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Relationship between age, education and blood zinc levels, with cognitive function in menopausal women

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ABSTRACT

Background: The increase in life expectancy results in an increase in the number of elderly, especially menopausal women. Aging can have an impact on the decline of cognitive function. The decline in cognitive function and being influenced by age can also be affected by education and blood zinc levels. However, various research results still need to be more conclusive regarding how much influence age, education, and blood zinc levels have on cognitive function.

Objectives: To determine the relationship between age, education, and blood zinc levels with the cognitive function of elderly menopausal women.

Methods: This research is analytical research with a cross-sectional design. The subjects of the study were menopausal women aged 60 years and over who was able to walk without help, as well as being able to read and write. Study subjects who suffered from a stroke, heart, kidney, mental function disorders, and used drugs for mental disorders, were not included in this study. Research subjects who met the eligibility criteria were carried out with physical examinations (age, height, weight, blood pressure) and laboratory examinations (blood sugar ad random and blood zinc levels), as well as undergoing cognitive function tests using MoCA-INA.

Results: A total of 65 study subjects met the eligibility criteria. Multivariate statistical analysis showed that there was a correlation between the cognitive function of the attention domain with age ($r=0.278$, $p=0.030$), the cognitive function of the visuospatial domain with education ($r=0.528$, $p=<0.001$), the cognitive function of the language domain with blood zinc levels ($r=-0.279$, $p=0.019$) and the cognitive function of the orientation domain with education ($r=0.319$, $p=0.012$).

Conclusions: The results of this study show that there is a meaningful relationship between age, education, and blood zinc levels, with cognitive function in elderly menopausal women.

Latar Belakang: *Peningkatan harapan hidup mengakibatkan peningkatan jumlah lansia terutama perempuan menopause. Penuaan dapat berdampak pada penurunan fungsi kognitif. Penurunan fungsi kognitif selain dipengaruhi oleh usia juga dapat dipengaruhi oleh pendidikan dan kadar zinc darah. Namun demikian, berbagai hasil penelitian masih belum konklusif terkait seberapa besar pengaruh usia, pendidikan dan kadar zinc darah terhadap fungsi kognitif.*

Tujuan: *: Untuk mengetahui hubungan antara usia, pendidikan dan kadar zinc darah dengan fungsi kognitif perempuan lansia menopause.*

Metode: *Penelitian ini merupakan penelitian analitik dengan desain potong lintang. Subjek penelitian adalah perempuan menopause berusia 60 tahun ke atas yang mampu berjalan tanpa bantuan, serta dapat membaca dan menulis. Subjek penelitian yang menderita penyakit stroke, jantung, ginjal, gangguan fungsi mental,* *dan menggunakan obat-obat untuk gangguan mental, tidak diikutkan dalam penelitian ini. Subjek penelitian yang memenuhi kriteria eligibilitas dilakukan pemeriksaan fisik (usia, tinggi badan, berat badan, tekanan darah) dan pemeriksaan laboratorium (gula darah sewaktu dan kadar zinc darah), serta menjalani pemeriksaan test fungsi kognitif menggunakan MoCA-INA.*

Hasil: *Sejumlah 65 subjek penelitian memenuhi kriteria eligibilitas. Analisis statistik multivariat menunjukkan terdapat korelasi antara fungsi kognitif domain atensi dengan usia (r=0,278, p=0,030), fungsi kognitif domain visuospasial dengan pendidkan (r=0,528, p=<0,001), fungsi kognitif domain bahasa dengan kadar zinc darah (r=-0,279, p=0,019), serta fungsi kognitif domain orientasi dengan pendidikan (r=0,319, p=0,012).*

Kesimpulan: *Hasil penelitian ini menunjukkan terdapat hubungan yang bermakna antara usia, pendidikan, dan kadar zinc darah, dengan fungsi kognitif pada perempuan lansia menopause.*

INTRODUCTION

The increasing life expectancy has an impact on the rising elderly population. Wan He et al. estimates that the percentage increase in the number of elderly people in Indonesia in the 2010-2030 period is 107.1%.[1] Increased life expectancy increases the risk of degenerative diseases such as dementia. The incidence and prevalence of dementia rise dramatically with age. One of the main symptoms of dementia is a decline in cognitive function.[2,3]

The proportion of the female elderly population in Indonesia is relatively high. The Central Statistics Agency projects the total female population aged 50 years and over in Indonesia in 2010-2035 to be 20.9 million. In 2020 it was estimated that the number of women living in menopause age in Indonesia was around 30.3 million people, and by 2025 it is estimated that there will be 60 million menopausal women.[4]

Menopause is an event in which there is a permanent cessation of menstruation due to the loss of ovarian activity. The term menopause refers to when menstruation has stopped for 12 consecutive months.[5] Menopause occurs mainly at the age of 47-55, with an average age of 51. Although menopause is a natural biological process, it will likely influence health greatly. Menstrual periods increase the risk of osteoporosis, cardiovascular disease, and increased degenerative cognitive disorders.[5]

A person aged 50 years and older needs a higher intake of micronutrients, such as essential vitamins and minerals. Trace elements are crucial co-factors for enzymes that involve the interaction of various enzymes necessary for the transmission of nerve impulses and detoxification. Changes in trace element levels can result in increased oxidative stress and decreased cognitive function.[6] Zinc is an essential trace element important in body fluids and tissues, which functions as a catalytic, structural, and regulatory function in the body.[7] Several studies have shown decreased zinc levels in postmenopausal women due to low intake or decreased food absorption.[8]

The association between age and deterioration of cognitive function in the elderly often shows a significant decrease in quality of life. Cognitive function abilities, including memory, attention/attention, language, and space/place orientation abilities, regress with age. Cognitive function in the elderly is influenced by the education and intellectual experiences built during his lifetime. Risk factors for decreased cognitive function include education, lifestyle, physical activity, social activity, nutrition such as zinc deficiency, as well as some medical conditions such as hypertension and diabetes mellitus.[9-11]

The relationship between age, education, and zinc with cognitive function in the elderly is still not conclusive. Research by Markiewicz-Zukowska et al. showed a positive correlation between zinc levels and age. The decrease in zinc levels will increase with age.[12] Conversely, meaningless results were found in Kheirkhah et al. research.[13] Research by Martin et al. shows a strong correlation between education and cognitive function.[14] Several studies state a relationship between zinc levels and cognitive function. A decrease in zinc levels will cause impairment in cognitive function.[13] Opposite results were found in a study conducted by Rembach et al.[15] Based on the various outcomes of these inconclusive studies, researchers want to know the relationship between age, education, and blood zinc levels with cognitive function.

METHODS

This research is an analytical study with a cross-sectional design conducted in Mampang Prapatan Village, South Jakarta. The subjects used in this study were residents living in the

Mampang area, menopausal women aged 60 years and over, randomly selected from 12 *Rukun Warga* (RW; hamlet). The inclusion criteria are women aged 50 years and over, who can walk without help, can read and write, and are willing to participate in research (sign informed consent) after receiving an explanation of this research. The exclusion criteria for this study are a history of suffering from stroke, heart, kidney, mental disorders, or taking medicines for depressive disorders or mental disorders.

The subjects of the study from 12 RW were selected from 6-7 people on each RW. The study subjects were given questionnaires about age, education, diseases that have been and are currently suffering, and drugs being used. Sixty-one people met the eligibility criteria. Sample size calculation using assumptions α=0.05, correlation coefficient 0.29, and 90% research power. This research has been approved by the Research Ethics Committee of the Faculty of Medicine Universitas Muhammadiyah Prof. Dr. HAMKA, Jakarta, Indonesia, with document number KEPKK/FK/006/07/2021.

Anthropometric measurements

Anthropometric measurements include height, weight, and body mass index (BMI) measurements. Height measurement using portable microtones in cm. Height measurement with an accuracy of 0.1 cm. Body weight was measured using sage portables scales in kg with an accuracy of 0.1 kg. Body mass index is calculated based on body weight (kg)/height (m^2) and is classified by categorization as follows; normal (< 23.0 kg/m^2), overweight (23-25 kg/m2), and obesity according to the criteria set for Asians (> 25 kg/m^2).

Laboratory examination

Laboratory examination includes blood sugar ad random, with a guide to normal values <140 mg/dL, and blood zinc examination, with a guide to normal values of 60-130μg/L. A total of 10 ml of blood samples for biochemical investigation are taken with vena puncture from the cubitus vein of each study subject. The blood sample was centrifuged at a speed of 3000 rpm for 15 minutes. The serum is separated and placed in an automatic analyzer.

Cognitive function examination using the Indonesian version of Montreal Cognitive Assessment (MoCA-INA)

The Indonesian version of the Montreal Cognitive Assessment (MoCA-INA) tests to evaluate cognitive function, including visuospatial ability/executive function, naming, memory, attention, language, abstraction, long-term memory, and orientation. The total highest score is 30 points, and a score of 26 and above is considered normal. The highest score for the visuospatial/executive function domain is 5, the naming domain is 3, the attention domain is 6, the language domain is 23, the abstraction domain is 2, the long-term memory domain is 5, and the orientation domain is 6.

Statistical analysis

First, a data normality test was performed on all variables using the Kolmogorov-Smirnov test. Basic characteristic data (age, blood pressure, weight, height, Body Mass Index, zinc levels, and MoCA-INA test) are normally distributed and displayed using mean and standard deviation. The assessment of the relationship between age, education, and zinc levels with cognitive function is based on the Pearson correlation test.

RESULTS

The average age is 58.64 ± 6.30 years, the average zinc level is 74.62 ± 10.62 μg/L, the average systolic blood pressure is 137.79 ± 24.32 mmHg, the average diastolic blood pressure is 80.20 ± 10.45 mmHg, the average BMI is 26.38 ± 4.12 kg/m2, and the average MoCA-INA is 18.57 ± 3.45. The average MoCA-INA score check result for the visuospatial domain is 2.70 ± 1.10, the naming domain is 2.69 ± 0.64, the attention domain is 3.93 ± 1.50, the language domain is 1.63 ± 0.83, the abstraction domain is 0.59 ± 0.71, the delayed memory domain is 0.39 ± 1.04, and the orientation domain is 5.59 ± 0.69 (Table 1).

Bivariate analysis between MoCA-INA and independent variables obtained meaningful results between cognitive function (MoCA-INA) and education (Table 2). Bivariate analysis between each cognitive domain with each independent variable showed there was a significant relationship between visuospatial and education (r =0.058, p<0.001), the language with zinc (r = -0.299, p=0.019), abstraction with diastolic blood pressure (r=-272, p=0.034), and between orientation with education (r=-0.139, p=0.012, Table 3).

DISCUSSION

Impaired cognitive function is essential to the diagnostic criteria for neurodegenerative disorders. Neurodegenerative is a common disease in the elderly.[16] The components of cognitive function consist of visuospatial, executive function, memory, attention, concentration, and language.

Education promotes the speed of cognitive function decline based on the theory of cognitive aging and the concepts of cognitive reserve and brain maintenance. Educational attainment is

Table 1. Basic characteristics of the subject of study

No.	Basic characteristics	Mean ± SD
1	Age (years)	58.84 ± 6.30
2	Zinc (mcg/L)	74.62 ± 10.62
3	Systolic blood pressure (SBP, mmHg)	137.79 ± 24.32
4	Diastolic blood pressure (DBP, mmHg)	80.20 ± 10.45
5	Education	3.69 ± 1.07
6	Age (years)	58.84 ± 6.30
7	Body mass index (BMI, kg/m^2)	26.38 ± 4.12
8	MoCA-INA	18.57 ± 3.45
	Visospatial	2.70 ± 1.10
	Naming	2.69 ± 0.64
	Attention	3.93 ± 1.50
	Language	1.63 ± 0.83
	Abstraction	0.59 ± 0.71
	Delayed memory	0.39 ± 1.02
	Orientation	5.59 ± 0.69

Table 2. Relationship between MoCA-INA and independent variables

	Pearson correlation	Sig (2-tailled)	95% Confidence interval	
			Lower	Upper
Age vs MoCA-INA	.111	.395	-.145	.353
Education vs MoCA-INA	.378	.003 *	.139	.575
Zinc vs MoCA-INA	-.056	.667	-.304	.198
SBP vs MoCA-INA	-.019	.882	-.270	.234
DBP vs MoCA-INA	-.125	.337	-.365	.131
BMI vs MoCA-INA	.222	.085	-.032	.449

Table 3. Relationship between each cognitive domain with each independent variable

	Pearson correlation	Sig (2-tailled)	95% Confidence interval	
			Lower	Upper
Visuospatial vs Education	.058	<.001	.318	.688
Attention vs Age	.278	.030	.028	.495
Language vs Zinc	-.299	.019	-.512	-.051
Abstraction vs DBP	-.272	.034	-.490	-.021
Orientation vs Education	.058	<.001	.318	.688

always related to cognitive function and the risk of dementia in late adulthood. A positive correlation between education and cognitive change may indicate that higher educational attainment is associated with a more significant improvement in cognitive performance, such as numeracy and vocabulary, over time.[14] Research from Opdebeeck et al. states that higher education is associated with higher cognitive abilities.[17] Cadar et al. and Lipnicki et al. also found the same results.[18,19] However, the opposite result was found in the research of Tucker-Drob et al.[20] Our research shows there is a meaningful relationship between education and cognitive function.

Zinc is an essential trace element for human health. Zinc is vital in growth, development, and cognitive function.[3,4] Zinc is found in body cells and large quantities in the cerebral cortex. The cerebral cortex plays a significant role in memory, attention, perception, cognition, awareness, mind, language, and consciousness.

A diet that is low in zinc and a decrease in homeostatic mechanisms will increase the incidence of zinc deficiency in the elderly. This may increase the risk of dementia and diabetes mellitus.[21] Zinc can also reduce oxidative stress associated with excitotoxicity through a variety of mechanisms including inhibition of the NMDAR and competition with copper for oxidation-reduction (redox) active binding sites on Amyloid beta (Ab).[21] Decreased zinc levels can cause synaptic dysfunction and facilitate calcium influx through NMDAR to activate Nicotinamide adenine dinucleotide phosphat (NADPH)-oxidase and nitric oxide synthase. The activation of these enzymes, along with mitochondrial dysfunction, will trigger oxidative stress. This will then result in impaired mitochondrial stability, the accumulation of phosphorylated tau, and the formation of neurofibrillary tangles (NFTs).[22]

Several research results show that zinc administration can reduce inflammatory markers and oxidative stress in the elderly. These results were found in research from Vural et al. and Markiewicz-Zukowska et al.[23,24] Different results were found by Rembach et al., researchers who stated that there was no connection between zinc and cognitive function.[15,25,26] Our results show that there is a relationship between blood zinc levels and cognitive function in the language domain.

CONCLUSION

The results showed a meaningful relationship between age and the cognitive function of the attention domain, education with the cognitive function of the orientation domain, and zinc with the cognitive function of the language domain. Although there are some limitations in this study, primarily related to the number of research subjects involved, the results of this study are expected to be helpful in anticipating cognitive function decline in menopausal older women by increasing education and sufficient zinc intake.

CONFLICT OF INTEREST

All authors stated there was no conflict of interest in the study. Data supporting the results of this study are available at the request of the relevant authors. Data is not publicly available due to privacy or ethical restrictions. Informed consent was obtained from all participants who participated in the study.

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