# Association between dietary intake of vitamin A, C, and E as antioxidants and cognitive function in the elderly at a nursing home

Jowy Tani[1], Ivan Riyanto Widjaja[1], Irwin Tedja[1], Irandi Putra Pratomo[1], Ira Siagian[1], Indra Fahri[1], Zarni Amri[2], Saptawati Bardosono[3]


## Abstrak

*Sebagaimana stres oksidatif adalah salah satu mekanisme utama yang menyebabkan perubahan degeneratif, antioksidan dari sumber makanan, seperti vitamin A, C, dan E, mungkin memiliki efek protektif terhadap stres oksidatif dan dapat mencegah atau menghambat gangguan kognitif pada lansia. Penelitian potong lintang ini dirancang untuk menentukan hubungan antara tingkat asupan vitamin A, C, dan E dengan adanya gangguan kognitif pada lansia serta faktor-faktor lain. Subyek meliputi 36 penghuni sebuah panti jompo di Jakarta, Indonesia. Data yang diperoleh meliputi asupan nutrisi harian seminggu sebelum wawancara yang dikonversi dari hasil semi-quantitative food frequency questionnaire (SFFQ), nilai Mini Mental State Examination (MMSE) dan hasil pengukuran antropometri. Penelitian ini menunjukkan sementara jenis kelamin, usia, pendidikan, status gizi, dan nilai asupan makronutrien tidak berhubungan secara bermakna dengan adanya gangguan kognitif, korelasi positif bermakna ditemukan antara pendidikan dan skor MMSE (p=0,036, r=0,351). Asupan vitamin A dan vitamin C ditemukan berhubungan bermakna dengan insidensi gangguan kognitif yang lebih rendah (masing-masing p=0,022 dan p=0,045). Selain itu, vitamin C juga ditemukan berkorelasi positif bermakna dengan nilai MMSE (p=0,031, r=0,359). Meskipun demikian, hubungan antara vitamin E dan adanya gangguan kognitif tidak bermakna (p=0,129). Asupan vitamin A dan C yang lebih tinggi mungkin dapat menghambat atau mencegah gangguan kognitif pada lansia. Asupan vitamin C yang lebih tinggi mungkin berkontribusi terhadap fungsi kognitif yang lebih baik. Penemuan ini mungkin disebabkan oleh efek protektif kedua vitamin antioksidan terhadap proses neurodegenerative yang disebabkan stres oksidatif.* ***(Med J Indones 2007; 16:261-6)***

## Abstract

*As oxidative stress is considered one of the major mechanisms underlying degenerative changes, antioxidants from dietary sources, such as vitamin A, C, and E, may have protective effects against oxidative stress and thus be able to prevent or delay cognitive impairment in the elderly. This cross sectional study was designed to determine the association between dietary intake of vitamin A, C, and E and the presence of cognitive impairment in the elderly, along with other factors. Subjects included 36 residents from a nursing home in Jakarta, Indonesia. The data obtained including daily nutrition intake values one week prior to sampling converted from semi-quantitative food frequency questionnaire (SFFQ) results, Mini Mental State Examination (MMSE) scores, and anthropometrical measurement results. This study showed that while sex, age, education, nutritional status, and macronutrients intake were not significantly associated with presence of cognitive impairment, significant positive correlation existed between education and MMSE score (p=0.036, r=0.351). Higher vitamin A and vitamin C intake were shown to be significantly associated with lower incidence of cognitive impairment (p=0.022 and p=0.045, respectively). Moreover, vitamin C was shown to have significant positive correlation with MMSE score (p=0.031, r=0.359). However, the association between vitamin E and the presence of impairment was not significant (p=0.129). Higher intake of vitamin A and C may delay or prevent cognitive impairment in the elderly. Higher intake of vitamin C may contribute to better cognitive functioning. The findings may be explained by the two antioxidant vitamins' protective effects against neurodegenerative processes cause by oxidative stress.* ***(Med J Indones 2007; 16:261-6)***


***Keywords:*** *antioxidant, vitamin A, vitamin C, vitamin E, cognitive impairment, the elderly*

Aging of the population is a problem affecting both developed countries and developing countries such as Indonesia. As percentage of the elderly in the total population increases, maintenance of cognitive function in the elderly has become a major public health concern.[1] While many causes of cognitive impairment in the elderly have been identified, Alzheimer disease

[1] *Fifth year medical student, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia*
[2] *Departement of Community Medicine, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia*
[3] *Departement of Nutrition, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia*

and vascular dementia are considered responsible for the cognitive impairment in the majority of cases.[2]

The current views on aging process consider that free radical damage is probably responsible for neuro-degenerative process of the brain and its subsequent cognitive impairment.[3] Antioxidants including vitamin A, C, and E, may be able to counter damage caused by oxidative stress and thus prevent or delay cognitive impairment in the elderly. To date, several animal studies have demonstrated that antioxidant nutrients may be able to counter the damage caused by oxidative stress.[4,5] Some observational studies have also shown that intake of certain antioxidants may decrease risk of Alzheimer's disease.[6,7]

Despite the growing evidence of antioxidant's protective effect against specific disease processes, to our knowledge, there is still lacking study investigating association between dietary intake pattern of antioxidant vitamins and general cognitive function in Indonesian elderly population, especially with participants that never took any antioxidants supplements.

We therefore conducted this cross-sectional study to investigate the association between dietary intake pattern of vitamin A, C, and E and cognitive function of an Indonesian elderly population, along with other factors. We consider it is important to identify dietary pattern beneficial for maintenance of cognitive function in the elderly, because the identification of such pattern will provide evidence for healthier dietary pattern in our society and decrease social burden placed by cognitive impairment in the geriatric population.

## METHODS

### Study Population

The cross-sectional study was conducted in March 2007 at a nursing home located at Cibubur, Jakarta, Indonesia. At the time of the study, the total population of the nursing home was 77. All nursing home residents aged at least 60 years old, had formal education more than 4 years, and had not taken supplements containing vitamin A, C, and/or E were eligible for participation in the study. Of 36 nursing home residents eligible for participation, all agreed to participate in the study and signed the written informed consent to be included in the study.

Data obtained from participants included age, sex, education (year of formal education taken), dietary assessment results, cognitive function assessment results, and anthropometric assessment results (included height, weight, upper arm circumference, and triceps skinfold thickness). Nutritional status of the participants was categorized based on body mass index (BMI), upper arm circumference, and triceps skinfold thickness categories.

### Dietary Assessment

Dietary intake data of the participants were obtained through interviews by researchers. A Semi-quantitative Food Frequency Questionnaire[8] (SFFQ) form was completed for each participant. The SFFQ form recorded all food items that had been consumed during the one week duration prior to the interview, the frequency of its consumption, and the portion consumed, based on participants' recall. The SFFQ also recorded whether any ingredient contained in any particular food item was not consumed. Initial food items listed in the SFFQ were based on food menu record that had been provided by the nursing home administrator. Food items consumed not listed in the initial list were added during the interview. Three-dimensional food model was used as an aid in the interview process.

The SFFQ data were then converted to macronutrients, vitamin A, vitamin C, and vitamin E daily intake values using NutriSurvey software (1995, Erhardt J, University of Indonesia, SEAMEO-TROPMED) based on United States Department of Agriculture National Nutrient Database Standard Reference Release-19.

### Cognitive Function Assessment

Cognitive function of the study participants was assessed using Indonesian version of Mini Mental State Examination[9] (MMSE). The MMSE was administered by clinical year medical students who had been trained for its administration.

The presence of cognitive impairment in the study participants were determined by applying a cut-off point to the participants' MMSE score; if a particular participant's MMSE score fall below the cut-off point, the participant was considered to have cognitive impairment. The cut-off point used in our study would based on the study result by Crum[10] (1993). The 25$^{th}$ percentile value of the group in the Crum study, as presented in table 1, which mean values of age and education of our study fitted in, would be use as the cut-off point. This was done to reflect the effects of age and education on MMSE score.

Table 1. Selected 25th percentile scores on MMSE[a] by age and educational level from the Crum[10] study (1993)

| Educational Level | Age | | | | | |
|---|---|---|---|---|---|---|
| | 60-64 | 65-69 | 70-74 | 75-79 | 80-85 | ≥85 |
| 0-4 year | 19 | 19 | 19 | 18 | 16 | 15 |
| 5-8 year | 24 | 24 | 24 | 22 | 22 | 21 |
| 9-12 year | 27 | 27 | 26 | 25 | 23 | 23 |
| ≥ 12 year | 28 | 28 | 27 | 27 | 26 | 25 |

[a] Mini Mental State Examination

**Data Analysis**

SPSS for Windows version 14 (SPSS Inc, Chicago, Illinois) was used for inputting, processing, and analyzing the data used in the study. To determine the possible effects of age and education on the presence of cognitive impairment, we analyzed the associations of age and education with the presence of cognitive impairment using independent samples T-test or Mann Whitney U test, as appropriate. As to determine the associations of categorized data such as nutritional status and sex with the presence of cognitive impairment, Chi-square or Fisher's exact test was used.

The associations between daily intake values of macro-nutrients, vitamin A, vitamin C, and vitamin E and the presence of cognitive impairment were determined using independent samples T-test or Mann Whitney U test, depend on the normality of the data distribution.

As extra analysis, we also determined correlation of MMSE score, the indicator of cognitive functioning, with other baseline characteristics including age, education, and daily nutritional intake values. Either Pearson or Spearmen test was used depend on the normality of the data distribution.

**RESULTS**

The baseline characteristics of the participants are presented in Table 2. The mean for age was 77.58 years and mean for education was 12.33 years. Most participants (72.2%) were female (n=26), and 16 (44.4%) of them had cognitive impairment. Based on BMI categorization, two-third (66.7%) of participant were overweight (n=24).

The association of sex and nutritional status with the presence of cognitive impairment in the participants is presented in Table 3. No significant association of sex (p=0.071), nutritional status based on BMI categorization (p=0.236), upper arm circumference categorization (p=0.593), or triceps skinfold thickness categorization (p=0.257) with the presence of cognitive impairment were found.

Table 2. Baseline characteristics of the sample (n = 36)

| Characteristic | No. (%) |
|---|---|
| Age, mean (SD), y | 77.58 (6.78) |
| Female (%) | 26 (72.2) |
| Education, mean (SD), y | 12.33 (3.07) |
| Weight, mean (SD), kg | 58.17 (11.44) |
| Height, mean (SD), cm | 152.26 (9.71) |
| BMI[a], mean (SD), $kg/m^2$ | 25.11 (4.56) |
| Upper arm circumference, mean (SD), cm | 27.34 (4.17) |
| Triceps skinfold thickness mean (SD), cm | 21.01 (13.26) |
| Intake | |
| Total energy, median (minimum-maximum), cal/d | 1545.35 (1038.90-2569.20) |
| Carbohydrate, median (minimum-maximum), g/d | 178.75 (114.40-384.10) |
| Protein, mean (SD), g/d | 53.20 (13.57) |
| Fat, median (minimum-maximum), g/d | 61.00 (40.01-88.44) |
| Vitamin A, median (minimum-maximum), mg/d | 548.55 (444.20-2466.50) |
| Vitamin C, median (minimum-maximum), mg/d | 101.15 (57.80-292.60) |
| Vitamin E, mean (SD), mg/d | 8.44(1.79) |
| Cognitive impairment present (%) | 16 (44.4) |
| MMSE[b] score, mean (SD) | 26.42 (2.73) |

[a]Body Mass Index [b]Mini Mental State Examination

Table 3. Association of sex and nutritional status with presence of cognitive impairment

| | | Cognitive Impairment | | p value |
|---|---|---|---|---|
| | | Present (n) | Not Present (n) | |
| Sex | Male | 2 | 8 | 0.071 |
| | Female | 14 | 12 | |
| BMI[a] category | Normal | 7 | 5 | 0.236 |
| | Overweight | 9 | 15 | |
| Upper arm circumference category | Underweight | 1 | 0 | 0.593 |
| | Normal | 6 | 7 | |
| | Overweight | 9 | 13 | |
| Triceps skinfold thickness category | Underweight | 11 | 10 | 0.257 |
| | Normal | 5 | 10 | |

[a] Body Mass Index

Association between age, education, and daily nutritional intake values with presence of cognitive impairment are presented in table 4. As presented, no significant association of age (p=0.304), education (p=0.083), and daily intake values of total energy (p=0.126), carbohydrate (p=0.102), protein (p=0.308), and fat (p=0.551) with the presence of cognitive impairment were found.

Table 4. Association of age, education, and daily nutritional intake values with presence of cognitive impairment

| | Cognitive Impairment | | p value |
|---|---|---|---|
| | Present | Not Present | |
| | Mean | Mean | |
| Age (y) | 78.88 | 76.55 | 0.304 |
| Education (y) | 11.31 | 13.15 | 0.083 |
| Total energy (cal/d) | 1411.54 | 1573.84 | 0.126 |
| Carbohydrate (g/d) | 174.74 | 201.89 | 0.102 |
| Protein (g/d) | 49.8 | 55.93 | 0.308 |
| Fat (g/d) | 59.34 | 62.12 | 0.551 |
| Vitamin A (mg/d) | 544.86 | 684.88 | 0.022 |
| Vitamin C (mg/d) | 96.74 | 126.48 | 0.045 |
| Vitamin E (mg/d) | 7.94 | 8.83 | 0.129 |

For association between intake of antioxidant vitamin and the presence of cognitive impairment, daily intake value of vitamin A and vitamin C were found to be significantly associated with the presence of cognitive impairment (p=0.022 and p=0.045, respectively). Higher intake of these antioxidant vitamins was associated with lower incidence of cognitive impairment in the participants. However, daily intake value of vitamin E was not significantly associated with presence of impairment.

Interestingly, as presented in table 5, our additional analysis result showed that significant weak positive correlation existed between daily intake value of vitamin C and MMSE score of the participants. Significant weak positive correlation also existed between formal education and MMSE score.

Table 5. Correlation of age, education, and daily nutritional intake values with MMSE[a] Score

| | r value | p value |
|---|---|---|
| Age (y) | -0.274 | 0.106 |
| Education (y) | 0.351 | 0.036 |
| Total energy (cal/d) | 0.106 | 0.539 |
| Carbohydrate (g/d) | 0.179 | 0.297 |
| Protein (g/d) | 0.130 | 0.451 |
| Fat (g/d) | -0.124 | 0.471 |
| Vitamin A (mg/d) | 0.246 | 0.148 |
| Vitamin C (mg/d) | 0.359 | 0.031 |
| Vitamin E (mg/d) | 0.058 | 0.735 |

[a] Mini Mental State Examination

## DISCUSSION

Our study showed that higher intake of vitamin A and vitamin C were associated with lower incidence of cognitive impairment in the participants, furthermore, higher vitamin C intake was significantly correlated with higher MMSE score, thus correlated with better cognitive functioning. To our knowledge, no study investigating association between dietary intake patterns of antioxidant vitamins and cognitive functioning, especially with participants' that never took antioxidant vitamin supplements, had been done in Indonesia before. The reason behind the exclusion of participants that had taken supplements contained antioxidant vitamins were that supplements intake was often short-term and may not reflected a person's long-term dietary pattern.

The strengths of our study are its assessment tools and the nursing home setting. MMSE is a relatively sensitive and specific tools that can be used to assess a person's cognitive functioning in short amount of time and its validity have been proven in many other studies. Furthermore, MMSE results are available as continuous numerical data, enabled us to quantitatively describe cognitive functioning of our participants. The other tool used in this study, SFFQ is a tool designed to provide dietary patterns of participants, and it was expected that in this study it would be able to provide reasonably accurate picture of the participants' long-term dietary pattern. By supplementing it with food list based on food provided to the participants one week prior to interview by the nursing home, it was expected to be able to decrease recall bias of the participants who may have diminished memory capacity.

The nursing home setting in this study enabled access to elderly who may otherwise be inaccessible. Its food providing policy that allowed the participant to freely decide the amount and type of food provided they wish to consume, are expected to reduce the possibility that SFFQ may not reflect the long-term dietary habit of the participants because of strict food providing policy. The particular nursing home also provide us with participants with relatively high education level (averaging 12.33 years of formal education), increasing the reliability of MMSE.

However, several limitation of this study must also be considered. First, SFFQ that was used in this study, although reasonably valid, is not the ideal dietary assessment tool. Comprehensive diet history would be able to obtain more accurate dietary information. Periodic monitoring of serum antioxidant vitamin levels of participants would achieve even better result.

Second, the SFFQ recalling duration of only one week, which originally designed to reduce recall bias, as participants with diminished memory capacity may provide unreliable information if asked to recall memory further than one week, may decrease the accuracy of long-term dietary pattern that was expected to be obtained. If the bias caused by possible memory unreliability could somehow be overcome, recall duration of more than one week may provided a more accurate picture of long-term dietary pattern.

Finally, the study haven't been able to exclude all possible confounding factors, such as social activities, presence of organic illnesses, presence of pseudo-dementia, alcohol intake, smoking habit, and many other factors that may had influenced participants' cognitive function. Adjustments with these factors would increase the reliability of the study.

The fact that no significant association of age, sex, education, nutritional status, and macronutrients intake with the presence cognitive impairment were found suggests that these variables may play limited role in the etiology of cognitive impairment. Nonexistence of significant association between vitamin E intake and the presence of cognitive impairment suggests that the vitamin's protective effect against cognitive impairment may be less significant compared to that of vitamin A or vitamin C.

The findings that higher vitamin A intake and vitamin C intake may prevent or delay cognitive impairments in the elderly, and higher vitamin C intake may contributes to better cognitive function, may be explained by antioxidant vitamins' effect to counter oxidative stress and thus prevents neurodegenerative processes in the elderly cause by free radical damage.

Several other studies had demonstrated certain antioxidant's effect in decreasing the risk of Alzheimer's disease. The protective effects of vitamin A and vitamin C against cognitive impairment may be explained by their protective effects against Alzheimer's disease. However, it is also possible that vitamin A and vitamin C also provided protection via other mechanisms. As our study did not assess the possible etiology of cognitive impairment in its participant, it would require more throughout studies, both epidemiologic and biochemical, to determine the exact mechanism(s) of the protective effect.

## CONCLUSION

In conclusion, the present result suggests that dietary pattern with higher intake of vitamin A and vitamin C may be associated with lower incidence of cognitive impairment in the elderly, and that higher intake of vitamin C may contribute to better cognitive function in the elderly.

### Acknowledgement

The authors express gratitude to Department of Community Medicine and Department of Nutrition FMUI for facilitating the study. We are also grateful to DR. Dr. Martina Wiwie SN, SpKJ(K) and Dr. Petrin R, SpKJ from Division of Geriatric Psychiatry, Department of Psychiatry FMUI for providing counsels concerning administration of Indonesian version of MMSE.

## REFERENCES

1. Mathers C, Stein C, Ma Fat D, Rao C, Inoue M, Tomijima N, et al. Global Burden of Disease 2000: version 2 methods and results. Geneva: World Health Organization; 2000. GPE Discussion Paper No. 50. 1001.
2. Sadock BJ, Sadock VA, editors. Kaplan & Sadock's Synopsis of Psychiatry. 9th edition. Philadelphia: Lippincott Williams & Wilkins; 2002.
3. Polidori MC. Antioxidant Micronutrients in the Prevention of Age-related Diseases. J Postgrad Med 2003;49:229-35.
4. Pellmar TC, Hollinden GE, Sarvey JM. Free radicals accelerate the decay of long-term potentiation in field CA1 of Guinea-pig hippocampus. Neuroscience 1991; 44:353-9.
5. Sack CA, Socci DJ, Crandall BM, Arendash GW. Antioxidant treatment with phenyl-alpha-tert-butyl nitrone (PBN) improves the cognitive performance and survival of aging rats. Neurosci Lett 1996;205:181-4.

6. Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Aggarwal N, et al. Dietary intake of antioxidant nutrients and the risk of incident Alzheimer disease in a biracial community study. JAMA 2002;287:3230-7.
7. Engelhart MJ, Geerlings MI, Ruitenberg A, van Swieten JC, Hofman A, Witteman JC, et al. Dietary intake of antioxidants and risk of Alzheimer disease. JAMA 2002; 287:3223-9.
8. Mahan LK, Escott-Stump S, editors. Krause's food, nutrition, and diet therapy. 11th ed. Philadelphia: Saunders; 2000.
9. Folstein MF, et al. Mini-mental state: A Practical Method for Grading the Cognitive State of Patients for the Clinician. J Psychiatr Res 1975;12:189.
10. Crum RM, Anthony JC, Bassett SS and Folstein MF. Population-based norms for the mini-mental state examination by age and educational level, JAMA 1993;18:2386-91.