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Research Article
Is Ratio of Omega-3/Omega-6 Fatty Acids Intake Related with the Level of Omega-3 in the Membrane of Erythrocyte among Institutionalized Elderly?

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Abstract
Background and Objective: Increased life expectancy also causes an increase in various diseases associated with inflammation. Omega-3 fatty acids are known to have anti-inflammatory effects but these effects are influenced by the presence of omega-6 fatty acids because they compete in the synthesis of eicosanoids. Therefore, the ratio of omega-3 and omega-6 fatty acid intake is important to consider. The ratio of omega-3 and omega-6 fatty acid intake will affect the level of omega-3 fatty acids in the blood. This study aimed to explore the relationship between the ratio of omega-3 / omega-6 fatty acid intake with the level of omega-3 fatty acid of erythrocyte membranes in the elderly in five registered nursing homes in South Tangerang City. **Materials and Methods:** This cross-sectional study involved 101 elderly subjects using proportional random sampling method. The ratio of omega-3 and omega-6 fatty acid intake was assessed using a semi-quantitative food frequency questionnaire (SQ-FFQ) and the omega-3 fatty acid levels of the erythrocyte membrane were measured using gas chromatography-mass spectrometry. We use Spearman's analysis to see the correlation. **Results:** The mean age of the participants was 75.5±7.6 years and the majority of participants were women (73.3%). Furthermore, the median ratio of omega-3 and omega-6 fatty acid intake was 0.08 (0.05-0.23) and the median value of erythrocyte membrane omega-3 fatty acids for ALA = 10.06 (4.9-24.9) μg mL^{-1}, EPA = 14.6 (5.06 - 81.02) ug mL^{-1}, DHA = 115.5 (20.6-275.09) ug mL^{-1}, total omega-3 = 144.1 (89.3 - 332.1) μg mL^{-1}. **Conclusion:** No correlation was found between the ratio of omega-3/omega-6 fatty acid intake with the level of omega-3 fatty acid erythrocyte membrane among institutionalized elderly. ($r = -0.06$, $p = 0.6$ for ALA; $r = 0.06$, $p = 0.5$ for EPA, $r = -0.07$, $p = 0.5$ for DHA and $r = -0.06$, $p = 0.5$ for total omega-3).

Key words: Elderly population, health problems, inflammaging, ratio of omega-3/omega-6 intake, level of omega-3 erythrocyte membrane, institutionalized elderly

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Increased life expectancy in various countries also causes an increase in the elderly population. The population of over 60 years in the world is expected to double from 901 million in 2015 to more than 2 billion by 2050[1]. The elderly population in Indonesia has surpassed 7 percent since 2000 and is expected to increase by a quarter by 2025[2]. The aging process causes inflammation, known as inflammaging, a condition that underlines the emergence of many chronic diseases and other adverse health problems in the elderly[3]. Omega-3 fatty acids are considered as one of the possible nutritional strategies that might be beneficial for healthy aging due to their anti-inflammatory effects[4].

In contrast, omega-6 fatty acids are associated with increased inflammation. Therefore, the ratio of omega-3 and omega-6 fatty acids is important to consider, because these two fatty acids compete with each other for the formation of eicosanoids[5]. The ratio of omega-3 fatty acids to omega-6 will affect the level of omega-3 fatty acids in the blood. Omega-3 fatty acid levels in the erythrocyte membrane are inversely correlated with inflammatory biomarkers in the elderly[6]. Food intake in the elderly itself needs to be considered, especially those in care institutions because the incidence of malnutrition in the elderly living in nursing home is reportedly higher than the population[7]. Therefore, this study aims to explore the association between the ratio of omega-3/omega-6 fatty acid intake with omega-3 fatty acid levels of erythrocyte membranes among the elderly in various nursing homes.

MATERIALS AND METHODS

Subjects collection and study design: This study used a cross-sectional design and conducted in five registered nursing homes in South Tangerang City with various socio-economic status. Data collection was conducted from July to August 2019. Subjects were obtained using proportional random sampling. Man or women aged ≥60 years, literate independently or with a companion, were included in this study. An informed consent form was signed by the study participants. Subjects with history of cancer, chronic kidney disease, abbreviated mental test (AMT) score <8 and geriatric depression score ≥10 were excluded. From 228 accessible individuals, 101 individuals fulfilled the inclusion criteria, completed all the research stages and included in the statistical analysis.

Data collection: Characteristics of subjects such as age, gender, educational level, smoking status, history of diabetes, dyslipidemia and cardiovascular disease were collected using an interview with the subjects. History of hypertension was collected using the measurement of blood pressure ≥140/90 mmHg or self-reported use of antihypertensive medication. Anthropometric measurement was done using body composition analyzer Tanita type SC-330 for body weight and knee height caliper for prediction of body height. Nutritional status was determined from the body mass index (BMI) based on the WHO category for Asia Pacific[8]. Functional status was measured using Barthel Index[9]. The physical activity was measured using physical activity scale for the elderly (PASE)[10-12]. The ratio of omega-3/omega-6 fatty acids intake was assessed using semiquantitative food frequency questionnaire. Venous blood samples were withdrawn to measure omega-3 fatty acids erythrocyte membrane levels using gas chromatography–mass spectrometry.

Statistical analysis: All data collected were analyzed using Statistical Package for the Social Science (SPSS) version 20.0. Nominal data were described using frequency, n (%). Kolmogorov-Smirnov test was used to determine data distribution and considered normal if the p-value is above 0.05. Normal distribution data was presented in mean and SD, while non-normal distribution data was presented using a median and minimum-maximum range. Spearman correlation test was used to determine the correlation between omega-3/omega-6 fatty acids intake ratio and the level of omega-3 erythrocyte membrane, $p<0.05$ was considered significant.

RESULTS

Table 1 shows the basic characteristics of the subjects. The mean age of subjects was 75.49±7.57years and 73.3% of subjects were women. Most subjects (40.6%) had low education level (elementary/junior high graduate), 92.1% subjects did not smoke, 76.2% subjects did not have diabetes mellitus, 65.3% subjects did not have dyslipidemia, 73.3% subjects did not have cardiovascular disease but 68.3% subjects had hypertension. Mean BMI of subjects was 21.79±4.00 kg m^{-2} with 37.6% of them categorized as normal BMI. Most of the subjects (65.3%) were independent but with sedentary physical activity (48.5%).

Table 2 shows the dietary intake of the elderly subjects in nursing home based on semiquantitative food frequency questionnaire (SQ-FFQ).We classified the intake based on the 2019 Indonesian recommended dietary allowance (RDA). Most subjects have low total energy and protein intake, 70.3 and 87.1% respectively. Most subjects had low total fat intake (47.5%) but there were 9.9% subjects who had high total fat intake.

Table 3 shows the intake of omega-3, omega-6 fatty acids and its ratio based on semiquantitative FFQ of elderly in nursing home. Most of the subjects have low omega-3 and omega-6 fatty acids intake, 89.1 and 90.2% respectively, with omega-3/omega-6 intake ratio as 0.08 (0.05-0.23).

The median level of omega-3 fatty acids in erythrocyte membrane was 10.06 (4.93-24.90) μg mL^{-1} for ALA; 14.63 (5.06-81.02) μg mL^{-1} for EPA; 115.48 (20.58-275.09) μg mL^{-1} for DHA and 144.11 (89.27-332.11) μg mL^{-1} for total omega-3 fatty acids (Table 4).

Table 5 shows the correlation between omega-3/omega-6 fatty acids intake ratio based on SQ-FFQ and the level of omega-3 fatty acids in erythrocyte membrane among elderly individuals in nursing homes. There were no significant

Table 1: Basic characteristics of subjects (n = 101)

Characteristics	Results
Age	75.49±7.57 †
60-69 years, n (%)	20 (19.8)
70-79 years, n (%)	54 (53.5)
80-89 years, n (%)	22 (21.8)
>90 years, n (%)	5 (5)
Gender	
Male	27 (26.7)
Female	74 (73.3)
Educational levels	
Very low, n (%)	7 (6.9)
Low, n (%)	41 (40.6)
Middle, n (%)	34 (33.7)
High, n (%)	19 (18.8)
Smoking status	
Non smoker, n (%)	93 (92.1)
Light smoker, n (%)	6 (5.9)
Heavy smoker, n (%)	2 (2)
Diabetes mellitus	
Yes, n (%)	24 (23.8)
No, n (%)	77 (76.2)
Hypertension	
Yes, n (%)	69 (68.3)
No, n (%)	32 (31.7)
Dyslipidemia	
Yes, n (%)	35 (34.7)
No, n (%)	66 (65.3)
Cardiovascular disease	
Yes, n (%)	27 (26.7)
No, n (%)	74 (73.3)
Nutritional status based on BMI	21.79±4.00 †
Underweight, n (%)	20 (19.8)
Normal, n (%)	38 (37.6)
Overweight, n (%)	20 (19.8)
Obese 1, n (%)	22 (21.8)
Obese 2, n (%)	1 (1)
Functional status	
Independence, n (%)	66 (65.3)
Mild dependency, n (%)	34 (33.7)
Moderate dependency, n (%)	1 (1)
Physical activity	
Sedentary, n (%)	49 (48.5)
Light, n (%)	30 (29.7)
Moderate to intense, n (%)	22 (21.8)

BMI: Body mass index, n: Total subjects, † Mean±SD

Table 2: The dietary intake based on semiquantitative FFQ of elderly subjects in nursing home (n = 101)

Variables	Results
Total energy (kcal day^{-1})	1167.93±207.16 †
Classification based on RDA	
Low (<80%), n (%)	71 (70.3)
Sufficient (80-120%), n (%)	30 (29.7)
High (>120%), n (%)	0 (0)
Protein (g day^{-1})	37.59±9.29 †
Classification based on RDA	
Low (<80%), n (%)	88 (87.1)
Sufficient (80-120%), n (%)	13 (12.9)
High (>120%), n (%)	0 (0)
Total fat (g day^{-1})	37.37±12.73 †
Classification based on RDA	
Low (<80%), n (%)	48 (47.5)
Sufficient (80-120%), n (%)	43 (42.6)
High (>120%), n (%)	10 (9.9)

† Mean±SD, ‡ Median (minimum-maximum)

Table 3: The Intake of Omega-3, omega-6 fatty acids and ratio of omega-3/Omega-6 based on semiquantitative FFQ of elderly in nursing home (n = 101)

Variables	Results
Omega-3 fatty acid (g day^{-1})	
ALA	0.52 (0.16-1.46) ‡
EPA	0.01 (0.00-0.40) ‡
DHA	0.04 (0.00-0.23) ‡
Total	0.6 (0.18-2.09) ‡
Classification based on RDA	
Low, n (%)	90 (89.1)
Sufficient, n (%)	9 (8.9)
High, n (%)	2 (2)
Omega-6 fatty acid (g day^{-1})	
LA	6.92±2.16 †
AA	0,07 (0.01-3.24) ‡
Total	7.31±2.35 †
Classification based on RDA	
Low, n (%)	81 (80.2)
Sufficient, n (%)	19 (18.8)
High, n (%)	1 (1)
Omega-3/omega-6 intake ratio	0.08 (0.05-0.23) ‡

† Mean±SD, ‡ Median (minimum-maximum)

Table 4: The level of Omega-3 fatty acids in erythrocyte membrane of elderly in nursing home (n = 101)

Variables	Results
Omega-3 fatty acids erythrocyte membrane level (μg mL^{-1})	
ALA	10.06 (4.93-24.90) ‡
EPA	14.63 (5.06-81.02) ‡
DHA	115.48 (20.58-275.09) ‡
Total (ALA+EPA+DHA)	144.11 (89.27-332.11) ‡

‡ Median (minimum-maximum)

Table 5: The correlations between ratio of omega-3/omega-6 fatty acids intake and level of omega-3 fatty acids in the erythrocyte membrane of elderly in nursing home

	Level of omega-3 fatty acids in erythrocyte membrane							
	ALA		EPA		DHA		Total	
Variables	r	p	r	p	r	p	r	p
Omega-3/omega-6 fatty acids intake ratio	-0.057	0.570[S]	0.060	0.553[S]	-0.071	0.482[S]	-0.064	0.525[S]

[S]Spearman correlation test

correlation between omega-3/omega-6 fatty acids intake ratio and omega-3 fatty acids erythrocyte membrane levels among elderly individuals in nursing homes (r = -0.026, p = 0.794 for ALA), (r = 0.009, p = 0.927 for EPA), (r = -0.064, p = 0.527 for DHA) and (r = -0.023, p = 0.817 for total omega-3).

DISCUSSIONS

In this study, no significant correlation was found between the ratio of omega-3/omega-6 fatty acid intake using SQ-FFQ with omega-3 levels in the erythrocyte membrane. This is probably due to the a number of other factors that can affect the levels of omega-3 in erythrocyte membrane. EPA and DHA can be formed endogenously from ALA even though the average conversion rate is less than 1%. These conversions can be influenced by LA because they compete for the same enzymes for conversion and also can be influenced by the estrogen hormone, as well as the genetic polymorphism of Fatty Acids Desaturases (FADS) and elongases[13]. Besides LA, ALA is also known to compete with other fatty acids in the process of elongation and desaturation such as omega-9 fatty acids (oleic acid), omega-7 fatty acids (palmitoleic acid) and trans fatty acids[14]. Most of the subjects in this study showed adequate intake of total fat based on the Indonesian RDA but not for omega-3 and omega-6 fatty acids. It is possible that the fat intake among elderly in nursing home is dominated by the other fatty acids besides omega-3 and omega-6, which may eventually influence the level of omega-3 fatty acids in the erythrocyte membrane. This study involved men and women who made sex differences likely to affect the omega-3 levels of erythrocyte membrane because estrogen is also known to influence the ALA to EPA and DHA conversion, although most of the elderly women in this study may have experienced menopause. Harris *et al.*[15] also found a slight difference in the omega-3 index between elderly men and women with an average age of 67 years.

Aging can affect the metabolism of omega-3 fatty acids. Older individuals tend to have higher levels of omega-3 fatty acids. The omega-3 index is said to have increased 7% per decade until the age of 70 with an increase in EPA and DHA levels of 13 and 6%, respectively[13,16]. Several studies have found that a correlation between omega-3 fatty acid intake and blood levels is not always clear in elderly. For example, in a study conducted by Plourde *et al.*[17] found that plasma DHA levels in the elderly were 4 times higher at 4 h postprandial and 2.5 times higher at 7 days postprandial compared to young adults after administration of DHA-labeled tracers (C-DHA). In this study the age range obtained was quite wide, ranging from 60-94 years, which might also affect the levels of omega-3 fatty acid in the membranes of erythrocytes.

Smoking status can also affect omega-3 fatty acid levels since smokers have lower level of omega-3 fatty acids and also a much higher omega-6/omega-3 ratio due to oxidative damage of unsaturated fatty acids and or changes in the metabolism of EPA and DHA in smokers[13,15]. In this study, there were 8 elderly subjects who smoked with 2 of them classified as heavy smokers. The existence of smoking behavior is also likely to affect the level of omega-3 fatty acids in the erythrocyte membrane.

A higher body mass index is also associated with lower levels of omega-3 fatty acids because in obesity there are higher levels of oxidative stress[18]. The presence of chronic diseases such as diabetes mellitus, hypertension and cardiovascular disease can also affect the level of omega-3 fatty acid. A study conducted by Gellert *et al.*[13] found a higher AA/ALA ratio in the erythrocyte membrane of women with diabetes mellitus and hypertension compared with those who did not, after adjusting for age and smoking status. It has been found in animal studies that obesity and diabetes can interfere with the expression and activity of enzymes involved in the synthesis of EPA and DHA derived from ALA[18].

The level of education and socioeconomic status can influence food intake choices, which of course will also affect the intake of omega-3 fatty acids. In a study conducted by Nordgren *et al.*[19], it was found that low levels of education and socioeconomic status increase the risk of suboptimal intake of omega-3 fatty acids. Physical activities also affect the level of omega-3 fatty acids of erythrocyte membranes because low physical activities were associated with obesity or diabetes[18]. Most subjects in this study have sedentary physical activity (48,5%), which can also be linked with 42.6% of subjects has a BMI $\geq$23, which then may have an effect on the level of omega-3 fatty acids in the erythrocyte membranes. Block *et al*.[20] found that high triglyceride levels were also associated with low levels of omega-3 fatty acids because high triglyceride levels were associated with coronary heart disease. In addition to the those factors, the lack of data regarding food sources of omega-3 and omega-6 fatty acids in the Indonesian food database can also affect the accuracy of the calculation of intake ratios in this study. Hence, the correlation between ratio of omega -3/omega-6 intake with the level omega-3 fatty acids in the membrane of erythrocytes are difficult to assess.

CONCLUSION

This study did not find an association between the ratio of omega-3/omega-6 fatty acids intake and omega-3 fatty acid levels of the erythrocyte membrane. This study is expected to reveal the mechanism of healthy aging that has not been explored much.

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