UNIVERSITI PUTRA MALAYSIA

DETERMINANTS OF BONE MINERAL DENSITY IN POSTMENOPAUSAL MALAY WOMEN

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By

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Chairperson: **Associate Professor Zaitun Yassin, Ph.D.**

Faculty: **Medicine and Health Sciences**

The objective of this study was to identify factors that determine the bone mineral density (BMD) in postmenopausal Malay women. A total of 113 subjects residing in the Klang Valley participated in the study on a voluntary basis. Study subjects were healthy Malay women aged between 50 to 65 years old who had attained menopause at least 5 years at the time of the study.

The BMD of total body, proximal femur, femoral neck, wards, trochanter and lumbar spine L2-L4 as well as fat mass (FM) and lean body mass (LBM) were measured using the dual energy X-ray absorptiometry (DEXA). Information on sociodemographic and reproductive history were collected using a questionnaire. Food intake was assessed using a three-day food record and a semiquantitative food frequency questionnaire. Physical activity was assessed using a three-day physical activity record, an open ended questionnaire and a pedometer. Knowledge, attitude and practice (KAP)

were assessed using a validated questionnaire. Body weight and height were measured using appropriate equipment and standard procedures. Dietary intake was analyzed using Nutritionist IV. Data were analyzed using SPSS Version 10.0. Stepwise regression analysis was used to determine the variables that were independently related to the BMD.

Stepwise regression analysis revealed that LBM, age, knowledge and protein intake explained 61.9% of the variance of proximal femur BMD. Meanwhile, LBM, knowledge, age, attitude towards osteoporosis and weight bearing exercise explained 64.3% of the variance of the femoral neck BMD. Age, LBM and knowledge explained 50.8% variance in the wards while 33.1% of the variance in the trochanter BMD was explained by LBM and age. As for the BMD of lumbar spine L2-L4, calcium intake and age were the most important variables (R^2= 0.440) while FM and calcium intake were the most important variables (R^2= 0.359) for total body BMD. In terms of reproductive history, only years since menopause was correlated with femoral neck BMD (r= -0.199, $p<0.05$). However, it failed to show any significant effect when entered into the stepwise regression.

In conclusion, this study found that dietary intake especially calcium and protein intake, weight bearing activities, FM, LBM, age and knowledge as well as positive attitude towards osteoporosis contribute towards the BMD. However, it appears that these factors exchange places in importance at different sites of bone. Thus, although a portion of the variation in BMD is determined by unmodifiable factors such as age, there are some lifestyle

factors such as dietary intake and weight bearing physical activity, which help to modify the predisposition to osteoporosis.

Abstrak tesis yang dikemukakan kepada senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

FAKTOR-FAKTOR PENENTU KETUMPATAN MINERAL TULANG DI KALANGAN WANITA MELAYU MENOPAUS

Oleh

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November 2002

Pengerusi: Profesor Madya Zaitun Yassin, Ph.D.

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Objektif kajian ini adalah untuk mengenalpasti faktor penentu ketumpatan mineral tulang (KMT) di kalangan wanita Melayu posmenopaus. Seramai 113 subjek yang tinggal di sekitar Lembah Klang telah menyertai kajian ini secara sukarela. Subjek kajian merupakan wanita Melayu yang sihat berumur di antara 50 hingga 65 tahun dan telah menopaus sekurang-kurangnya lima tahun ketika kajian ini dijalankan.

KMT jumlah tubuh, pinggul, pangkal pinggul, wards dan trokanter dan lumbar L2L4 serta jisim lemak (JL) dan jisim otot tanpa lemak (JOTL) telah diukur dengan menggunakan 'dual energy X-ray absorptiometry' (DEXA). Maklumat sociodemografi dan sejarah reproduktif telah dikumpul dengan menggunakan borang soal selidik. Pengambilan makanan telah ditentukan dengan menggunakan borang rekod pengambilan makanan tiga hari dan borang kekerapan pengambilan makanan semikuantitatif. Aktiviti fizikal telah direkod dengan menggunakan borang rekod aktiviti fizikal tiga hari dan alat pedometer. Tahap pengetahuan, sikap dan amalan (KAP) telah ditentukan

dengan menggunakan borang soal selidik yang telah divalidasi. Pengambilan makanan dianalisis dengan menggunakan program Nutritionist IV. Data telah dianalisis dengan menggunakan SPSS Versi 10.0. Analisis regrasi kaedah 'stepwise' telah digunakan untuk menentukan faktor yang mempengaruhi KMT secara bebas.

Hasil analisis regrasi kaedah 'stepwise' menunjukkan bahawa JOTL, umur, skor pengetahuan dan pengambilan protein menjelaskan 61.9% variasi KMT pada tulang pinggul. Manakala JOTL, skor pengetahuan, umur, sikap terhadap osteporosis dan aktiviti menanggung berat badan menjelaskan 64.3% variasi KMT di pangkal pinggul. Umur, JOTL dan tahap pengetahuan menerangkan 50.8% variasi di bahagian wards manakala 33.1% variasi KMT di bahagian trokanter dijelaskan oleh JOTL dan umur. Bagi bahagian lumbar L2L4, pengambilan kalsium dan umur merupakan angkubah yang sangat penting (R^2= 0.440) manakala JL dan pengambilan kalsium merupakan angkubah yang sangat penting (R^2= 0.359) bagi KMT jumlah badan. Bagi sejarah reproduktif, hanya jangkamasa selepas menopaus berkait dengan KMT di bahagian pangkal pinggul (r= -0.199, $p<0.05$). Walau bagaimanapun, ia gagal menunjukkan sebarang perkaitan yang signifikan selepas dimasukkan ke dalam analisis regrasi kaedah 'stepwise'.

Kesimpulannya, kajian ini mendapati bahawa pengambilan diet terutamanya pengambilan kalsium dan protein, aktiviti menanggung berat badan, jisim lemak, JOTL, umur serta skor pengetahuan dan sikap terhadap osteoporosis menyumbang kepada KMT. Walaubagaimanapun, kepentingan faktor-faktor

ini berbeza mengikut bahagian tulang yang berlainan. Walaupun, sebahagian daripada variasi dalam KMT ini ditentukan oleh faktor-faktor yang tidak boleh diubahsuai seperti umur, faktor-faktor gaya hidup lain seperti pengambilan diet dan aktiviti fizikal yang boleh membantu mengubah kecenderungan terhadap osteoporosis.

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DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citations, which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UPM or other institutions.

RANI A/P SARMUGAM

Date:

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LIST OF ABBREVIATIONS

BMD	Bone Mineral Density
BMC	Bone Mineral Content
BMAD	Bone Mineral Areal Density
DEXA	Dual Energy Absorptiometry
RDA	Recommended Dietary Allowance
BMI	Body Mass Index
WHR	Waist Hip Ratio
WHO	World Health Organization
OR	Odds Ratio
RR	Relative Risk
CI	Confidence Interval

CHAPTER 1

INTRODUCTION

Bone is composed of hydroxyproline rich protein matrix crystals called hydroxipatite and a small amount of other substances such as collagen and some non-collagenous proteins such as osteonectin, osteocalcin and osteopontin. There are two types of bone tissues; cortical and trabecular. Each bone in the human body is composed of both types of these bone tissues. However, the relative proportion of these tissues differs according to the sites, for example the vertebrae consists of 50% trabecular bone and 50% of cortical bone and the femoral neck consists of 30% trabecular bone and 70% of cortical bone (Geusens, 1998). The cortical bone which predominates in the shafty long bones is the outer layer of the bone. It is compact, dense and has a slow bone turnover. Meanwhile the trabecular bone forms the internal support network for the cortical shell in the bone ends, vertebrae and other sites. It has a higher turnover rate compared to the cortical bone.

As living tissues, bone tissues are constantly removed and replaced throughout the life cycle. The cells that are responsible for the bone formation are called osteoblast while osteoclast cells cause bone resorption. An increase in osteoclastic activity or decreased osteoblastic activity will cause net bone loss.

After the peak bone mass has been attained, the amount of bone resorbed by osteoclasts is balanced by the amount of new bone formed by osteoblasts. However from menopause onwards, the bone resorption will increase at a rate higher than the bone formation (Genant et al., 1999) due to increased osteoclast activity or decreased osteoblast activity. A negative balance will occur when bone formation does not fully compensate for the amount of bone resorption, which in time will cause the trabecular bone especially, to become porous and its load carrying capacity to be reduced by 75% (Melton III et al., 1990). This causes the brittle bones to become fragile and increases the risk of fracture when a minimal force is applied.

The situation described above is called osteoporosis. It is defined by WHO (1994) as a systemic skeletal disease characterized by low bone mass and microarchictectural deterioration of bone tissues, leading to enhanced bone fragility and a consequent increase in fracture risk.

Riggs and Melton (1986) classified osteoporosis as Type I osteoporosis and Type II osteoporosis (Table 1.1). Type I or postmenopausal osteoporosis is mainly contributed by estrogen deficiency due to menopause. It leads to impaired intestinal and renal tubular calcium absorption that contributes to the negative calcium balance after menopause. Meanwhile, Type II or senile osteoporosis is mainly caused by the aging process. Two most important factors related to Type II osteoporosis are the decline of osteoblast function and impaired production of 25-hydroxyvitamin D which leads to decrease of calcium absorption and secondary hyperparatyroidism.

Table 1.1: Types of involutional osteoporosis

	Type I	Type II
Age (year)	51-75	>70
Sex ratio (F:M)	6:1	2:1
Type of bone loss	Mainly trabecular	Trabecular and cortical
Rate of bone loss	Accelerated	Not accelerated
Fracture sites	Vertebrae and distal radius	Vertebrae and hip
Parathyroid function	Decreased	Increased
Calcium absorption	Decreased	Decreased
Metabolism of 25-OH-D to $1,25(OH)_2D$	Secondary decrease	Primary decrease
Main causes	Factors related to menopause	Factors related to aging

Source: Riggs and Melton III, 1986

Senile osteoporosis (Type II) begins at age 40. From then on, the bone mass will decrease at approximately 0.6 to 0.7% yearly and continues throughout life. On the other hand, postmenopausal osteoporosis (Type I) starts once a woman reaches menopause until 15 to 20 years later with about 1% up to 5% loss of trabecular bone yearly (Hurley and Khosla, 1997).

Table 1.2 shows the risk factors of osteoporosis (Suzuki, 1998). The individual factors are also known as unmodifiable risk factors such as genetic, race and sex, which cannot be altered. The modifiable factors are the nutritional and lifestyle factors such as calcium intake and regular exercise, which can be altered in order to prevent osteoporosis.

Table 1.2: Risk factors for osteoporosis

Individual factors
Race
Heredity /Genetic
Sex (female higher risk than male)
Age (postmenopausal women in particular)
Body build (slender, small and thin person)
Nutritional factors
Calcium deficiency
Alcohol and smoking
Excessive intake of salt and phosphorus
Weight loss due to extreme weight control (inappropriate diet)
Physical factors
Insufficient exercise (long term bed ridden)
Muscle paralysis (by stroke etc.)
Decrease in exercise capacity
Zero gravity (astronauts)
Disease or drug related factors
Premenopausal ovariectomy or hypogenitalism
Gastrectomy
Anorexia nervosa
Steroid use
Source: Suzuki,1998

Statement of the Problem

Osteoporosis has become one of the major public health issues. It has drawn a lot of attention from health care professionals as well as the public due to increase in life expectancy, number of elderly and the cost associated with fractures.

The recent National Institute of Health (NIH) Consensus Statement (2000) reported that the direct financial expenditure for treatment due to osteoporotic fractures is estimated to be around US $10 to US $15 billion annually. Besides, there is also indirect financial loss due to lost of wages or productivity of the patient or caretaker due to osteoporosis.

Apart from the Medicare cost, osteoporotic fractures also lead to significant bone pain, disability and disfigurement causing a decrease in the quality of life (Barret-Connor, 1995). It also has a significant effect on the physical and psychosocial aspect of the patients and their families. Death related to respiratory disease from bed rest and hospitalization due to hip fractures is about 12% to 20% (NIH Consensus Statement, 2000).

In the United States of America (USA), 10 million individuals already have osteoporosis and 18 million more have low bone mass, placing them at high risk of getting osteoporosis (NIH Consensus Statement, 2000). The Asian Osteoporosis Study reported that the age adjusted rate of osteoporosis for men and women per 100,000 were 180 and 459 for Hong Kong, 164 and 442 for Singapore, 88 and 218 for Malaysia, 114 and 289 for Thailand (Table 1.3). The rates for both sex doubled from 65 to 75 years old and increased exponentially from the age of 75 onwards. Even though the rates in this region is slightly lower than the rate in the USA, it is expected that it will continue to rise along with the increase in life expectancy, rapid economic development and urbanization (Lau et al., 2001).

In Malaysia, there are about 1.2 million elderly, which is about 6.8% of the total population (Department of Statistics, 1999). This percentage is projected to increase to 8.3% by 2010 and 11.3% by 2020 (Ministry of Health, 1999).

Table 1.3: Hip fracture discharge (number and rates per 100,000) by age, sex and country (region) in 1997– 1998)

	Hong Kong		Singapore		Malaysia		Thailand		US white	
Age groups (years)	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Men										
50-54	26.0	15.8	19.0	22.0	50	13.8	6	27.1	41	33
55-59	43	30.8	23	34.5	58	20.1	9	35.8		
60-64	74	53.0	25	48.6	83	37.6	9	35.2	44	81
65-69	108	89.5	38	98.6	90	58.3	17	77.2	67	123
70-74	164	189	128	210	95	96.5	21	144	64	119
75-79	222	404					19	227	87	338
80-84	272	932	212	611	331	320	17	421	129	851
85+	236	1639					27	727	181	1894
Age adjusted to US white		180		164		88		114		187
Women										
50-54	18	13.4	15	14.1	32	9.2	2	9.5	66	60
55-59	41	35.2	26	34.0	76	26.5	15	59.1		
60-64	81	64.4	54	81.1	112	48.2	24	88.9	93	117
65-69	209	174	99	195	179	103	35	148	149	252
70-74	354	359	135	408	274	230	56	361	258	437
75-79	573	820					61	657	394	850
80-84	635	1405	1051	1369	892	644	43	898	509	1679
85+	1003	3012					30	605	799	3099
Age adjusted to US white		459		442		218		269		535

Source: Lau et al., 2001