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Prevalence and factors associated with vitamin B_{12} deficiency in elderly from Viçosa/MG, Brasil

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Abstract

The prevalence of vitamin B_{12} nutritional deficiency increases with age and it is particularly common in elderly people. The objective this study was determining its prevalence and the factors associated with this condition in non-institutionalized elderly from Viçosa, Minas Gerais State, Brazil.

***Methods:* a cross-sectional, population-based study was conducted in order to identify the prevalence and the factors associated with vitamin B_{12} deficiency among the elderly population in Viçosa (MG). Data were collected from August 2011 to June 2012, by means of a household survey and hematological and biochemical tests performed in 340 elderly.**

***Results:* the prevalence of vitamin B_{12} deficiency in this group was 17.4% (95% CI, 13.4% - 21.4%). Cognitive impairment appears to be an important factor related to vitamin B_{12} deficiency.**

***Conclusions:* the current paper contributes to studies that emphasize some factors that may affect elderly performance in their natural aging process, especially when these factors are associated with cognitive impairment and lead to significant disability and loss of quality of life. Thus, the herein presented results were able to provide more comprehensive knowledge on the relation between B_{12} deficiency and its impact on this population. They also proved to be relevant for planning public health programs and initiatives that target on this age group.**

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Key words: *Vitamin B_{12}. Nutritional deficiency. Elderly.*

PREVALENCIA Y FACTORES ASOCIADOS A LA DEFICIENCIA DE VITAMINA B_{12} EN ANCIANOS DE VIÇOSA/MG, BRASIL

Resumen

La prevalencia de deficiencia nutricional de vitamina B_{12} aumenta con la edad y es especialmente común en la población mayor. El objetivo de este estudio consistió en determinar su prevalencia y los factores asociados a esta carencia en mayores no institucionalizados de Viçosa, Estado de Minas Gerais, Brasil.

***Métodos:* estudio poblacional interseccional, realizado para identificar la prevalencia y los factores asociados a deficiencia de vitamina B_{12} entre la población de mayores en Viçosa (MG). Los datos fueron recopilados desde agosto de 2011 hasta junio de 2012 mediante una encuesta en los hogares y pruebas hematológicas y bioquímicas realizadas en 340 mayores.**

***Resultados:* la prevalencia de deficiencia de vitamina B_{12} en este grupo fue del 17,4% (95% CI, 13,4% - 21,4%). La deficiencia cognitiva se presenta como un factor importante relacionado con la deficiencia de vitamina B_{12}.**

***Conclusiones:* el informe actual contribuye a los estudios que destacan ciertos factores que podrían afectar al rendimiento de las personas mayores en su proceso de envejecimiento natural, especialmente cuando estos factores están asociados con deficiencia cognitiva y dan lugar a una discapacidad significativa así como pérdida de calidad de vida. Así, los resultados aquí presentados han servido para aportar un conocimiento más comprensivo sobre la relación entre deficiencia de B_{12} y su impacto sobre este grupo de población. También han demostrado su relevancia de cara a la planificación de programas e iniciativas de salud pública centrados en este grupo de población.**

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Palabras clave: *Vitamina B_{12}. Deficiencia nutricional. Mayores.*

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Introduction

Vitamin B_{12} (cobalamin) is essential to the human body and responsible for maintaining neurological functions, red blood cell production and DNA synthesis[1]. The human body does not produce this micronutrient, thus it must be obtained by the regular intake of animal-origin proteins and fortified cereal products[1-3].

Vitamin B_{12} deficit in the elderly population caused by stomach problems and inadequate diet has been studied. In the case of inadequate diet, this deficit results from inadequate health conditions due to the loss of teeth (the decreased ingestion of red meat is the main cause), reduced appetite and tolerance to milk and its derivatives[2,4]. Therefore, the low levels of vitamin B_{12} found in the elderly population may be associated with gastric atrophy and the production of low intrinsic factors. These two items are responsible for the poor absorption of this micronutrient and it results in vitamin B_{12} deficiency. Once associated with the evolution of some comorbidities - anemia, neuropathies and cognitive impairments –, vitamin B_{12} deficiency represents a major public health problem[2,3,5-7].

Literature reports that approximately 10% of the non-institutionalized elderly population has vitamin B_{12} deficiency. This prevalence increases with age and reaches 20% in octogenarians[2,8-10]. However, the actual prevalence is difficult to measure: studies use different cutoff points to analyze this vitamin deficiency at plasma levels. There are also variations in laboratory test methods used to measure it[1,11,12].

Studies on the prevalence of vitamin B_{12} deficiency are scarce in Brazil. Xavier *et al*. (2010) found prevalence of vitamin B_{12} deficiency in 11% adult and elderly individuals. Their study compared different methods used to detect this deficiency and showed lower vitamin B_{12} levels among the elderly. This result was obtained by measuring the methylmalonic acid (MMA). This measurement is considered to be a new alternative, since the serum dosage of vitamin B_{12} still has some restrictions due to sensitivity problems[13]. Almeida *et al*. (2012) conducted a clinical study on cognitive aging and evaluated mild cognitive impairment and serum levels of vitamin B_{12} and folic acid[14]. These authors observed that the investigated levels were lower in elderly people with mild cognitive impairment, in comparison to those with Alzheimer's disease. The Brazilian studies on the elderly population are focused on mental or neurological disorders such as dementia, Alzheimer's, Parkinson's and psychiatric disorders, which are common diseases in old age[15-18]. In addition, there are still scarce studies on this topic, especially population-based studies regarding the community elders.

Thus, the current study tackles the epidemiology of vitamin B_{12} nutritional deficiency, by determining its prevalence and the factors associated with this condition in non-institutionalized elderly from Viçosa County, Minas Gerais State, Brazil.

Materials and Methods

The current study is part of the project named "Capacidade funcional e autonomia de idosos com Síndrome Metabólica na Estratégia Saúde da Família de Viçosa-MG" (Functional capacity and autonomy of elderly people with Metabolic Syndrome enrolled in the Family Health Strategy Program of Viçosa-MG). It is a cross-sectional study conducted in all Family Health Strategy (ESF - Estratégia Saúde da Família) units in Viçosa / MG, from August 2011 to June 2012. The sample consisted of individuals aged 60 years old or older, from both genders, assisted in the County's ESFs, including its urban and rural areas.

The sample size calculation considered 95% confidence level, 65% MS prevalence[11] and 5% tolerated error. Thus, the sample comprised 331 elderly, to which 20% was added to cover possible losses, so the sample totaled 398 elderly. The final sample consisted of 402 elderly. The present study interviewed 402 elderly, and 340 (56.12%) agreed to undergo biochemical tests. Thus, 340 elderly were effectively studied. The sample size calculation was performed using Epi-Info 3.5.1 software.

Data collection was performed in all the ESFs, during two meetings. At the first meeting, the elderly were informed about the research goals and signed the Informed Consent Form. Subsequently, a questionnaire was applied to collect the elderly's socioeconomic and demographic features (date of birth, gender, marital status, education). The participants' socioeconomic classification was performed by applying the questionnaire of the Brazilian Association of Research Companies[29]. Then, anthropometric assessment was carried out.

Data were collected using a semi-structured questionnaire with mostly closed and pre-coded questions. The questionnaire was directly applied to the elderly. However, if they presented some difficulty, the respondent close to them could help. Approximately 25.7% of the elderly were assisted in some section of the questionnaire, and the assistance was mostly provided by family members (95%).

The biochemical tests consisted of complete blood counts, 15 mL blood sample was collected from each individual by a technician from the Clinical Analysis Laboratory of the Health Division at the Federal University of Viçosa. All the studied participants were instructed to fast for 12 hours before the blood collection[20].

Vitamin B_{12} levels were measured by the DXi *immunoenzymatic analyzer*, from Beckman Coulter, using electrophoresis.

According to the World Health Organization (1968), vitamin B_{12} measurement may be interpreted according to the following concentrations: deficiency (levels below 80 pg/mL), suggesting deficiency (between 80 and 140 pg/mL) indefinite diagnosis (between 140 and 200 pg/mL) and normal (from 200 to 960 pg/mL)[21].

According to this criterion, vitamin B_{12} deficiency was the analyzed dependent variable, and it was defined as plasma levels below 140 pmol/L[21].

The herein analyzed independent variables were:

a) Sociodemographic features: gender (female, male), age (60-69, 70-79 and 80 years old and over), education level (five years or more, up to four years and never studied).
b) Indicators of health conditions and use of health services: history of depression, cardiovascular diseases; cognitive impairment, anemia, number of self-reported diseases (up to four diseases and five or more diseases), functional capacity (adequate and inadequate), nutritional status (normal weight, underweight and overweight), changes in food intake in the last three months (without reduction and with reduction) and hemoglobin (g/dL) and folic acid (ng/mL) levels.

Cognitive impairment was assessed through Mini-Mental State Examination (MMSE), which is composed of questions grouped into seven categories. Each one of them evaluated the deficit of specific cognitive functions: time orientation, local orientation, record of three words, attention and calculation, remembering three words, language and visual constructive capacity. MMSE score could range from a minimum of 0 to a total of 30 points[22]. Elderly with scores equal to or lower than 13 were classified as "carriers of some cognitive impairment" and those with scores higher than 13 were classified as "without cognitive impairment"[22,23].

Anemia was evaluated by measuring plasma hemoglobin levels lower than 12 g/dL for women and 13 g/dL for men in the age group over 60 years old[21].

Nutritional status was calculated using body mass index (BMI), dividing the weight in kilograms by the height in squared meters (kg / m^2). Thus, the herein adopted cutoff points to assess the nutritional status were suggested by Lipschitz[24,25]: low weight (22kg/m^2), normal weight (22-27kg/m^2) and overweight (>27kg/m^2).

The functional capacity assessment was based on reports from individuals in a range of 12 types of activities among those of daily living (ADLs) and instrumental activities of daily living (IADLs). The herein included ADLs were: bathing, dressing, eating alone, toileting, walking from one room to another in the house and getting out of bed towards the chair. The instrumental activities of daily living (IADLs) were: preparing or cooking food, using the phone, leaving the house and taking a bus, taking medication, handling money, shopping, cleaning the house, washing and ironing[26].

Twelve (12) functional activities from the report were analyzed and divided into categories: 1) without difficulty; 2) with little difficulty; 3) with great difficulty; 4) unable; 5) does not apply. Subsequently, these categories were summed. As for the statistical analysis, the functional capacity variable was dichotomized into appropriate and inadequate[25]. Thus, individuals who reported some difficulty in performing six or more activities (categories 2 and 3), or individuals who reported they had difficulty in performing at least three out of 12 activities (category 4) were considered to have inadequate functional capacity[26].

The EpiInfo software version 6.04 was used to data storage and the Stata software version 9.0 was used to analyze them. The normal distribution of quantitative variables was assessed using Kolmogorov-Smirnov test. Descriptive analysis of the variables was presented by measuring the adequate central and variability tendencies as well as the frequency distribution.

The association among categorical independent variables and the presence of vitamin B_{12} deficiency were estimated by bivariate analysis using Pearson's chi-square test (χ^2). The significance level adopted in all comparisons was $\alpha = 5\%$.

As for the regression analysis, Poisson regression with robust variance was used in order to obtain estimates of prevalence ratios of vitamin B_{12} deficiency and the respective confidence intervals of 95% (CI 95%).

Bivariate analyses were performed among the dependent and independent variables, and the prevalence ratio (PR) was obtained through Poisson regression as association measure. The multivariate analysis incorporated the variables associated with the outcome from the bivariate analysis, with $p<0.25$, and those with significant association at the level of $p<0.05$ were kept in the final model.

The current study was approved by the Ethics Committee on Human Research of the Federal University of Viçosa (N. 039/2011).

Results

The proportion of men and women was equivalent among the 345 elderly included in the current study, in which women accounted for 49.9%. The mean age was 69.55 years old (SD = 7.51 years) with predominance of the age group from 60 to 69 years old (57.31%).

This sample showed mean level of vitamin B_{12} of 242.43 pg/mL (SD = 109.13), corresponding to the normal range for individuals from both genders according to WHO (1968)[21]. The minimum value was 49 pg/mL and the maximum value was 726 pg/mL. The current study found 15.7% suggestive prevalence of vitamin B_{12} deficiency and 21.27% indeterminate diagnosis.

The total prevalence of vitamin B_{12} deficiency was 17.4% (95% CI 13.4% - 21.4%). According to table I, there was significant difference in the prevalence of vitamin B_{12} deficiency regarding education and income, and it was higher in those with no education.

The mean hemoglobin serum level among those with B_{12} deficiency was 13.71 g/dL (SD = 1.35 g/dL)

Table I
Prevalence and prevalence ratio (PR) of vitamin B_{12} deficiency, according to sociodemographic variables, in elderly individuals from Viçosa, Minas Gerais, 2012

Variables	*N*	*Prevalence (%)*	*RP ($IC_{95\%}$)*	*p*
Sex				
Female	171	15.8	1	
Man	174	19.0	1.20 (0.72 – 1.99)	0.48
Age				
60-70 years	197	13.7	1	
70-80 years	109	21.1	1.54 (0.88 – 2.68)	0.13
> 80 years	39	25.6	1.87 (0.90 – 3.86)	0.09
Education				
> 5 years	42	33.3	1	
1-4 years	221	18.1	2.47 (1.05 – 5.83)	**0.03**
illiterate	82	7.3	4.55 (1.75 – 11.85)	**<0.01**

in comparison to the mean of 13.78 g/dL (SD=1.30 g/dL) found among those without deficiency. These differences were not statistically significant (p=0.7). Regarding the folic acid, the means were significantly different (p=0.04), and elderly with vitamin B_{12} deficiency showed the average of 68.34 ng/mL, whereas those with no deficiency showed 83.00 ng/mL.

The herein studied comorbidities showed statistically significant association between cognitive impairment and vitamin B_{12} deficiency among the elderly. Among those who self-reported up to four diseases, there was higher prevalence of vitamin B_{12} deficiency; however, this result did not show statistically significant difference, as it can be seen in table II.

Among the elderly with inadequate functional capacity, 14.7% showed vitamin B_{12} deficiency. However, the association between inadequate functional capacity and vitamin B_{12} deficiency was not statistically significant, and there were no significant differences in the prevalence of vitamin B_{12} deficiency according to the elderly nutritional status and food intake (Table II).

The multivariate analysis found that elderly individuals with cognitive impairment showed prevalence of vitamin B_{12} deficiency 1.84 times higher (95% CI 1.10 - 3.07) than those without such comorbidity. This was the only factor independently associated with vitamin B_{12} deficiency.

Discussion

The current study found mean serum level of vitamin B_{12} of 242.43 pg/mL and 17.4% (95% CI, 13.4% -21.4%) in the elderly showing deficiency of this vitamin. The results showed to be higher than those found by Framingham, who found 12% vitamin B_{12} deficiency in the elderly[21]. Lower vitamin B_{12} deficiency prevalence (4.5%, 5.0% and 6.0%) was also found in population studies conducted by MacFarlane *et al*. (2011) in the Canadian Health Measures Survey, and in those by Andrés *et al*. (2008) and Clarke *et al*. (2003), respectively[28,29,3]. Xavier *et al*. (2010) found high prevalence of vitamin B_{12} deficiency in elderly people (11%). They compared different methods used to detect this deficiency among adult and elderly individuals and found lower vitamin B_{12} levels within the second group[13]. Despite their results, population studies related to aging and vitamin B_{12} deficiency are still conflicting, since the literature lists several definitions about the herein presented deficiency, which may range from 2 to 20%, depending on the definition used in the study[5,11 29]. Despite these issues, the prevalence observed among Viçosa elderly emphasizes the importance of actions to prevent this deficiency within this age group, in order to delay or minimize its consequences.

According to the bivariate analysis, the educational level was an important factor in vitamin B_{12} deficiency. It was observed that the low education level was associated with the higher prevalence of this micronutrient deficiency. Ferreira *et al*. (2011) and Castro-Costa *et al*. (2011) conducted population studies on the elderly's socio-demographic features and associated low education with cognitive impairment and with the presence of functional incapacity in performing the activities of daily living[30,31].

The cognitive impairment showed to be a factor independently associated with vitamin B_{12} deficiency among the studied elderly. Different studies show that low concentrations of this vitamin are related to cognitive decline, due to neurological degeneration and the presence of spinal cord demyelination and damage to the cerebral white matter[33]. Cross-sectional studies conducted by Balk *et al*. (2006) and Vogel *et al*., (2009) showed positive associations between low vitamin B_{12}

Table II
Prevalence and prevalence ratio (PR) of vitamin B_{12} deficiency, according to variables such as health and nutrition status in elderly individuals from Viçosa, Minas Gerais, 2012

Variables	*N*	*Prevalence (%)*	*PR ($IC_{95\%}$)*	*P*
History of depresion				
No	280	17.5	1	
Yes	65	16.9	0.97 (0.72 – 1.86)	0.48
History of cardiovascular disease				
No	303	17.2	1	
Yes	142	19.0	1.54 (0.88 – 2.68)	0.13
Cognitive impairment			1.87 (0.90 – 3.86)	0.09
No	230	13.9	1	
Yes	107	25.2	1.81 (1.09 – 2.34)	**0.02**
Anemia				
No	305	16.7	1	
Yes	40	22.5	1.34 (0.66 – 2.73)	0.41
Number of disease				
0-4	214	19.6	1	
>5	131	13.7	0.70 (0.40 – 1.22)	0.34
Functional capacity				
Adequate	290	17.9	1	
Inadequate	54	14.7	0.83 (0.39 – 1.74)	0.61
Nutritional status				
Normal	33	30.3	1	
Under weight	136	16.9	1.79 (0.85 –3.76)	
Over weight	143	15.4	0.91 (0.51-1.63)	0.75
Food intake				
Without reduction	314	16.9	1	
With reduction	31	22.6	1.34 (0.75 – 2.85)	0.47

levels and lower scores on cognitive tests performed by elderly individulas[31-34,]. This profile is consistent to that observed in the current study. On the other hand, the cohort study conducted by Clarke *et al*. (2007) found no association between cognitive decline (checked by MMSE scores) and decreased vitamin B_{12} levels. These authors found high concentrations of homocysteine, which was linked to slow cognition decrease[32].

The present study found significant association between folic acid levels and vitamin B_{12} deficiency. There is consensus among studies that lower folic acid levels are correlated with the worst cognitive performances, especially regarding memory and psychomotor speed[14]. There are also studies that report significant association between reduced vitamin B_{12} levels and cognitive impairment combined with low folic acid concentrations[8,14]. Thus, the biochemical and health results found in these studies suggest that the reduced levels of folic acid and vitamin B_{12} amplify the negative effect on the elderly cognitive performance. However, it is important to consider that methodological differences between the current study and the available literature (such as sample size, source population and the use of different diagnostic criteria), may limit the comparisons[11,29].

The mechanisms by which the decrease in folic acid is associated with cognitive changes need to be further elucidated. One possible explanation is the evidence that there is an inverse relation between folic acid and homocysteine levels[14,34]. The folate in the biochemical chain is responsible for promoting methionine amino acid regeneration from homocysteine. Thus, patients with low folic acid levels may show elevated homocysteine levels, which, in turn, is neurotoxic and may lead to cognitive and degenerative changes[35].

The current study found no link between vitamin B_{12} deficiency and the occurrence of anemia. The same re-

sult was obtained in the Leiden 85-Plus study conducted by den Elzen *et al*. (2008), who made adjustments using confounding variables without changing the results[33]. This study goes against the literature, which reports information on the isolated measurement of vitamin B_{12}. This data is not sufficient to result in the elderly anemic condition. Studies, such as that conducted by den Elzen *et al*. (2008), also refer to different tests and cutoff points to measure vitamin B_{12} and hemoglobin concentrations using biochemical information, such as homocysteine and folic acid concentrations, to complement the studied associations[33]. Despite the associations, it was observed that anemia did not remain independently associated with vitamin B_{12} deficiency in this study. It may partly due to the small sample size, which was insufficient to demonstrate this relation and also due to the multideficient and multifactorial character of anemia.

Vitamin B_{12} deficiency may also be related to the elderly's diet. Pernicious anemia, which results from vitamin B_{12} deficiency, often affects this population[12]. However, this is a limitation of the current study, since the results were significantly different among the elderly with and without food reduction. It is believed that this analysis may get different results by checking the elderly's type of diet and the occurrence of vitamin supplementation. In addition, the literature states that vitamin B_{12} deficiency can be effectively reversed at low costs, when there is supplementation of this micronutrient in the early onset of symptoms such as fatigue and mental disorders[2]. The OPEN (2011) study suggests that this supplementation should be done in the elderly population even in the absence of established clinical symptoms[30].

The current study showed other limitations that should be pointed out. Homocysteine levels were not investigated. The researches were consistent regarding the relation between high levels of this amino acid and the occurrence of brain injury and psychiatric disorders[35]. Since it is a cross-sectional study, it was not possible to establish the cause and effect relationship between vitamin B_{12} deficiency and cognitive impairment. Despite these aspects, it is believed that the current paper contributes to studies that emphasize some factors that may interfere in the elderly performance during the natural aging process, especially when they are associated with cognitive impairment. It, in turn, may lead to significant disability and to the loss of elderly's quality of life. Therefore, the herein presented results could provide a comprehensive knowledge about the relation between vitamin B_{12} deficiency and its impact on this population.

Conclusion

The mean level of vitamin B_{12} found in the current study was 242.43 pg/mL. It was found 17.4% prevalence of vitamin B_{12} deficiency in the studied group. This result was higher than that found in other investigated population studies. Cognitive impairment was an important vitamin B_{12} deficiency-related variable and it elucidated the association between vitamin B_{12} levels and health condition indicators among the elderly. This fact reinforces the need for actions to ensure the maintenance of an adequate nutritional status among the elderly, under the perspective of a healthy aging.

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