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Association Between 25(OH)D Serum Levels with Calcaneus Bone Mass Density in Elderly at Rural Public Health Care Clinics of Jakarta Islamic State University in 2017

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***Abstract*-Osteoporosis is systemic bone disease marked by decline of bone mass density (BMD) and deterioration of bone microarchitecture so that bones become brittle and break easily. With the increasing of life expectancy, number of elderly in Indonesia will increase simultaneously. Estimated 10% of Indonesian population at the year 2020 will be above 60 yo. These elderly population risk developing degenerative disease such as osteoporosis. Serum 25(OH)D and calcium level regulated along with bone calcium deposit by hormonal signals dynamics. To identify the relationship between serum 25(OH)D and calcium level with calcaneus BMD in elderly at rural area. This study use analytic cross-sectional design conducted at KPKM Reni Jaya UIN Syarif Hidayatullah Jakarta in February-Mei 2017 with consecutive sampling. Calcium and 25(OH)D level obtained from peripheral blood serum while calcaneus BMD was measured using Hologic Sahara Quantitative Ultrasound. Respondent were given informed consent before enrolled in this study. Data were checked for variance and normality using boxplot, histogram, kurtosis and skewness ratio before undergoing statistical analysis using RealStats add in for Microsoft Excell 2016. Data gathered from 60 respondent shows a prevalence of 68.3% BMD classified as osteoporosis which was significantly (p<0.05) dominated by women (53.3%). Statistical analysis shows a significant association (p<0.05) between low level of serum 25(OH)D and BMD. Respondent weight also shows significant association (p<0.05) although, no significant association shown between Body Mass Index and BMD. Low level of serum calcium also shows significant association (p<0.05) toward BMD condition. Binary logistic regression analysis shows that serum calcium level significantly alter probability of developing osteoporotic BMD appearance in elderly. The serum pre-hormone 25(OH)D and calcium deficiency related to the deterioration of calcaneus bone mass density in osteoporosis condition. Development of osteoporosis most likely occurred to elderly women with a low serum calcium and vitamin D level.**

Keywords: 25(OH)D; calcium; bone mass density; osteoporosis; elderly

I. BACKGROUND

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture [1]. Two hundred million people worldwide suffered with osteoporosis according to the International Osteoporosis Foundation (IOF) by 2050 and estimated 50% of fracture incidence will come from east and south east asia region [2]. Modifiable risk factor for osteoporosis included body mass index, calcium deficiency, lack of physical activity, glucocorticoid consumption and the presence of chronic illness [1].

Bone mass density (BMD) measurement using Dual X-ray Absorptiometry (DXA) shows osteoporosis with t-score value ≤ -2.5 SD and osteopenia with t-score ≤ -1.0 SD. However, these cut off point depended heavily on the type of technology used to measure bone density and the location of bone investigated. DXA is the gold standard for bone density measurement but Quantitative Ultrasound (QUS) widely used in developing countries and rural setting for screening purposes and much cheaper and mobile compared to DXA. Calcaneus density measurement using QUS have a different cut off t-score which is ≤ -1.9 SD for osteoporosis and -1.89 -3 SD for osteopenia [3].

Indonesia at the year 2020 were estimated to have a 10% elderly (>60 yo) population [4]. Degenerative disease such as osteoporosis in elderly will become an additional burden to the national health care system. Supplementation of calcium to maintain normal calcium level within the body can reduce the morbidity and mortality of osteoporosis. Serum calcium was regulated by free active vitamin D by increasing intestinal absorption, kidney reabsorption and bone resorption. 25(OH)D or 25 hydroxyvitamin D is a pre-hormone that upon activation in the kidney become 1,25(OH)2D and circulated in bound form with albumin and vitamin D binding protein (VBD) [5] [6] [7].

This study aims to evaluate relationship of between bone mass density and serum 25 hydroxy vitamin D and

serum calcium level among elderly at the Rural Public Health Care Clinics of Jakarta Islamic State University.

II. METHOD

In this analytical cross-sectional study, the subjects comprised of 60 respondents (age ≥ 60 years) were recruited from the Rural Public Health Care Clinics of Jakarta Islamic State University. Subjects were given informed consent and recruited by consecutive sampling in February-May 2017. Ethical approval for the study protocol was obtained from the ethics committee of the Faculty of Public Health University of Indonesia. Subjects had no previous BMD assessment and required to have body mass index ≤ 27 kg/m^2.

All subjects were interviewed and checked for physical examination, age, weight and height were recorded and BMI was calculated. Blood samples were collected from all subjects for serum calcium and 25(OH)D measurement by clinical laboratory (Prodia Lab). Cut off point used for hypocalcemia at 8.9 mg/dl and 20 ng/ml for hypovitaminosis of vitamin D [8]. Bone mineral density was assessed using Hologic Sahara Quantitative Ultrasound. Osteoporosis is defined as having a T-score ≤ -1.9 at calcaneus bone. All measurement data collected and analyzed using Microsoft Excell 2016 add in for statistical analysis (Real Stat) available for download at http://www.real-statistics.com/free-download/.

Data checked for normality using boxplot, histogram, kurtosis and skewness ratio. Binary logistic regression analyses performed on the data to assess correlation between BMD and the various indicated variables. Chi-square test was performed to identify differences in categorical variables and independent t-test for numerical variables. Multivariate analysis of all numerical variables against BMD performed using Hotteling T-Square test. Significance levels of less than 5% were considered significant.

III. RESULTS AND DISCUSSION

Table I showed that mean values of weight, height, and hypovitaminosis D condition were significantly lower ($p<0.05$) in osteoporosis compared to osteopenia respondent, while their mean hypocalcemia value significantly higher compared to osteopenia respondent (6.86 vs 6.43 mg/dl, respectively, $p<0.05$). The mean values of BMI for both group were slightly below 25 kg/m2, which indicated that our respondents was normal weight. Multivariate analysis of numerical variables also shows significant difference ($p<0.05$).

TABLE I. MEAN VALUES RELATED TO OSTEOPOROSIS AND OSTEOPENIA

Parameter	Osteoporosis		Osteopenia		p value*
	Mean (SD)	N	Mean (SD)	N	
Age	65.45 (4.45)	41	65.4 (4.98)	19	0.38
Weight (kg)	56.64 (7.53)	41	62.32 (9.1)	19	0.01
Height (cm)	152.45 (7.58)	41	156.99 (8.61)	19	0.03
BMI (kg/m^2)	24.17 (2.69)	41	24.59 (3.02)	19	0.19
Hypo vitamin D (ng/ml)	12.98 (3.81)	25	14.9 (2.96)	13	0.03
Normovitamin D (ng/ml)	25.73 (5.21)	16	25.88 (3.45)	6	0.3
Hypocalcemia (mg/dl)	8.68 (0.12)	21	8.43 (0.3)	3	0.03
Normocalcemia (mg/dl)	9.19 (0.14)	19	9.25 (0.38)	17	0.31

*independent t-test or its parametric alternative Mann Whitney test

Table II showed the prevalence of osteoporosis in elderly of the Rural Public Health Care Clinics of Jakarta Islamic State University was at 68.33% which was dominated by women (53.33%). The likelihood of female to have osteoporosis was 3.2 times greater compare to male. Hypocalcemia also increase the likelihood of having osteoporosis in elderly by 5.6 times with coefficient of regression (-2.19) that showed the lower value will increase the probability of osteoporosis. The prevalence of hypovitaminosis D of the elderly in the Rural Public Health Care Clinics of Jakarta Islamic State University was 41.67%. However, hypovitaminosis D did not increase the likelihood of developing osteoporosis in the elderly of the Rural Public Health Care Clinics of Jakarta Islamic State University.

TABLE II. CATEGORICAL PARAMETER

Parameter	Osteoporosis	Osteopenia	p value (OR)
Gender			p<0.05 (3.2)
Men	53.33%	16.67%	
Women	15.00%	15.00%	
Elderly			p>0.05
Early	53.33%	25.00%	
Middle	15.00%	6.67%	
BMI			p>0.05
Normal	43.33%	13.33%	
Overweight	25.00%	18.33%	
25(OH)D			p>0.05
Low	41.67%	21.67%	
Normal	26.67%	10.00%	
Calcium			p<0.05 (5.6)
Low	35.00%	5.00%	
Normal	33.33%	26.67%	

*Chi Square or fisher exact test

Analysis of women subgroup in Table III. showed a prevalence of hypovitaminosis and hypocalcemia at 50% and 38.64% respectively. Hypocalcemia condition was significant in both elderly population and elderly women subpopulation while hypovitaminosis D only become a significant condition in elderly women subpopulation. This result in accordance with recent study by Kharroubi et al (2017) that showed a significant association of women with vitamin D deficiency with BMD [8]. However, our data shows no significant association of BMI with osteoporosis which may be caused by a greater prevalence of normal BMI (56.66%) in our data. Osteoporosis was found to associated with low weight and BMI value (Klibanski et al., 2001) which was not found in our respondent. Although, numerical analysis did show that body weight and height had a significant association with osteoporosis (Table.I).

TABLE III. FREQUENCY OF VITAMIN D AND CALCIUM LEVEL IN ELDERLY WOMEN

Parameter	Osteoporosis	Osteopenia	P value
Hypo vitamin D (ng/ml)	50.00%	25.00%	p<0.05
Normovitamin D (ng/ml)	25.00%	0.00%	
Hypocalcemia (mg/dl)	38.64%	0.00%	p<0.05
Normocalcemia (mg/dl)	36.36%	25.00%	

*Chi Square or fisher exact test

Elderly women or postmenopausal women was frequently found to have osteoporosis because of the low estrogen level that lead to loss of bone mineral density [9]. Elderly people showed no changes in vitamin D absorption. However, there was age-related changes for vitamin D metabolism and calcium absorption that renders the increase intake of vitamin D and calcium was needed to reduce morbidity [10].

This study showed the importance of 25(OH)D as a serum marker for vitamin D deficiency in association with loss of bone mineral density. Furthermore, 25(OH)D as vitamin D pre-hormone that upon activation work to their respective target organ via vitamin D receptor. Active vitamin D will increase calcium intestinal absorption, kidney reabsorption and reduce bone resorption which is an interesting opportunity to be used as a therapeutic supplementation in bone metabolic disorder such as osteoporosis.

IV. CONCLUSION

The serum pre-hormone 25(OH)D and calcium deficiency related to the deterioration of calcaneus bone mass density in osteoporosis condition. Development of osteoporosis most likely occurred to elderly women with a low serum calcium and vitamin D level.

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