Original article

Correlation Between Age, Body Mass Index, And Blood Selenium Level with Glutathione Peroxidase Activity Among Elderly in South Jakarta

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Abstract:

Oxidative stress contributed in aging process and several degenerative diseases. Selenium was an important trace element due to as a component of antioxidants enzymes (selenoproteins), including glutathione peroxidase for protection against free radical. ***Objective:*** We aimed to study the correlation between blood selenium level and plasma glutathione peroxidase activity in elderly. ***Materials and Methods:*** Cross sectional study was held in 5 elderly communities in south Jakarta. Body mass index, blood selenium level and plasma glutathione peroxidase activity were measured in 95 elderly aged between 60-86 years old. Nonparametric correlation was used for correlation analysis. ***Results and Discussion:*** The median of subject's age was 69 years old (60-86) and for body mass index was 23.57 (13.59-36.05). The median of selenium level among subject was 0.19 (0.023-0.56). The mean of plasma glutathione peroxidase activity was 164.45 U/L ± 68.07. There was no correlation among variables. However, plasma glutathione peroxidase activity decreased with increasing age and body mass index although it was not significant. ***Conclusion:*** There was no correlation between blood selenium level and plasma glutathione peroxidase activity. Detection of plasma selenium level is needed to confirm this result.

Keywords: Selenium, Glutathione Peroxidase, Antioxidant, Elderly

Introduction

Globally people above 60 age years in 2017 are approximately 962 million, 13% from population, and increase 3% per year. In 2030 this population will be estimate reach 1.4 billion, and 2.1 billion in 2050.[1]

Population of Indonesian elderly were increase from 5.45% in 1980 to 9.77% in 2010. It has been estimated in 2020 the population would reach 11.34%.[2]

The health status has wide variation with increasing age. Some older people have physical capacity same like the younger and the other have declined of physical capacity. The transition of epidemiology cause change of disease pattern, where chronic degenerative disease such hypertension, arthritis, stroke, diabetes are more and more increase.[1, 2]

Aging can describe as degenerative process decline in physical function to maintain homeostasis leading to an increase possibility of death. The imbalance between oxidative stress and antioxidant defense trigger macromolecular damage, at the end can cause degenerative disease and death. Accumulation of cellular oxidative stress are caused by free radical from intrinsic process like metabolism product, random error biochemical reaction, nutrition intake, and also extrinsic factors.[3, 4]

Selenium were trace element which had important role in protection system from oxidative stress. Maintaining optimal level of body selenium were crucial to prevent oxidative stress. Selenium deficiency related to increasing risk of several

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chronic disease including cancer, and coronary artery disease. In recent year, selenium researches are an interested study due to its important role as selenoprotein antioxidant to against free radical.[5, 6] In our body, selenium would bind with amino acid to form selenoproteinglutathione peroxidase (GPx), a selenium dependent enzyme plays critical role in reduction of lipid and hydrogen peroxides. If GPx activity is decreased, more hydrogen peroxide is present, leads to tissue damage. Same as others proteins, glutathione peroxidase contains from several amino acids. For examples GPx-1, consist of 181 kinds of amino acid, the essential amino acids and non-essentials.[7]

There are four subspecies of GPx that catalyze the reduction of free radical in specific tissue location. 70% GPx found in cytosol and 30% in mitochondria matrix. GPx-1 found in most cells, including red blood cells, hepatocyte, and kidney tissue, GPx-2 found in gastrointestinal tract, GPx-3 is selenoprotein in plasma as glycoproteins, and GPx-4 interact with complexes lipid in cell membrane.[8]

Glutathione peroxidase catalyze reduction of hydrogen peroxides and organic hydroperoxides. If this free radical is not reduced, leads to cellular damage, including DNA and other proteins damage. During the process, glutathione is needed in reduced form (GSH) and transform to be oxidized glutathione (GSSG). GSSG is radical so it must be reduced to GSH immediately.[9, 10, 11]

Recently, study about selenium in elderly still rarely. Baierle et al[12] in 2015 found negative correlation between GPx activity with plasma carbonyl in elderly population. In 2012, Savory et al[13] analyzed the effect of supplementation 200 µg selenium to obese patient for 3 weeks. The result showed that selenium supplementation could reduce lipid peroxidation. Cardoso et al[14] in 2014 found lower selenium level in Alzheimer patient compared to the mild cognitive impairment patients and the healthy group. The aim of this study was to assess the correlation between selenium level with GPx activity in Indonesian elderly. We hypothesized blood selenium level would have positive correlation with GPx activity.

Materials and Methods

Source population and Study population

Cross sectional study was held in 3 different sub-districts in Jakarta, that were Cilandak, KebayoranBaru, and Pesanggrahan. Participants were recruited from a consecutive sampling in several Integrative Healthcare Center for elderly. The inclusion criteria were men or women aged 60 years old and over as well as willing to follow all procedures and signed the informed consent. Subject would be excluded if smoking or drinking alcohol in recent 1 year, had severe pain at lower extremity, or fever. We examined anthropometric assessment, blood selenium level, and plasma GPx activity.

Study variables & their indicator

Anthropometric Assessment

Body mass index data was obtained from weight and height measurement. Due to limitations in elderly, we used knee height measurement to obtain body height. Body weight measurement used SECA 803 digital body weight scale, and the knee height measurements used knee height caliper. The result of knee height would be conversed to body height used a formula[15]

Men Height = (1,924 x Knee height) + 69,38

Women Height = (2,225 x Knee height) + 50,25

Blood Selenium Level

Blood sample was taken without fasting first. After vena puncture, whole blood from EDTA tube was added with1 mL ofconcentrated nitric acids, and heated up in waterbath for 1 hour. After that, 0.5 ml hydrogen peroxide was added to the sample and heated up for 2 hours. The sample must be filtered with Whatman paper before measurement. Blood selenium level was determined in whole blood by inductively coupled plasma-optical emission spectrometer (ICP-OES).

Glutathione Peroxidase Activity

GPx activity was determined in plasma using colorimetric method by spectrophotometry (Thermo Fisher Scientific®) at 340 nm and 37°Cusing a commercially available kit (Glutathione peroxidase Ransel kit, Randox®). Fifty microliters of heparinized plasma were diluted with diluting agent, incubated for 5 minute and added 1 ml of Drabkin's reagent. The solution was mixed well and read as an initial absorbance of sample after one minute and read again after 1 and 2 minutes.

Statistical analysis

Descriptive statistics were used to summarize subject characteristic including age, gender, education, and nutrition status. Age, body mass

index, and selenium level were categorized into 2-4 groups. Correlation analysis spearman were used to examine the correlation between age, body mass index, selenium level with GPx activity. The statistical analysis used SPSS program.

Result

Participants of this study were 23 men and 72 women aged 60-86 years old. Subjects characteristic were summarized in table 1. Most of participants were women (75.8%) and 24.2% were men. For education background, 38.9% had low education.

Table 1. Subject baseline characteristic

Variable	Result
Age, years, median (min-max)	69 (60-86)
Gender	
Men, n (%)	23 (24.2)
Women, n (%)	72 (75.8)
Education	
Low education, n (%)	37 (38.9)
Well education, n (%)	30 (31.6)
High education, n (%)	28 (29.5)
Body mass index, kg/m^2, median (min-max)	23.57 (13.59-36.05)
Nutritional status	
Underweight, n (%)	5 (5.3)
Normoweight, n (%)	38 (40)
Overweight, n (%)	29 (30.5)
Obese, n (%)	23 (24.2)
Blood selenium level, μg/dl, median (min-max)	0.19 (0.0023-0.56)
Optimal level, n (%)	74 (77.9)
Low level, n (%)	21 (22.1)

GPx activity in older age group (> 70 years old) was lower than the younger (figure 1A). Mean of GPx activity in older age group was 158.5 μmol/min/L, while the mean of younger age group was 169.2 μmol/min/L. Statistical analysis with independent T-Test showed there were no significantly different in two age groups. (p>0.05). In nutritional status, GPx activity was lower in overweight and obese groups than the normal weight group (figure 1B). Median of GPx activity in obese group was 136.7 μmol/min/L with range 44.2 - 262.9 μmol/min/L. Anova test result showed there no significantly different among those groups (p>0.05). In blood selenium level groups, mean of GPx activity in low level group was 164.1 μmol/min/L lower than optimal level group (figure 1C). There no significantly different found in statistical analysis used independent T-Test (p>0.05). We analyzed the correlation between age, body mass index, and blood selenium level with GPx
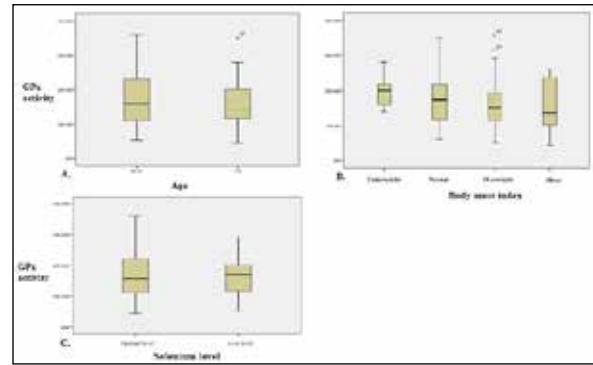

Figure 1. A. GPx activity in age groups B. GPx activity in body mass index groups C. GPx activity in blood selenium level. There were no significant different between GPx activity in all groups (P>0.05)

activity used spearman correlation analysis. GPx activity decreased by age and body mass index in this study, but no significant correlation found (p>0.05).GPx activity increase by increasing blood selenium level, although we not found the significant correlation between them (p=0.05).

Discussion and Conclusion

In our study, range of age's subject was 60-86 years old. The women participants were greater than men participants. This condition was in accordance with the data from *Badan Pusat Statistik* Republic of Indonesia that showed elderly (aged ≥ 60 years old) were 8.97% from Indonesian population, consist of 47.48% men and 52.52% women. Most of elderly in Indonesia aged 60-69 years old (63%) and the rest aged 70 years old and over. For educational background, more than half of Indonesian elderly were only junior high school graduates or lower. In recent study, 38.9% participants had low education background.[16]

GPx was an enzymatic antioxidant system which protect the cells from oxidative stress. Harman in 1956 described oxidative stress in aging process.[3,17,18]

In this study GPx activity was lower in the older age group. Previous in vitro studies demonstrated that levels of GPX1 protein and enzymatic activity were significantly reduced in human endothelial progenitor cells (EPC) derived from old subjects, but the blood levels of selenium were not significantly different between young and old subject. It meant that decreasing of GPX1 levels in EPC of old individuals appeared was not depend on blood selenium level. As seen in our result, there was no correlation between blood selenium level with plasma Gpx activity, however the subjects who had low level selenium tend to had

low level Gpx activity. Espinoza et al[19] in 2008 found an inverse association between GPx and age, indicating that for each 1-year increase in age, GPx activity decrease by 2.9 μmol/min/L. Our result also exhibited that Gpx activity decreased with increasing age. Decrease in GPx activity as the consequence of high level of oxidative stress which occur in aging process due to its role as antioxidant.[20]

Besides in aging process, oxidative stress increase in several condition including obesity.[13, 20, 21] The study of Furukawa et al in 2004 showed that fat accumulation would increase systemic oxidative stress. This condition in obesity might relate to dysregulated adipocytokines production. Lipid peroxidation marker significantly correlated with BMI and waist circumference.[21] In this study, 23 subjects were obese. Their GPx activity were lower than the normal group, but no significantly different among this groups. The Gpx might be used to eliminate free radical and overcome oxidative stress, thereby its activity was low in obese group. Obesity was one condition that increase oxidative stress due to low grade inflammation.

Study of selenium has been an interest study since its discovery as an important component of antioxidant enzymes, including glutathione peroxidase.[6, 22, 23] There are a few of human studies that implicate low body selenium status in reduce longevity or health span.[24,25] EVA study in France 2005 explored the relationship between baseline plasma selenium concentrations and mortality. This 9-year longitudinal study indicate that low plasma selenium concentrations were associated with higher mortality.[26,27] In selenium deficiency condition, transformation selenocysteine into GPx during translation decreased cause increasing GPx mRNA degradation[27]. In this study, GPx activity was lower in low blood selenium level, but no significantly correlation between selenium level with GPx activity. It might be caused by the difference sample source in analyzing selenium and Gpx. Selenium level was analyzed from the hemolysate, while Gpx activity was analyzed in plasma. Regarding that, plasma selenium assessment is needed to determine plasma selenoprotein GPx status for the future study. Glutathione peroxidase as antioxidant doesn't work independently to prevent oxidative stress. Therefore, further research is needed to assess other antioxidants and other chronic inflammation condition which influence glutathione peroxidase status.

In conclusion, glutathione peroxidase activity in elderly in south Jakarta was tend to decreased with increasing age and body mass index. Moreover, its activity also decreased in low level of selenium, although the correlation analysis was not significant.

Recommendations

The future research of relationship between GPx, other antioxidants, stress oxidative, and chronic diseases may greatly improve our understanding to maintain the quality of life in elderly.

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