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Nutritional Status, Physical Activity, Oxidative Stress, and Cognitive Function in Pre Elderly and Elderly

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ABSTRACT

This study aimed to analyse the relation of nutritional status, physical activity or oxidative stress with cognitive function of pre-elderly and elderly. A comparative cross-sectional study was conducted on 40 pre-elderly and 35 elderly subjects who were admitted to the Integrated Development Post Program (*Posbindu*) between September 2014 and January 2015. Anthropometric measurements (weight and height), physical activity, and biochemical data (oxidized low-density lipoprotein[Ox-LDL] and serum malondialdehyd [MDA]) were obtained. Nutritional status was assessed through body mass index (BMI), while the cognitive function was measured by Rey Osterrieth Complex Figure (ROCF) and Digit Span Backward. The data were analysed using an independent t-test and Spearman's test with a confidence level of 95%. The study showed that the prevalence of malnutrition among the pre-elderly and elderly were 60.0% and 80.0%, respectively. Concerning physical activity, those who belonged to inactive-sedentary activity based on physical activity level (PAL) ratio were 55.0% and 45.7%, respectively. There were no significant differences in Ox-LDL, MDA levels and cognitive function ($p>0.05$). Significant negative correlations existed between Ox-LDL and immediate visual memory function ($r=-0.289$; $p<0.05$), as well as between Ox-LDL and delayed visual memory function ($r=-0.288$; $p<0.05$). The conclusion that visual memory function was only correlated with Ox-LDL.

Keywords: cognitive function, elderly, oxidized low-density lipoprotein, pre-elderly

INTRODUCTION

Aging is associated with biochemical changes and increased production of free radicals due to mitochondrial dysfunction (Sanz *et al.* 2006). The damage to DNA, proteins, and lipids from free radicals increases with age, which accumulates and contributes to dementia (Semba *et al*. 2007). These changes will lead to increased oxidative stress associated with various pathological conditions and disease progression in the elderly. One of the oxidative stress markers is the level of lipid peroxidation or oxidized LDL (Ox-LDL) and its derivative product, i.e., malondialdehyde (MDA) (Parthasarathy *et al.* 2010).

Oxidative stress is a common characteristic of aging and neurodegenerative disorders including Alzheimer's disease (Arimon *et al.* 2015). Alzheimer's disease (AD) is an age-related neurodegenerative disease clinically characterised by progressive memory loss and irreversible cognitive decline. Aging is related to the decrease in physical activity performance. Physical activity is known to be one of the antidotes to adverse changes associated with advancing age. Elderlies who are categorized as physically active have a better antioxidant capacity, which may be due to the suppression of oxidative stress (Solberg *et al*. 2013). Inactive elderlies have a higher risk of degenerative diseases (Coelho *et al*. 2014).

The nutritional status shows a health performance that can be represented by body mass index (BMI). Early detection of nutritional status in the elderly is an essential effort in monitoring health. Several studies have found an association between nutritional status and functional disorders. According to Orsitto (2015), malnutrition in the elderly is a global problem. Undernourishment is associated with some aging syndromes, including cognitive decline. Therefore, a study on the relationship between nutritional status, physical activity or oxidative stress, and the de-

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creased in cognitive functions in pre-elderly and elderly is of capital importance.

This study aimed to analyse the relationship between nutritional status, physical activity or oxidative stress markers (e.g., oxidized low-density lipoprotein/Ox-LDL and MDA) and the cognitive function in pre-elderly and elderly.

METHODS

Design, location, and time

This comparative cross-sectional study was conducted in September 2014 to January 2015 at the Health Service Post for the Elderly (*Posbindu*) in Depok City. Blood Ox-LDL and MDA analyses were carried out in the Laboratory of Physiology and Biochemistry, Faculty of Medicine, University of Brawijaya. A professional psychologist performed cognitive function assessment at the office of the urban village of Limo in Depok, West Java, Indonesia.

Sampling

The subjects in this study were pre-elderly and elderly with inclusion criteria as follows, 1) men or women aged 45-74 years, 2) had dyslipidemia, 3) were able to perform daily activities independently, and 4) no history of chronic diseases. The sample size was calculated based on the prevalence of metabolic syndrome among the elderly (14.9%) (Kamso 2007) and deviation of the sample on population (10%), and the minimum subject was 49 people. There were 116 elderly who volunteered to be the subjects of the research, but only 75 of them met the inclusion criteria. Ethical clearance for this study was apu proved by the Health Research Ethics Committee of the Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo General Hospital, Jakarta. It was obtained in the form of Ethical Approval No. 94/UN2.F1/ETIK/2015 and written informed consent was obtained from each.

Data collection

The data collected in this study were primary data, i.e., subjects characteristics and blood biochemical parameters. Subject characteristics included biographical data (age, sex, physical activity) obtained by interview using questionnaires, and anthropometric data which comprised weight and height. Height was measured using microtome with precision set at 0.1 cm, while weight was measured using a digital weighing scale with an accuracy of 0.1 kg.

Meanwhile, blood biochemical data included oxidative stress markers, i.e., Ox-LDL and MDA. Blood sampling was conducted simuls taneously in the morning (at 7-8 a.m.), before activities and after fasting for at least 10 hours. The blood samples were analysed for Ox-LDL by using ELISA reader and MDA levels by using the spectrophotometric method.

Cognitive function assessment was performed using Backward Digit Span and Rey-Osterrieth Complex Figure (ROCF) tests. Attention, concentration and short-term verbal memory performance were assessed by digit span test, which was routinely applied in psychological studies as a stand-alone test or part of a series of psychological assessment (Jones & Macken 2015). ROCF is extensively used in the neuropsychological assessment, particularly when assessing the perceptual organization, visuospatial constructional ability and visual memory (Ogino *et al*. 2009). Statistical analyses performed were independent t-test and Spearman's test with a confidence level of 95%.

RESULTS AND DISCUSSION

Characteristics of the subjects

There were two age groups of subjects composed of men and women, i.e., 40 pre-elderly (45-59 years) and 35 elderly (60-74 years) people. The mean age of the pre-elderly group was 53.73±4.01 years, while that of the elderly group was 64.97±4.75 years. The nutritional status of subjects is important to note because it provides preliminary information related to a person's health. Table 1 showed that most of the subjects in both groups were categorized as undernourished based on their BMI (60.0% of the pre-elderly and 80.0% of the elderly). The mean physical activity level (PAL) of pre-elderly subjects was classified as sedentary (1.64±0.19), while the elderly subjects were at a moderate level (1.70±0.22).

The increase in age and prevalence of degenerative diseases are some of the causal factors of cognitive decline, which will lead to Alzheimers Disease (AD) and other types of dementia. Cognitive decline reduces the daily social activities, meaning that the elderly become unproductive and the public health problems may arise; which in turn bring economic burden to the family, society, and government regarding health care.

Several studies have found the relation between nutritional status and functional disorders and dependency on others. According to Orsitto (2015), malnutrition in the elderly is the world's major problem, including in industrialised coun-

Table 1. Distribution of subjects by nutritional status and physical activity

Variables	Pre-elderly (n=40)		Elderly (n=35)	
	n	%	n	%
BMI (kg/m^2)[a]				
Underweight (<18.5)	1	2.5	2	5.7
Normal (18.5-25.0)	16	40.0	7	20.0
Overweight (25.1-27.0)	10	25.0	12	34.3
Obese (>27.0)	13	32.5	14	40.0
Physical activity				
Inactive (PAL ≤1.4)	4	10.0	2	5.7
Sedentary (1.5≤ PAL ≤1.6)	22	55.0	16	45.7
Moderate (1.7≤ PAL ≤1.9)	11	27.5	12	34.3
Active (PAL ≥2.0)	3	7.5	5	14.3

[a]Depkes RI (2010), [b]FAO (2001), [c]45-59 years old, [d]60-74 years old, PAL=Physical activity level, BMI=Body mass index

tries. Poor nutritional status is associated with some aging syndromes, including cognitive decline. Otherwise, Dainy *et al*. (2016) reported that high BMI in elderly was correlated with high triglyceride serum level. Kamso (2007) also stated that overweight elderly has four times higher risk of metabolic syndrome, which is one of the risk factors for the AD.

Early detection of malnutrition in the elderly is an important strategy to improve health. The percentage of subjects who were at risk of malnutrition in the present study was in line with the results of studies by Guigoz (2006) and Han, Li & Zheng (2009), stating that 24% to 36% of the elderly were at risk of being malnourished. According to Chapman (2006), if malnutrition occurred, the elderly would experience decreased functional status, muscle strength and mass, as well as bone density; dysfunction of the immune system; anemia; slow wound healing; and increased morbidity and mortality. Orsitto (2015) suggested that nutritional intervention and assistance program should be given to the elderly who were at risk of malnutrition.

Table 1 also showed that most of the subjects in both groups had inactive-sedentary lifestyles (65.0% of the pre-elderly and 50.7% of the elderly). The nutritional status and physical activities in both groups were relatively similar. The previous study indicated that physical activity was one of the required factors for healthy aging (Buchner 2009). Being physically active is associated with improved blood pressure, lipid profiles, lipoprotein levels, and inflammatory markers (Lohne-Seiler *et al*. 2014). Conversely, physical inactivity is associated with the risk of various diseases such as cardiovascular disease, type 2 diabetes, obesity, and AD (Coelho *et al*. 2014). According to Chau *et al*. (2013), a sedentary lifestyle would be detrimental to one's health and considered as the initiator of type 2 diabetes, cardiovascular disease, and death. Inactive and sedentary subjects should improve or increase their daily physical activities, and reduce the amount of time spent sitting or television viewing in order to maintain their health. In this study, most of the subjects were classified as sedentary, which showed that the subject tended to be at risk of having the AD. The pre-elderly group had the same level of physical activity as the elderly, which was considered dangerous because the pre-elderly should be more active to prevent them from the AD (later on).

Oxidative stress markers and cognitive functions of subjects

Oxidative stress is an imbalance between free-radical production and antioxidant defenses. MDA is one of the substances produced as the end product of lipid peroxidation in the body due to free radical reactions. Table 2 showed the mean result of oxidative stress markers (Ox-LDL and MDA levels) and cognitive function. There were no significant differences between pre-elderly and elderly ($p>0.05$) groups, which may indicate that the health condition of the pre-elderly group is almost similar to that of the elderly. In other words, there was early aging. This condition should be a concern in order to meet the success of windows opportunity in 2030 to achieve a healthy and productive pre-elderly.

Our findings showed that Ox-LDL and MDA levels in the elderly subjects were higher than those in pre-elderly subjects. These results

Table 2. Mean results of oxidative stress markers and cognitive functions

Variables	Pre-elderly[1]	Elderly[2]	p[3]
Oxidative stress			
Ox-LDL(pmol/ml)	1.55±0.50	1.77±0.49	0.058
MDA (nmol/ml)	3.38±0.58	3.63±0.77	0.110
Cognitive functions			
Attention	2.98±1.23	2.74±1.32	0.432
Immediate visual memory	10.68±7.65	8.34±6.68	0.168
Delayed visual memory	11.05±7.40	7.94±5.99	0.052

[1]45-59 years old, [2]60-74 years old, [3]Independent sample test

were in line with previous research demonstrating that Ox-LDL levels continued to increase with advancing age (Purwantyastuti *et al.* 2005). The increased Ox-LDL level is linear with MDA levels because MDA is the product of LDL peroxidation (Parthasarathy *et al*. 2010). Subjects' MDA levels in this study were higher than those of the previous study, indicating that the mean MDA level in the elderly was 3.18±0.30 nmol/ml (Winarsi *et al*. 2013). High levels of MDA may lead to Alzheimers Disease (Schrag *et al*. 2013).

The pre-elderly group had higher cognitive test scores (attention and visual memory function) than the elderly group as presented in Table 3. The standard minimum score for attention test was four, while the minimum score for visual memory test was nine. The attention scores in both groups were below the normal standard. Meanwhile, the visual memory scores in the pre-elderly group were normal, while the ones in the elderly group were below the normal standard. The statistical results of the cognitive function test showed that there were no significant differences among the groups.

The results of cognitive function and oxidative stress tests showed that the pre-elderly group was better than the elderly group, although the nutritional status and physical activities in both groups were relatively similar. These findings were following Petralia *et al*. (2014) who stated that cognitive decline was associated with age caused by the decrease in hippocampal neurogenesis and dendritic network alterations in the brain.

Correlation of nutritional status, physical activity, or oxidative stress with cognitive function

Table 3 showed that cognitive function (visual memory) was only correlated with Ox-LDL. Ox-LDL was positively correlated with the results of immediate and delayed ROCF test. It indicated that the level of Ox-LDL might affect the subjects' cognitive functions. Gironi *et al*. (2011) and Mariani *et al*. (2005) stated that brain cells had a high metabolic rate, oxygen consumption, and lipid contents. It made the brain highly susceptible to oxidative stress. Therefore, the level of oxidative stress could be a causal factor of cognitive impairment.

Parameters of physical activity and nutritional status in the present study were not correlated with the results of cognitive tests. It may need more extensive observation and consideration on various risk factors to study cognitive impairment. In theory, physical activity and nutritional status are considered as the modifiable risk factors for the AD. As established in the study by Norton *et al*. (2014), 9.6 million AD cases worldwide were caused by modifiable risk factors, including physical activity. Moreover, a study of Blondell *et al*. (2014) showed that physical activity had neuroprotective properties, thereby preventing a decline in cognitive function and delaying the onset of dementia symptoms.

Nutritional status is also important in determining the cognitive state of the elderly and preventing the potential decline in cognitive function. Qiu *et al.* (2009) stated that vascular

Table 3. Association of oxidative stress marker, physical activity and nutritional status to cognitive functions

Variables	Attention		Immediate visual memory		Delayed visual memory	
	r	p	r	p	r	p
Ox-LDL	-0.115	0.328	-0.289	0.012*	-0.288	0.012*
MDA	0.044	0.710	-0.179	0.123	-0.156	0.181
Physical activity	0.139	0.233	0.117	0.319	0.057	0.625
Nutritional status	0.115	0.325	0.132	0.258	0.102	0.385

*[3]Independent t-test, significant at $p<0.05$

risk factors and disorders (including nutrition-related disorders) had been proven to have potential risk roles in the pathogenesis and clinical manifestation of AD based on the increasing evidence. However, the association between nutritional status and cognitive impairment is very complex, because more nutrients are involved in this relationship. Several studies found that nearly all the nutrients play a role in maintaining cognitive capacity in the elderly (Johansson *et al*. 2009). Therefore, elderlies are encouraged to do dietary diversification in their daily consumption in order to maintain their good nutritional status that will lead to robust (non-frail) elderly. Badrasawi *et al.* (2016) showed that mini-mental stat exam (MMSE) scores were significantly higher in robust than frail elderly groups.

Our findings indicated that it is important to pay attention to the intake of foods rich in antioxidants in order to prevent the increase in Ox-LDL and MDA levels in pre-elderly, which may lead to a decline in cognitive function. High levels of MDA reflect lipid oxidation in the cell membrane (Gupta & Chari 2006). This condition can be improved in various ways, for example, by consuming antioxidant supplements. The early study indicated that antioxidant supplements could prevent oxidative stress caused by exogenous factors or pathological conditions (Hulbert 2010). Gonzalez *et al.* (2010) also recommended that the consumption of EPA and DHA should be increased to reduce the risk of cognitive impairment that might have implications in the helplessness state of the elderly.

CONCLUSION

Most of the elderly and pre-elderly subjects were at risk of malnutrition, and their physical activities were at a sedentary level. Ox-LDL and MDA levels in the elderly were higher than those in the pre-elderly subjects. The pre-elderly had better scores in cognitive function tests than the elderly subjects. Ox-LDL levels had a negative correlation with immediate and delayed visual memory functions. It indicates that high ox-LDL level is associated with a decline in cognitive functions in elderly and pre-elderly.

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