitive decline of 26.1%, which is significantly higher ($p=0.006$) than those with blood zinc concentrations within the expected range, which presented a prevalence of 8.8%. Among the sociodemographic characteristics, the decline was significantly more prevalent in those aged 80 years or more, with less schooling, and widowed or single (without a partner). Among the clinical variables, only the history of EVA was associated with the presence of decline (18.9% and 8.9% in older adults without EVA); the other diseases were not associated (data not

Table 1. Mean score (standard error – SE) of the domains of the Cognitive Abilities Screening Instrument – short form (CASI-S) in relation to the presence of zinc deficiency of community-dwelling older adults of the region of Campinas-SP, 2019 (n=591).

Domains	CASI-S Domains Mean (SE)		
	Adequate Serum Zinc	Inadequate Serum Zinc	p-value*
Memory	2.9 (0.02)	2.8 (0.11)	0.018
Temporal Orientation	3.7 (0.04)	3.6 (0.24)	0.980
Verbal Fluency	7.1 (0.09)	6.1 (0.58)	0.117
Evocation	7.3 (0.09)	6.5 (0.52)	0.133
Total score	27.7 (0.19)	25.4 (1.07)	0.022

Note: *Mann-Whitney test.

Source: Authors.

shown). Among the lifestyle variables, smoking and alcohol consumption showed no significant difference but, among the older adults who reported physical activity, the prevalence of decline was significantly lower compared with those inactive or insufficiently active (6.7 and 11.7% respectively, p=0.039). Finally, among the indicators of nutritional status, the prevalence of decline was significantly higher in those who presented nutritional risk by MNA (26.4%, compared with 5.7% in those without nutritional risk, p<0.001).

Table 3 presents the results of the univariate logistic regression analysis. In the multiple model, the chance of cognitive decline was 3 times higher in older adults with serum zinc deficiency (OR=3.80; 95%CI=1.30-11.12). Other characteristics that were associated with the presence of cognitive decline were low schooling (OR=3.12; 95%CI=1.49-6.50), marital status without a partner (OR=1.88; 95%CI=1.04-3.42), risk of malnutrition according to MNA (OR=3.98; 95%CI=2.36-6.71), and reported history of EVA (OR=2.70; 95%CI=1.04-6.98).

Discussion

The results presented here show that among the cognition domains evaluated in the study, only memory was associated with zinc deficiency. The prevalence of zinc deficiency was 3.9% and 9.4% for cognitive decline and we observed a strong association between cognitive decline with serum zinc deficiency in community-dwelling older adults. The decline was also associated with low schooling, marital status without a partner, risk of malnutrition according to MAN, and report of a history of EVA.

Regarding the domains analyzed by CASI-S, zinc deficiency was significantly associated with the memory domain. Although few studies have evaluated this association, a study conducted in a long-term care facility for older adults in Poland also reports a correlation between zinc deficiency and memory impairment[18]. The study by Alghadir *et al.*[19] showed similar results, with lower serum zinc concentrations strongly associated with worse cognitive performance in long-term memory tests, praxis, thinking, attention, and concentration.

The literature describes many hypotheses to explain these findings. Among them, we can highlight the higher concentration of zinc found in the hippocampus region in the brain, a region that seems to be more vulnerable to the deficiency of this micronutrient. This region of the brain plays a critical role in memory, learning, and neurogenesis[18,20]. Another hypothesis that may explain this change is that zinc can decrease the absorption of glutamate and dopamine transporters and exhibit various effects on calcium, potassium, sodium, and chloride channels, whereas recent evidence shows that zinc can also be released in glycinergic synapses[20,21]. This process is also considered important for memory, suggesting zinc plays a role in its formation.

The prevalence of zinc deficiency observed in our study was lower than the values described in other studies with older adults. Two international studies reported prevalences between 10% and 36%[22-24], while a Brazilian study conducted with 70 participants aged >50 years in two cities of the state of Rio Grande do Sul showed a considerably higher prevalence of 26.4%[25]. Note that these studies adopted different reference values for defining disability, which may partly justify this difference.

Table 2. Prevalence of cognitive decline in relation to health, lifestyle, and nutritional status variables of community-dwelling older adults of Campinas-SP, 2019 (n=591).

Variables	Prevalence of cognitive decline			
	N (%)	N (%) No decline	N (%) With decline	p-value**
Serum Zinc				
Mean (Standard Error), µg/dL	93.4 (0.6)	93.4 (0.6)	93.2 (2.7)	0.765
Adequate*	568 (96.1)	518 (91.2)	50 (8.8)	
Inadequate	23 (3.9)	17 (73.9)	6 (26.1)	0.006
Gender				0.297
Male	184 (31.1)	170 (92.4)	14 (7.6)	
Female	407 (68.9)	365 (89.7)	42 (10.3)	
Age Group				0.050
60-69	305 (51.6)	279 (91.5)	26 (8.5)	
70-79	233 (39.4)	213 (91.4)	20 (8.6)	
≥80	53 (9.0)	43 (81.1)	10 (18.9)	
Schooling (years of study)				0.002
≥5	235 (39.8)	225 (95.7)	10 (4.3)	
0-4	340 (57.5)	296 (87.1)	44 (12.9)	
Not informed	16 (2.7)	14 (87.5)	2 (12.5)	
Marital status				0.043
With a partner	351 (60.0)	325 (92.6)	26 (7.4)	
Without a partner	234 (40.0)	205 (87.6)	29 (12.4)	
Encephalic vascular accident (EVA)				0.045
No	549 (93.7)	500 (91.1)	49 (8.9)	
Yes	37 (6.3)	30 (81.1)	7 (18.9)	
Smoking habit				0.337
Non-smoker	352 (59.6)	322 (91.5)	30 (8.5)	
Smoker or former smoker	239 (40.4)	213 (89.1)	26 (10.9)	
Alcoholism				0.683
Non-alcoholic	365 (61.8)	329 (90.1)	36 (9.9)	
Alcoholic or former alcoholic	226 (38.2)	206 (91.2)	20 (8.8)	
Practice of physical activity				0.039
Active	267 (45.2)	249 (93.3)	18 (6.7)	
Insufficiently active or not active	324 (54.8)	286 (88.3)	38 (11.7)	
Body mass index (BMI)				0.135
Malnutrition	49 (8.3)	42 (85.7)	7 (14.3)	
Eutrophic	186 (31.5)	164 (88.2)	22 (11.8)	
Excess weight	356 (60.2)	329 (92.4)	27 (7.6)	
Nutritional risk				<0.001
No risk	474 (80.2)	447 (94.3)	27 (5.7)	-
Risk of malnutrition	106 (17.9)	78 (73.6)	28 (26.4)	-
Not informed	11 (1.9)	10 (90.9)	1 (9.1)	

Note: *Adequate serum zinc is ≥70 µg/dL for women and ≥74 µg/dL for men. **T-student test for difference of serum zinc mean; Pearson's chi-square test for other variables.

Source: Authors.

The lack of specific reference values for older adults may compromise the analysis of the presence of zinc deficiency in this population, making reassessing and standardizing these parameters important since the prevalence analysis is important to guide public policies for risk groups. In our study, we used as reference standard the values (70 µg/dL for women and 74 µg/dL for men) indicated by the IZiNCG in its reanalysis of National Health and Nutrition Examination

Table 3. Results of the logistic regression model of the association between cognitive decline, serum zinc deficiency and other independent variables in community-dwelling older adults of Campinas-SP, 2019 (n=591).

Variables	Gross OR* (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Serum Zinc				
Adequate	1.0	-		
Inadequate	3.66 (1.38-9.69)	0.009	3.80 (1.30-11.12)	0.015
Schooling (years of study)				
≥5	1.0	-	1.0	
0-4	3.34 (1.65-6.79)	0.001	3.12 (1.49-6.50)	0.002
Marital status				
With a partner	1.0		1.0	
Without a partner	1.77 (1.01-3.09)	0.045	1.88 (1.04-3.42)	0.038
Nutritional risk				
No risk	1.0		1.0	
Risk of malnutrition	3.38 (2.11-5.42)	<0.001	3.98 (2.36-6.71)	<0.001
Encephalic vascular accident (EVA)				
No	1.0		1.0	
Yes	2.38 (0.99-5.70)	0.052	2.70 (1.04-6.98)	0.040

Note: *OR: Odds Ratio. Logistic regression analysis. Category "not informed" suppressed from the analysis of schooling and nutritional risk.

Source: Authors.

Survey II study from the United States (NHANES II: 1976-1980)[14], a population-based survey that provides data for serum zinc concentrations in a representative sample of healthy people. It describes specific values for children and pregnant women, men, and women over 10 years of age, but without a specific range for older adults[14].

The prevalence of cognitive decline in our study was 9.4%. The prevalence of cognitive decline found in the literature varies greatly[26-28], partly also due to the different measurement instruments available and cut-off points used in the literature.

A study conducted with older residents in the municipality of Ibicuí, Bahia showed a 18.7% prevalence of cognitive deficit, much higher than what our study reported[26]. A systematic review evaluated 48 studies in China and described a 14.7% prevalence of mild cognitive impairment (a condition in which the older person has cognitive decline, but no negative impact on daily living activities)[27]. Another review study found a 17.3% general prevalence in the selected studies, ranging from 0.5% to 41.8%, and the authors argue that differences in the characteristics of the studies, such as mean age and schooling of the sample, diagnostic criteria, cognitive tests used, and operationalization of these criteria, may be responsible for this variability[28].

This is the first national study that analyzes the association between zinc deficiency and cognitive decline and even the international literature has few studies on the subject. Alqabbani and AlBadr[24] in a study conducted in Saudi Arabia with 400 participants aged 65 years or older, from primary care centers, showed that 36% of the participants presented zinc deficiency and 35% of the participants presented impaired cognitive functions, with a significant positive correlation between the serum zinc status and cognitive functions[24]. These prevalences were higher than those described in our study, but we emphasize that the use of different instruments for cognitive assessment and differences between the cutoff points for zinc deficiency may partially justify these differences.

Another study conducted in Poland[18] analyzed the relationship of serum zinc and mental and physical status of 100 older people living in a long-term care (LTC) facility for older adults. The findings showed that serum zinc concentrations were lower in individuals with alterations in cognitive function and also in participants with signs of depression compared with those without depression[18].

Although most zinc is protein-bound, some specific subpopulations of neurons contain vesicles filled with weakly bound or free zinc ions

(Zn^{2+}). The first reported and most abundant population of neurons containing zinc is glutamatergic[29], and zinc released from the vesicles of these neurons into the synaptic cleft can modulate the activity of the N-methyl-D-aspartate receptor (NMDA) in a dose-dependent and reversible manner[20]. However, zinc can also modulate the activity of other glutamate receptors, such as αamino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), metabotropic receptors, and receptors for other neurotransmitters such as adenosine, dopamine, and serotonin[29].

In our study, cognitive decline was also associated with schooling, a sociodemographic variable that helps in understanding it as a multifactorial condition[11].

According to the literature, schooling is the main protective factor for cognitive decline in advanced age[30,31]. Gomes *et al.*[32], in their integrative review, emphasize that environmental factors, such as schooling, could favor neuronal growth and neuroplasticity and thus delay the emergence of cognitive decline. Other studies have also pointed out the relationship between low schooling and cognitive decline, including with older Brazilian adults[11,32,33].

In our study, we found an association between cognitive decline and not having a partner. Recent studies have shown that being married or having a partner is associated with better mental and physical health and longer life expectancy, whereas divorce and widowing have harmful effects on a number of health outcomes, including self-rated health, cardiovascular health, and risk of inflammation[34,35]. Sociopsychological resources can explain this association, with being married relating to greater access to involvement, support, and social integration, which are factors for better health and well-being, which may include better cognitive health[34]. In addition, higher levels of social involvement (that is, degree of participation in community or society) can reduce the risk of dementia, improving cognitive reserves, favoring the ability to deal with neuropsychological damage by using compensatory cognitive approaches[34,36]. Spouses expand their social support networks, connecting them, for example, to their friends and family. Daily communication with the spouse also provides cognitive stimulation and can increase neural plasticity, maintaining and improving cognitive reserves[34,35]. On the other hand, divorce and widowing can harm health and increase stress[35,37,38], besides usually resulting in the loss of economic, social, and psychological resources, which may be associated with a higher risk of cognitive decline and dementia[35,38].

We also evidenced that the risk of malnutrition was associated with higher chances of cognitive decline. In aging, changes in body composition and cognitive fragility are clearly implicated in frailty and sarcopenia syndromes[39,40]. Our results corroborate those of Mantzorou *et al.*[41], who in a study conducted in seven cities in Greece with a sample of 2,092 older adults, described that 35.0% of them had a higher risk of malnutrition and 11.3% had malnutrition, whereas 34.4% of the participants had impaired cognitive function and 32.3% had depressive symptoms, with malnutrition more frequent in participants with cognitive decline and depressive symptoms.

Regarding the clinical history of the older adults, in our study only self-reported encephalic vascular accident (EVA) was associated with cognitive decline, which is consistent with literature results[42,43]. EVA is one of the main causes of death and disability worldwide, with a considerable proportion of those who have suffered an EVA developing persistent and significant cognitive deficits that affect functional capacity[42,43]. The EVA can increase the risk of cognitive decline by at least 5 to 8 times, being considered a risk factor for this impairment[43,44]. Merriman *et al.*[42], in their review study, indicate that 50% of EVA survivors reported cognitive decline 6 months after the clinical episode, also associating it with worse quality of life and increased disability[42,45]. According to the study by Drozdowska *et al.*[46], cardiovascular risk factors may be predictors of age-related cognitive decline and dementia since these factors are predecessors to EVA and, therefore, it seems plausible that post-EVA cognitive decline may be a manifestation of vascular neurodegenerative processes[46]. However, note that the pattern of post-EVA cognitive decline is typically diffuse in nature and can affect several cognitive domains[42,45].

Our study has some limitations. Since it is a cross-sectional study, we cannot establish causal relationships. We also did not calibrate the interviewers for the blood aliquot collection, which may lead to information bias. This was not possible due to the procedure being performed by a nursing team of the unit itself in some places. However, all professionals followed the protocol common to any venous collection, and to ensure standardization, the study coordinator supervised all biological collections, and was responsible for the identification of the tubes, storage in the thermal boxes, and transportation of samples with ice to the contracted laboratory.

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The absence of cutoff points for specific zinc deficiency for the older population may also have impacted on the results obtained since metabolic conditions change as the years progress and parameters used for young adults may be inappropriate to older adults.

However, note that we conducted the study with a large sample of community-dwelling older adults, a group characterized as an ideal audience for screening for initial cognitive decline, allowing further implementation of preventive measures at the primary care level. Furthermore, to date, no national publications have been found to evaluate the prevalence of zinc deficiency and its relationship with cognitive decline in older adults. Even in international studies, this relationship is scarcely discussed, especially relating to memory. Thus, our study may relevant to guide national public policies aimed to encourage older adults' consumption of zinc.

Conclusion

The results of our study showed that cognitive decline had a strong association with zinc deficiency. Therefore, we recommend reflections on the implementation of public policies, programs, and educational actions aimed at the older population, especially on promoting healthy eating in primary health care networks, to avoid future changes that may compromise the cognitive capacity of the older individual.

Collaborations

MF Marchetti worked in data collection and analysis and writing of the manuscript. LP Corona worked in the research coordination, study design, analysis plan and review of the writing of the manuscript. CN Freiria and GM Silva worked in data collection, database preparation and revision of the manuscript. M Milanski, FSA Borim and TRP Brito worked in the review of the analysis and manuscript. All the authors listed read and approved the final manuscript. I state that all authors contributed significantly to the manuscript and are in accordance with its content.

Acknowledgements

To the Conselho Nacional de Pesquisa e Desenvolvimento (CNPq), the Pró-Reitoria de Pesquisa of UNICAMP and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

The authors thank Espaço da Escrita – Pró-Reitoria de Pesquisa of UNICAMP – for the language services provided.

Funding

Conselho Nacional de Pesquisa e Desenvolvimento (CNPq) (Process 408262/2007-6); the Pró-Reitoria de Pesquisa of UNICAMP (FAEPEX Processes numbers 2854/18 and 3150/19); and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

References

1. Instituto Brasileiro de Geografia e Estatística (IBGE). *Mudança Demográfica no Brasil no Início do Século XXI – Subsídios para as Projeções da População - 2015*. Rio de Janeiro: MS/IBGE; 2015.
2. Clegg ME, Williams EA. Optimizing nutrition in older people. *Maturitas* 2018; 112:34-38.
3. Sales MC, Oliveira LP, Cabral NLA, Sousa SES, Almeida MG, Lemos TMAM, Lyra CO, Lima KO, Sena-Evangelista KCM, Pedrosa LFC. Plasma Zinc in institutionalized elderly individuals: Relation with immune and cardiometabolic biomarkers. *J Trace Elem Med Biol* 2018; 50:615-621.
4. Saueressig C, Silva VLD, Antunes LDC, Dall'Alba V. Níveis de zinco sérico em pacientes internados com depressão. *J Bras Psiquiatr* 2016; 65(3):239-244.
5. Chasapis CT, Ntoupa AP, Spiliopoulou C, Stefanidou M. Recent aspects of the effects of zinco n human health. *Arch Toxicol* 2020; 94(5):1443-1460.
6. Choi S, Hong DK, Choi BY, Suh SW. Zinc in the Brain: Friend or Foe? *Int J Mol Sci* 2020; 21(23):8941.
7. Gower-Winter SD, Levenson CW. Zinc in the central nervous system: From molecules to behavior. *Biofactors* 2012; 38(3):186-193.
8. Warthon-Medina M, Moran VH, Stammers AL, Dillon S, Qualter P, Nissensohn N, Serra-Majem L, Lowe NM. Zinc intake, status and indices od cognitive function in adults and children: a systematic review and meta analysis. *Eur J Clin Nutr* 2015; 69:649-661.
9. Garcia TER, Marcelo-Pons M, Martínez-Arnau F, Serra-Catalá N, Santamaría-Carrillo Y, Cauli O. Blood zinc levels and cognitive and functional evaluation in non-demented older patients. *Exp Gerontol* 2018; 108:28-34.
10. Portbury SD, Adlard PA. Zinc Signal in Brain Diseases**.** *Int J Mol Sci* 2017; 18(12):2506.
11. Pereira XBF, Araújo FLC, Leite TIA, Araújo FAC, Bonfada D., Lucena EES. Prevalência e fatores associados ao deficit cognitivo em idosos na comunidade. *Rev Bras Geriatr Gerontol* 2020; 23(2):e200012.
12. Rolizola PMD, Freiria CN, Silva GM, Brito TRP, Borim FSA, Corona LP. Insuficiência de vitamina D e fatores associados: um estudo com idosos assistidos por serviços de atenção básica à saúde. *Cien Saude Colet* 2022; 27(2):653-663.
13. Damasceno A, Delicio AM, Mazo DFC, Zullo JFD, Scherer P, Ng RTY, Damasceno BP. Validation of the brazilian version of mini-test CASI-S. *Arq Neuropsiquiatr* 2005; 63(2-B):416-421.
14. Hotz C, Peerson JM, Brown KH. Assessment of the Risk of Zinc Deficiency in Populations and Options for Its Control**.** *Food Nutr Bull* 2004; 25(1):137-151.
15. Hennigar SRH, Lieberman HR, Fulgoni VL, McClung JP. Serum Zinc Concentrations in the US Population Are Related to Sex, Age, and Time of Blood Draw but Not Dietary or Supplemental Zinc. *J Nutr* 2018; 148(8):1341-1351.
16. World Health Organization (WHO). *Global recommendations on physical activity for health*. Geneva: WHO; 2010.

17. Guigoz Y, Vellas B, Garry PJ. Mini Nutritional Assessment: a practical assessment tool for grading the nutritional state of elderly patients. *Open J Nurs* 1994; 4(5):15-59.
18. Markiewicz-Żukowska R, Gutowska A, Borawska MH. Serum zinc concentrations correlate with mental and physical status of nursing home residents. *PloS One* 2015; 10(1):e0117257.
19. Alghadir A, Gabr SS. Al-Eisa E. Assessment of the effects of glutamic acid decarboxylase antibodies and trace elements on cognitive performance in older adults. *Clin Interv Aging* 2015; 10:1901-1907.
20. Cherasse Y, Urade Y. Dietary Zinc Acts as a Sleep Modulator. *Int J Cell Sci Mol Biol* 2017; 18(11):2334.
21. Zhang Y, Keramidas A, Lynch JW. The free zinc concentration in the synaptic cleft of artificial glycinergic synapses rises to at least 1 muM. *Front Mol Neurosci* 2016; 9:88.
22. Cheong M, Chew STH, Oliver J, Baggs G, Low YL, How CH, Tan NC, Huynh DTT, Tey SL. Nutritional Biomarkers and associated factors in community-dwelling older adults: Findings from the SHIELD study. *Nutrients* 2020; 12(11):3329.
23. Kvamme JM, Grønli O, Jacobsen BK, Florholmen J. Risk of malnutrition and zinc deficiency in community-living elderly men and women: the Tromsø Study. *Public Health Nutr* 2014; 18(11):1907-1913.
24. Alqabbani HM, Albadr NA. Zinc status (intake and level) of healthy elderly individuals in Riyadh and its relationship to physical health and cognitive impairment. *Clin Nutr Exp* 2020; 29:10-17.
25. Rocha TJ, Korb C, Schuch JB, Bamberg DP, Andrade FM, Fiegenbaun M. SLC30A3 and SEP15 gene polymorphisms influence the serum concentrations of zinc and selenium in mature adults. *Nutr Res* 2014; 34(9):742-748.
26. Nascimento RASA, Batista RTS, Rocha SV, Vasconcelos LRC. Prevalência e fatores associados ao declínio cognitivo em idosos com baixa condição econômica: estudo MONIDI. *J Bras Psiquiatr* 2015; 64(3):187-192.
27. Xue J, Li J, Liang J, Chen S. The prevalence of mild cognitive impairment in China: A systematic review. *Aging Dis* 2018; 9(4):706-715.
28. Pessoa RMP, Bomfim AJL, Ferreira BLC, Chagas MHN. Diagnostic criteria and prevalence of mild cognitive impairment in older adults living in the community: a systematic review and meta-analysis. *Rev Psiquiatr Clín* 2019; 46(3):72-79.
29. Frederickson CJ, Koh JY, Busch AI. The neurobiology of zinc in health and disease. *Nat Rev Neurosci* 2005; 6:449-462.
30. Chapko D, McCormack R, Black C, Staff R, Murray A. Life-course determinants of cognitive reserve (CR) in cognitive aging and dementia - a systematic literature review. *Aging Ment Health* 2018; 22(8):915-926.
31. Kim H, Lee S, Ku BD, Ham SG, Park WS. Associated factors for cognitive impairment in the rural highly elderly. *Brain Behav* 2019; 9(5):e01203.
32. Gomes ECC, Souza SL, Oliveira AN, Leal MCC. Treino de estimulação de memória e a funcionalidade do idoso sem comprometimento cognitivo: uma revisão integrativa. *Cien Saude Colet* 2020; 25(6):2193-2202.
33. Silva JG, Caldeira CG, Cruz GECP, Carvalho LED. Envelhecimento ativo, qualidade de vida e cognição de idosos: um estudo transversal em uma cidade de Minas Gerais. *REAS/EJCH* 2020; 12(1):1-10.
34. Liu H, Zhang Z, Choi SW, Langa KM. Marital Status and Dementia: Evidence from the Health and Retirement Study. *J Gerontol B Psychol Sci Soc Sci* 2020; 75(8):1783-1795.
35. Liu H, Zhang Y, Burgard SA, Needham BL. Marital Status and cognitive impairment in the United States: evidence from the National Health and Aging Trends Study. *Ann Epidemiol* 2019; 38:28-34.
36. Sommerland A, Ruegger J, Singh-Manoux A, Lewis G, Livingston G. Marriage and risk of dementia: systematic review and meta-analysis of observacional studies. *J Neurol Neurosurg Psychiatr* 2018; 89(3):231-238.
37. Liu H, Waite L. Bad marriage, broken heart? Age and gender differences in the link between marital quality and cardiovascular risks among older adults. *J Health Soc Behav* 2014; 55(4):403-423.
38. Brown SL, Lin IF, Vielee A, Mellencamp KA. Midlife marital dissolution and the onset of cognitive impairment. *Gerontologist* 2021; 61(7):1085-1094.
39. Gómez-Gómez ME, Zapico SC. Frailty, Cognitive decline, Neurodegenerative diseases and nutrition interverts. *Int J Mol Sci* 2019; 20(11):2842.
40. Dye L, Boyle NB, Champ C, Lawton C. The relationship between obesity and cognitive health and decline. *Proc Nutr Soc* 2017; 76(4):443-454.
41. Mantzorou M, Vadikolias K, Pavlidou E, Serdari A, Vasios G, Tryfonos C, Giaginis C. Nutritional status is associated with the degree of cognitive impairment and depressive symptoms in a Greek elderly population. *Nutr Neurosci* 2018; 23(3): 201-209.
42. Merriman NA, Sexton E, Donnelly NA, McCabe G, Walsh ME, Rohde D, Gorman A, Jeffares I, Pender N, Willians D, Horgan F, Doyle F, Wren MA, Bennett KE, Hickey A. Managing cognitive impairment following stroke: protocol for a systematic review of non-randomised controlled studies of psychological interventions. *BMJ Open* 2018; 8(1):e019001.
43. Qu Y, Zhuo L, Hu Y, Chen W, Zhou Y, Wang J, Tao Q, Hu J, Nie X, Zhan S. Prevalence of post-stroke cognitive impairment in China: A community-Based, Cross-sectional study. *PLoS One* 2015; 10(4):e0122864.
44. Wu JX, Xue J, Zhuang L, Liu CF. Plasma parameters and risk factors of patients with post-stroke cognitive impairment. *Ann Palliat Med* 2020; 9(1):45-52.
45. Mijajlovic MD, Pavlovic A, Brainin M, Heiss WD, Quinn TJ, Ihle-Hansen HB, Hermann DM, Assayag EB, Richard E, Thiel A, Kliper E, Shin YI, Kim YH, Choi SH, Jung S, Lee YB, Sinanovic O, Levine DA, Schlesinger I, Mead G, Milosevic V, Leys D, Hagberg G, Ursin ML, Teuschl Y, Prokopenko S, Mozheyko E, Bezdenezhnykh A, Matz K, Aleksic V, Muresanu DF, Korczyn AD, Bornstein NM. Post-stroke dementia – a comprehensive review. *BMC Med* 2017; 15(1):11.

46. Drozdowska BA, Elliott E, Taylor-Rowan M, Shaw RC, Cuthbertson G, Langhorne P, Quinn TJ. Cardiovascular risk factors indirectly affect acute post-stroke cognition through stroke severity and prior cognitive impairment: a moderated mediation analysis. *Alzheimers Res Ther* 2020; 12(1):85.

Article submitted 08/07/2021
Approved 16/02/2022
Final version submitted 18/02/2022

Chief editors: Romeu Gomes, Antônio Augusto Moura da Silva