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THE COMPARISON OF PLASMA MALONDIALDEHYDE LEVELS AMONG OSTEOPOROTIC AND NON-OSTEOPOROTIC POSTMENOPAUSAL WOMEN

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ABSTRACT

Introduction: Osteoporosis is a bone metabolic disorder due to decreased of bone matrix and minerals. Oxidative stress refered as an elevation of reactive oxygen species (ROS) in the cells causing structural damages and functional loss, is contributed in the process of osteoporosis, but its association still in controversy. Herewith we report the comparison of the plasma malondialdehyde (MDA) levels, one of oxidative stress markers among osteoporotic postmenopausal women and without osteoporosis. **Methods:** An observational analytic study with cross-sectional approach among 40 postmenopausal women, grouped into two groups, osteoporosis (n=20) and non-osteoporosis (n=20) based on bone mineral density (BMD) score. The plasma MDA levels were measured from venous blood using ELISA. The difference between plasma MDA levels among both groups was analyzed using an independent T-test. **Results:** The characteristics of demography and clinic among both groups are relatively similar. However, there is a difference in the body weight and BMI. Furthermore, there is no significant differences of MDA levels between the two groups (292,03±61,02ng/ml for group with osteoporosis, and 315,25±73,86ng/ml for non-osteoporosis, p=0,286). **Conclusions:** There is no significant difference in plasma MDA levels among osteoporosis and non-osteoporosis postmenopausal women.
Keywords: Osteoporosis, MDA, oxidative stress, postmenopause

INTRODUCTION

Osteoporosis is a bone metabolic disturbances appeared by a decrease of bone mass resulted from bone minerals and matrices reduction as well as micro-architectural damage to bone tissue (1). Osteoporosis is often referred to as a silent disease because it shows no signs and physical symptoms until a fracture occurs. Data of the International Osteoporosis Foundation (IOF) shows 1 of 4 Indonesian women aged 50 - 80 years, has a risk of osteoporosis (2). The etiology of osteoporosis is an imbalance of osteoblasts and osteoclasts activities on bone remodeling whereas osteoclasts are more active than osteoblasts result in decreased bone mass (3,4).

Recently, there are several studies proved that oxidative stress is contributed in the process of osteoporosis, especially that occurs in postmenopausal women. Oxidative stress is refered as an imbalance of ROS and antioxidants in the body. Oxidative stress induces structural damages on biological substances, such as nucleic acids, lipids, and proteins by triggering membrane lipid peroxidation, then leads to the formation of some reactive aldehydes such as MDA (5). MDA play an pathogenic role in degenerative diseases such as osteoporosis because of its ability to bind some proteins causing functional damage and accelerating molecular turnover (6). MDA can be detected from serum, plasma, and tissue samples, using various methods and commonly used as an oxidative stress markers in many diseases such as osteoporosis, cancer, asthma, stroke and cardiovascular attack (7).

The association of the MDA levels and the incidence of osteoporosis is controversial. Several studies have shown that there is an elevation of MDA levels among osteoporosis patients, compared to the non-osteoporosis. Some studies also reported that

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osteoclastic and osteoblastic activities may be correlated with an imbalance between oxidant and antioxidant levels in postmenopausal-related osteoporosis (8,9). On the other hand, some studies show that there is no difference between in the level of MDA among osteoporosis compared to non-osteoporosis patients, and the level of MDA does not associated with lumbar BMD or bone turnover markers (10). Due to these controversial evidence, herewith we report the comparison of the level MDA among osteoporosis and non-osteoporosis postmenopausal women.

MATERIALS AND METHODS

A cross-sectional study among 40 postmenopausal women in Semarang City, Central Java, Indonesia who met the inclusion and exclusion criteria. The protocol was approved by the Faculty of Medicine Diponegoro University Ethics Committee with ethical clearance certificate number 209/EC/KEPK/FK-UNDIP/V/2019.

Participants who received long-term corticosteroid and calcium therapy, and suffered from chronic disease (diabetes mellitus, renal failure, and chronic liver disease) were droped out from the study. The demographic characteristics of the participants were obtained. BMD was measured at the lumbar spine (L2-4) and femoral bone by dual-energy x-ray absorptiometry (DEXA).

Plasma MDA was determined from venous blood samples, obtained from the brachiocephalic vein using the ELISA-competitive principle (Elabscience E-EL-0060 MDA kit) and measured spectrophotometrically at a wavelength of 450 nm ± 2 nm. The level of MDA then determined by plotting the absorbances of the samples to the standard curve.

Demographic and clinical data including age, body weight, body height, basal metabolic index (BMI), hypertension history, dyslipidemia history, gout history, long-term medication history, and plasma MDA levels were classified based on the presence of osteoporosis into two groups: The first group is participants without osteoporosis, and the second group, for who has osteoporosis, then analyzed using SPSS software version 17.0 for Windows.

The categorical scale data such as hypertension history, dyslipidemia history, gout history, and long-term medication history were cross-tabulated using the Chi-square test. While for numerical scale data including age, body height, body weight, BMI, and plasma MDA levels were analyzed using two-independent sample T-test.

RESULTS

The demographic and clinical characteristics of participants, which classified based on the presence of osteoporosis are depicted in Table 1. The age of participants are between 59 and 81 years old, with the average is 65,63 years old. The mean of body weight and height of the study participants are 55,78 kg and 1,51 m, respectively. The study participants were then divided by standard categorization of BMD T-score into the group of non-osteoporosis (20 participants) and osteoporosis (20 participants).

The results of the crosstabulation analysis for two groups showed that there were no significant difference on the ages, body height, hypertension history, dyslipidemia history, gout history, and long-term medication history between both groups ($p=0,664$ for age, $p=0,401$ for body height, $p=0,490$ for hypertension $p=1,000$ for dyslipidemia, $p=0,605$ for gout history and $p=0,327$ for the long-term medication history) but no for body weight and BMI among the osteoporosis group and the non-osteoporosis group ($p<0.05$).

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Table 1. Demographic data of both groups

Variables	Groups		p	OR (95%CI)
	Non-osteoporosis (n=20) Mean ± SD, n (%)	Osteoporosis (n=20) Mean ± SD, n (%)		
Age (Year old)	65,25 ± 3,55	66,00 ± 5,60	0,664	
Body weight (Kg)	61,55 ± 7,31	50,00 ± 4,86	0,000	
Body height (cm)	151,75 ± 4,58	150,40 ± 5,43	0,401	
Body mass index (Kg/m^2)	26,80 ± 3,62	22,13 ± 2,15	0,000	
Hypertension				
Yes	7 (17,5)	5 (12,5)	0,490	0,619 (0,168-2,435)
No	13 (32,5)	15 (37,5)		
Dyslipidemia				
Yes	15 (37,5)	16 (40)	1,000	1,333 (0,304-5,937)
No	5 (12,5)	4 (10)		
Gout				
Yes	3 (7,5)	1 (2,5)	0,605	0,298 (0,038-3,154)
No	17 (42,5)	19 (47,5)		
Long-term medication				
Yes	9 (22,5)	6 (15)	0,327	0,524 (0,143-1,924)
No	11 (27,5)	14 (35)		

BMI : body mass index; *Independent T-test with significance at the level of 0.05

The result of the analysis of the mean difference between the two groups is depicted in Table 2. Herewith we found that there is no significant difference in plasma MDA levels among osteoporosis and non-osteoporosis postmenopausal women (p>0,05).

Table 2. Comparison of plasma MDA levels in postmenopausal women

Variables	Groups		p
	Non-osteoporosis (n=20) Mean ± SD, n (%)	Osteoporosis (n=20) Mean ± SD, n (%)	
MDA (ng/ml)	292.03±61.02	315.25±73.86	0.286

*Independent T-test with significance at the level of 0.05

DISCUSSION

Oxidative stress refers to increased intracellular ROS, which damages the various biological subtances including proteins, lipids, and nucleic acids, resulting in the structural damages and the functional loss of these molecules. Lipid peroxidation produces hydrogen peroxides, which then produce various reactive intermediates, such as MDA (14). The main target of peroxidation is lipids found in many biological membranes and lipoproteins. Examination of MDA levels as the final product of lipid peroxidation can be used to measure damage to lipids caused by free radicals so that examination of MDA levels can be used as one of the oxidative stress biomarkers (15).

Our study depicted that the mean of plasma MDA levels in osteoporotic-postmenopausal women were higher than those in the group without osteoporosis, but it was not statistically significant. This findings is consistent with previous studies conducted by M. Zinnuroglu et al (2012) which showed that there is no differences in MDA levels among osteoporosis and non-osteoporosis postmenopausal women (9) and previous research conducted by Qian Wu et al (2015) which proved that there is no correlation between MDA levels with BMD (11). Other

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study also concluded that the MDA levels may not help for determining the postmenopausal osteoporosis severity (12). In contrast, previous studies conducted by V. Akpolat et al (2013) demonstrated that there is significant differences in MDA levels between osteoporosis and non-osteoporosis groups (13).

There are several factors maybe contributed on this study such as the endogenous antioxidants (SOD, catalase, GSH) status and exogenous antioxidants obtained from the participant diet (15), unfortunately we did not recalled the history of diet. Furthermore, there are several disadvantages of use of MDA for detecting of oxidative stress status. Researchers use MDA as an oxidative stress biomarker such as its unstable nature, especially if the examination is delayed, so maybe it is better if we also confirmed with the other parameters of oxidative stress. The variety of MDA examination methods is also related to the specificity of the results of the examination. The HPLC (High-Performance Lipid Chromatography) method is the best MDA examination method with specificity at this time.

CONCLUSION

In conclusion, although MDA is one of an oxidative stress marker contributed in the mechanisms of postmenopause-related osteoporosis, our study reported that there was no difference of plasma MDA levels among osteoporosis and non-osteoporosis postmenopausal women.

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REFERENCES

1. Bouxsein ML, Genant HK. *The Breaking Spine*. United States, USA; 2010.
2. Kementerian Kesehatan RI. *Situasi Lansia Di Indonesia Tahun 2017*. Jakarta; 2017.
3. Kementerian Kesehatan RI. *Data Dan* Kondisi *Penyakit Osteoporosis Di Indonesia*. Jakarta; 2015.
4. Sozen T, Ozisik L, Calik Basaran N. An overview and management of osteoporosis. *Eur J Rheumatol*. 2016;4(1):46-56.
5. Ozgocmen S, Kaya H, Fadillioglu E, Aydogan R, Yilmaz Z. Role of antioxidant systems, lipid peroxidation, and nitric oxide in postmenopausal osteoporosis. *Mol Cell Biochem*. 2007;295(1-2):45-52.
6. Barrera G, Pizzimenti S, Daga M. Lipid Peroxidation-Derived Aldehydes, 4-Hydroxynonenal, and Malondialdehyde in Aging-Related Disorders. *Antioxidants*. 2018;7(8):102.
7. Khoubnasabjafari M, Ansarin K, Jouyban A. Reliability of malondialdehyde as a biomarker of oxidative stress in psychological disorders. *BioImpacts*. 2015;5(3):123-127.
8. Sendur OF, Turan Y, Tastaban E, Serter M. Antioxidant status in patients with osteoporosis: A controlled study. *J Bone Spine*. 2009;76(5):514-518.
9. Zinnuroglu M, Dincel AS, Kosova F, Sepici V, Karatas GK. Prospective evaluation of free radicals and antioxidant activity following 6-month risedronate treatment in patients with postmenopausal osteoporosis. *Rheumatol Int*. 2012;32(4):875-880.
10. Zhu SY, Zhuang JS, Wu Q, Liu ZY, Liao CR, Luo SG, et al. Advanced Oxidation Protein Products as a Novel Marker of Oxidative Stress in Postmenopausal Osteoporosis. *Med Sci Monit*.

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2015;21:2428-2432.
11. Zhu SY, Zhuang JS, Wu Q, Liu ZY, Liao CR, Luo SG, et al. Advanced oxidation protein products induce pre-osteoblast apoptosis through a nicotinamide adenine dinucleotide phosphate oxidase-dependent, mitogen-activated protein kinases-mediated intrinsic apoptosis pathway. *Aging Cell*. 2018;17(4).
12. Maggio D, Barabani M, Pierandrei M, Polidori MC, Catani M, Mecocci P, et al. Marked Decrease in Plasma Antioxidants in Aged Osteoporotic Women : Results of a Cross-Sectional Study. *J Clin Endocrinol Metab.* 2003;88(4):1523-1527.
13. Akpolat V, Bilgin HM, Celik MY, Erdemoglu M, Isik B. An Evaluation of Nitric Oxide, Folate, Homocysteine Levels and Lipid Peroxidation in Postmenopausal Osteoporosis. *Adv Clin Exp Med.* 2013;22(3):403-409.
14. Hassan HA, Lipid peroxidation end-products as a key of oxidative stress: Effect of antioxidant on their production and transfer of free radicals. 2012, in: Lipid Peroxidation (ed. A. Catala). Tech Publishing, Croatia, pp. 63–87.
15. Trimbake SB, Sontakke AN, Dhat VV. Oxidative stress and antioxidant vitamins in leprosy. *Int J Res Med Sci.* 2013;1(3):101-104.