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Correlation of estradiol serum levels with classification of osteoporosis risk OSTA (Osteoporosis Self-Assessment Tools for Asian) in menopause women

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ABSTRACT

Background: In postmenopausal women, decreasing estrogen levels is a marker of ovarian dysfunction. Hypoestrogenic state has known increasing the risk of osteoporosis.

Objective: To determine the correlation between estradiol serum levels with classification of osteoporosis risk OSTA (Osteoporosis Self-Assessment Tools for Asian) in menopausal women.

Methods: This study was case series study which examined estradiol serum in menopausal women by ELISA and assess the osteoporosis risk using osteoporosis risk classification OSTA. Total 47 samples were collected at Dr. H. Adam malik, Dr. Pirngadi, and RSU Networking in Medan. This research was conducted from May to December 2016. Data were statistically analyzed, and presented with Spearman test.

Results: In this study we found the mean levels of estradiol in menopausal women was 18.62 ± 16.85 ng / ml with OSTA osteoporosis risk score of 2.09 ± 2.45. There were a significant positive correlation between estradiol and risk of osteoporosis OSTA with correlation coefficient r = 0.825 and p <0.05.

Conclusion: There is a strong positive correlation between serum levels of estradiol with OSTA osteoporosis risk assessment in menopausal women.

Keywords: Estradiol, OSTA, menopause women

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INTRODUCTION

Osteoporosis a problem of elderly is getting attention of the world, including Indonesia. This is motivated by the increasing age expectancy.[1] The number of elderly in Indonesia is expected increase 41% in the period 1990-2025, while menopausal women in 2000 accounted for 15.5 million, will rise to 24 million in 2015.[2] The increase in the number of elderly in Indonesia raises fears of an epidemic disease osteoporosis.[2,3] According to the results of data analysis conducted by the Center for Nutrition Ministry of Health in 14 provinces shows that the problem of osteoporosis in Indonesia has reached a level that needs to be wary is 19.7%. That is why the tendency of osteoporosis in Indonesia six times higher than in Netherlands. The five provinces with the highest risk of osteoporosis in Indonesia including South Sulawesi (27.7%), Central Java (24.02%), Yogyakarta (23.5%), North Sumatra (22.82%), East Java (21.42%) and East Kalimantan (10.5%).[4]

In 2006, based on the analysis of data and the risk of osteoporosis by the Department of Health in Indonesia together with Fonterra Brands Indonesia, the prevalence of osteoporosis in Indonesia has now reached 41.75%. That is, every two from five of Indonesia's population are at risk for osteoporosis. This is higher than the prevalence in the world which is only one from three women have risk of osteoporosis.[4]

Postmenopausal osteoporosis has become a problem of morbidity and mortality in the world. Osteoporosis is characterized by low bone density that increases bone fragility and risk of fracture. The risk of osteoporotic fractures ranges between 30-40% in the whole of human life.[5] In postmenopausal women, osteoporosis if not administered properly, complications of fracture can cause morbidity.[6,7]

In postmenopausal women, estrogen levels decrease which became a marker of loss of ovarian function. It has long been known that estrogen plays an important role in determining bone health in women, ie in maintaining a balance of work osteoblast (bone formation) and osteoclasts (bone resorption).[8,9] In postmenopausal women the average concentration of serum estradiol reach 10-20 pg / ml. With the reduction in estradiol levels can cause complaints in the various organs of the woman and cause a decrease in bone mass rapidly as a marker of the beginning of the process osteoporosis.[9,10]

Prevention and diagnosis of osteoporosis should be done early. Gold standard osteoporosis examination is the examination of Dual Energy X-Ray

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Absorptiometry (DXA) in various positions such as lumbar spine, pelvis and distal radius. But examination of DXA has some limitations, namely the examination fee is quite expensive, the use of ionizing radiation, and requires radiologists who are competent in accurately diagnosing of osteoporosis. Therefore began to develop various instruments as a screening to determine risk of osteoporosis clinically in Asian countries.[10]

Several types of questionnaires were Osteoporosis Self-Assessment Tool (OST, OSTA), Osteoporosis Risk Assessment Instrument (Orai), Simple Calculated Osteoporosis Risk Estimation (SCORE) and Osteoporosis Index of Risk (OSIRIS).[11] All of this questionnaire using a variable weight and age to identify risk osteoporosis.[12,13] One type questionnaire to determine the risk of osteoporosis that can be used in Southeast Asian populations is a Osteoporosis Self-Assessment Tool (OSTA). In this study we aimed to determine the correlation between estradiol serum levels with classification of osteoporosis risk OSTA in postmenopausal women.

METHODS

This study is case series study to determine the correlation of serum levels of estradiol with osteoporosis risk classification OSTA (Osteoporosis Self-Assessment Tools for Asian). This research was conducted from May to December 2016. Total 47 samples were collected at Dr. H. Adam malik, Dr. Pirngadi, and Satellite Hospitals in Medan. The target population is women who are not getting menstrual period at least 12 consecutive months in the department H. Adam Malik Hospital, Pirngadi Hospital and Satellite Hospitals Medan.

After the approval from the ethics committee to do research, research began to gather research subjects appropriate inclusion and exclusion criteria. Women with history of malignancy, diabetes mellitus, heart disease, on treatment of hormone replacement therapy, and history of smoking and alcohol were excluded.

Then do the collection of blood serum estradiol taken from venous blood as much as 3cc. Do anamnesis regarding age and weight then calculated based on the formula OSTA and classified based on the risk of osteoporosis OSTA. Data were collected and analyzed statistically.

Statistical analysis

After sample size was fulfilled, data were statistically analyzed. The data was analyzed descriptively to determine sample characteristics and distribution of each variable. Correlation between estradiol serum levels and osteoporosis risk OSTA was analyze analytically by Spearman test, with $p<0.05$ significance. Analysis was done using SPSS software 6.0.

Table 1 Baseline Characteristics

Characteristics	N	%
Category Age		
≤ 50 years	8	17.0
>50 years	39	83.0
Menopause onset		
1-2 years	15	31.9
3 – 4 years	13	27.7
≥5 years	19	40.4
BMI		
Normal weight	18	38.3
Overweight	7	14.9
Obesity	22	46.8
Serum Estradiol Levels		
≤ 20 pg / ml	37	79.4
≥ 20 pg / ml	10	21.7
OSTA Osteoporosis Risk		
Low	42	89.4
Moderate	5	10.6

RESULTS

Characteristics of study subjects based on age, duration of menopause, body mass index, and levels of estradiol and risk of osteoporosis OSTA described in the following table.

Based on table 1, it can be seen that the characteristics of the study subjects age generally is the age group >50 years as many as 39 people (83%) with duration of menopause is generally ≥ 5 years as many as 19 people (40.4%), while for the body mass index (BMI) more with obese by 22 people (46.8%), in the rest were normal weight and overweight, may not find study subjects included underweight group. Based on the characteristics of the risk of osteoporosis OSTA generally found in low-risk group 42 (89.4%), 5 (10.6%) in the moderate risk group, may not find study subjects included high-risk group.

Based on table 2, 47 samples were obtained from the lowest levels of estradiol was 8.77 ng/ml and the highest was 89.10 ng /ml (mean =18.62 ± 16.85 ng/ml). Score the risk of osteoporosis (OSTA) is -2.00 lowest and the highest was 10.20 with a mean of 2.09 ± 2.45. For the characteristics of IMT obtained with the lowest score of 18.67 kg/m^2 and the highest 37.34 kg/m^2 with a mean of 25.38 ± 4.13 kg/m^2. For ages the youngest was 46 years old and the oldest was 60 years old with a mean age of 53.45 ± 3.09 years.

Table 2 **Average levels of estradiol, OSTA, BMI and age in postmenopausal women**

Variable	Mean	SD	Min - Max
Estradiol levels	18.62	16.85	(8.77 - 89.10)
OSTA	2.09	2.45	(-2.0 - 10.20)
IMT	25.38	4.13	(18.67 - 37.34)
Weight	63.89	11.57	(45 - 98)
Age	53.45	3.09	(46.0 - 60.0)

Table 3 **Estradiol levels of correlation with Osteoporosis Risk Classification OSTA**

	r	P value
Correlation Estradiol serum levels and OSTA	0.825	0.0001

Based on Spearman correlation test between serum estradiol levels with risk of osteoporosis OSTA showed that there is a significant positive correlation, with the strength of the correlation r = 0.825 and p <0.05.

DISCUSSION

This study found that the majorities (79.4%) of postmenopausal women have relatively low levels estradiol (≤ 20 pg / ml) and the levels of risk of osteoporosis are generally (89.4%) in low level too. Statistical analysis by Spearman correlation test showed significant positive correlation, with the strength of the correlation is very strong (r = 0.825). Low levels of serum estradiol which is common in post-menopausal women can be explained by the literature that Estradiol (E2, or 17β-estradiol) is a steroid hormone that derived from cholesterol targets in various tissues in female reproductive organs.[14] In women, estradiol is synthesized primarily by the ovarian follicles whereas testosterone in men, estradiol produced by the testes and the conversion of androgens ekstraglandular.[15] In postmenopausal women the average concentration of serum estradiol reach 10-20 pg/ml.[9,10] Levels of estradiol in women menopause is lower compared to women of reproductive age in each phase of the menstrual cycle.

Aromatization process that occurs in the peripheral associated with women's weight. Obese women have higher estrogen levels compared with lean women because of increased peripheral aromatization. Circulating estradiol levels after menopause is around 10-20 pg / mL, which is largely derived from the peripheral conversion of estrone, which in turn is mainly derived from peripheral conversion of androstenedione.[16] Circulating levels of estrone in postmenopausal women is higher than estradiol, about 30-70 pg/ ml. Women entering menopause will occur in ovarian function is decreased so that the production of the hormones estrogen and progesterone also decreased.[8,17]

Bone metabolism is regulated by bone cells (osteoblasts, osteoclasts) which can react to stimuli. Specific stimulation is regulated by the cell receptor found on the cell membrane or within the cell. The receptors are located in the cell membrane binding stimuli from the outside and then send that information to the cell nucleus via transduction mechanisms.[12, 18, 19,20,21,22]

The results of this study also found that most post-menopausal women are generally at risk of osteoporosis OSTA rate is low (89.4%). The pathogenesis of osteoporosis is complex include the role of bone cells, hormones, cytokines, mineral and biomechanical factors.[11,19] Based on the North American Menopause Society in 2010, a major risk factor for osteoporosis in post-menopausal women are age, genetics, lifestyle factors (such as lower intake of calcium, vitamin D, smoking), body mass index and status menopause.[23,24,25]

Weight training will give emphasis on the bones and cause bone to contract thereby stimulating bone formation. Decreased physical activity may reduce bone mass prolonged. Affluent physical activity will produce greater bone mass. The incidence of osteoporosis in a person with enough physical activity at age 25 to 55 years will be less than the physical activity minimal.[23,24,25]

A decrease in muscle mass and a low BMI often found in menopause. Low BMI associated with Bone Mass Density (BMD) is low in the general population, including the menopause. Research shows that the effect of body weight on bone mass is greater on the body weight bearing for example on the femur or tibia.[24, 25]

Research in the past decade has demonstrated the role of leptin in the control of bone mass. Leptin is produced by adipocytes and contributes to the regulation of energy homeostasis through suppression of appetite and increase energy use.[25] Peripheral Leptin works in the bone to increase osteoblast proliferation and synthesis of bone matrix which results in improved bone mass.[26,27]

Leptin also suppress the production of RANKL which lead to decrease in bone resorption. The second effect of this activity resulted in an increase in bone mass. Leptin also has immunomodulating complex and can work as pro-inflammatory cytokines that activate inflammatory cells and promote the secretion of pro-inflammatory cytokines such as IL-1, TNF and interferon gamma (IFN). Because leptin is associated with BMI, leptin levels are low which reflects the decline in the status of nutrisi.[24,25,26]

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Estrogen is not only produced by the ovaries but also in adrenal glands and fat tissue. Fat tissue can alter the androgen hormone into estrogen. The more fatty tissue that is owned by a woman, the more estrogen produced. Decreased bone mass in women with excess body weight with a high fat content would be jarang.[27] The results of this study are also in accordance with the table OSTA, the low risk category of osteoporosis include age 45-64 years with body weight 60 kg - 64 kg, for postmenopausal women mean age was 53.45 years and mean weight was 63.89 kg.

CONCLUSION

There is a significant positive correlation between serum levels of estradiol and osteoporosis risk value assessed by OSTA with correlation coefficient r = 0.825. It shows that serum estradiol levels can be used as a routine examination and one additional factor that needs to be administered in the treatment of osteoporosis in postmenopausal women.

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