

RISK FACTORS OF OSTEOPOROSIS IN OBESE POSTMENOPAUSAL WOMEN OF KARACHI, PAKISTAN

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ABSTRACT

Low serum vitamin D3 (Vit D3) and calcium levels as well as high parathyroid hormone (PTH) levels are the most important risk factors in osteoporosis especially after menopause. This study was performed to observe the differences in serum calcium (mg/ml), vitamin D3 (ng/ml) and parathyroid hormone (PTH) (pg/ml) level in obese post-menopausal women as compared to normal weight (control) post-menopausal women. This was a cross sectional study. Data were collected through a questionnaire from different localities of Karachi city. We selected 13 control (18.5-22.9 Kg/m²) and 71 obese (BMI > 25 Kg/m²) females of age group 40-55 years with ceased menstruation for at least one year. BMI of subjects was calculated by using their weight (Kg) and height (m) and Asian BMI cut-offs were used to categorize the females. Blood samples collected from respective subjects, after sampling serum and plasma was separated. Levels of Vitamin D3 and PTH hormone were estimated with the help of ELISA Kit, while serum Calcium was through colorimetric method. Serum calcium and Vit D3 levels of obese menopausal women were significantly reduced. However, PTH levels of obese postmenopausal women were found significantly elevated than control females that indicate greater risk of bone turnover after menopause especially in obese women.

Keywords: Menopause, Obesity, Serum calcium, Vit D3, PTH

INTRODUCTION

Menopause is marked with rapid bone loss due to estrogen decline particularly in the early years after menopause (Suresh & Naidu, 2006). Calcium ion is a fundamental structural element of the skeleton, and plays a basic role to sustain the strength of bones and joints. Insufficient nutrition along with endocrine disorders leads to osteoporosis (Sheweita & Khoshal, 2007). Parathyroid hormone, vitamin D and calcitonin play a vital role to regulate calcium ion concentration by the intestinal calcium absorption, excretion through kidneys, and bone uptake and release of calcium

(Guyton&Hal, 2006).

Various endocrine factors like estrogen and PTH involved in maintaining bone health and blood calcium level in the human body (Garneo & Delmas, 2004). Usually at the age of 40–50 yearsthe reproductive phase of females ceased and ultimately there is cessation of the cycle, which is called menopause (Guyton & Hal, 2006). Bone loss is triggered by estrogens deficiency after the menopause as well as age related processes (Garcia-Perez *et al.*, 2004). Estrogens deficiency may induce calcium loss after menopause thus intestinal calcium uptake decreases in such women (Qureshi *et al.*, 2010; Nordin *et al.*, 2004). Serum 25-hydroxyvitamin D (25OHD) concentration if less than 12 ng/mL then it is called vitamin D deficiency, and insufficiency when 12–20 ng/mL (Ross, 2011). Vitamin D deficiency is linked with many of the same health risks as obesity, such as cardiovascular disease, certain cancers, high blood pressure, osteoporosis, and secondary hyperparathyroidism (Forrest & Stuhldeher, 2011; Holick *et al.*, 2011; Holick, 2005). Obesity interferes with vitamin D and endocrine system (Snijder *et al.*, 2005; Shirazi *et al.*, 2013; Bolland *et al.*, 2006; Blum *et al.*, 2008). Hyperparathyroidism is reported in obesity, however there is inverse association of obesity with serum 25OHD levels (Snijder *et al.*, 2005; Shirazi *et al.*, 2013). Increased adiposity cause decrease bioavailability of vitamin D for intestinal calcium uptake (Bolland *et al.*, 2006; Blum *et al.*, 2008). Deficiency of serum 25OHD causes a reimbursement elevation in PTH synthesis and secretion to sustain serum calcium levels.

Low levels of Vitamin D increased the parathyroid hormone (PTH) concentration (Holick, 2005; Bilezikian *et al.*, 2014). Both PTH and 25OHD play essential roles in maintaining serum calcium levels (Bilezikian *et al.*, 2014). Raised serum PTH for a longer period of time increases the osteoclast activity and excretion of phosphorous through urine, thus reducing the bone mass (Holick, 2005; Bilezikian *et al.*, 2014). Incidence of osteoporosis is much prevalent in Pakistan. Osteoporosis frequency in women of age group 75-84 years is about 97% and 55% of women with age group 45-54 years prompted to osteoporosis (Habiba *et al.*, 2002). The National Osteoporosis Foundation suggested that lifestyle modification reduce the risk of osteoporosis after menopause. Healthy life style may reduce the risk up to 20–40% the risk of bone turn over in advanced age (Weaver *et al.*, 2016). Aging, housing structures, non exposure to sunlight, and clothing, restrictions of females to the indoor are major contributing factors of vitamin D deficiency in our society (Khan *et al.*, 2012). This study was performed to examine the

differences in serum calcium, vitamin D3 and parathyroid hormone (PTH) level in obese post-menopausal women as compared to normal weight (control) post-menopausal women.

METHODOLOGY

This experiment was performed in Karachi city of Pakistan between, January 2015 to April 2015. Research ethics committee of Federal Urdu University of Arts Science and Technology approved the study procedure. We included women aged 40-55 years with ceased menstruation for at least 12 month and had a natural menopause. The home visits included the use of a face-to-face questionnaire and written consent was obtained from each subject. A total of 84 postmenopausal women were volunteered for the study which included 13 normal weight/control (BMI=18.5-22.9 Kg/m²) and 71 obese(BMI>25Kg/m²). Asian BMI cut-offs were use to categorized the females (Low *et al.*, 2009).Subjects with hysterectomy, hormone replacement therapy and suffering from any chronic disease were not included.BMI of subjects was calculated by using their weight (Kg) and height (m).A fasting venous blood sample of 5ml was taken. Serum and plasma was separated for further estimation.For Estimation of PTH, Intact PTH ELISA kit used: (Catalog # 950.090.096 Diaclone SAS, France). Vitamin D level was determined through ELISA (Calibotech Inc., USA) and Serum Calcium through by colorimetric method using Spectrum kit.

Statistical analysis was achieved using the SPSS statistical software (SPSS, Chicago, IL, USA). Statistical analysis Mean \pm SD of all the variables was determined. Student's *t*-test was applied to see the significance of difference of parameters between two groups. P values $<$ 0.05 were accepted as significant.

RESULTS AND DISCUSSION

The results revealed that the mean age of normal control postmenopausal women (n=13) was (49.31 \pm 1.01) years, while mean age of obese women (n=71) was (50.21 \pm 0.63) years. The findings evaluated the significant differences in the average BMI values of control (22.14 \pm 0.023) kg/m² and obese postmenopausal women (35.93 \pm 0.72) kg/m². BMI of obese females were significantly higher than control females (P<0.001).

Serum calcium level of obese postmenopausal women (5.48 \pm 0.18 mg/ml) showed significant reduction as compare with normal weight females (8.11 \pm 0.33) (P<0.05). Normal weight females average Vitamin D level was (34.43 \pm 4.67) ng/ml and obese femaleswere (11.99 \pm

0.67) ng/ml respectively. Obese postmenopausal women exhibited a considerable reduced level of vitamin D ($P < 0.001$). Normal weight females average PTH level was (14.73 ± 2.08) pg/ml and obese females were (30.95 ± 2.05) pg/ml respectively. Parathyroid hormone of obese postmenopausal women exhibited a considerable elevation as compare with normal weight females ($P < 0.01$) (Fig 1).

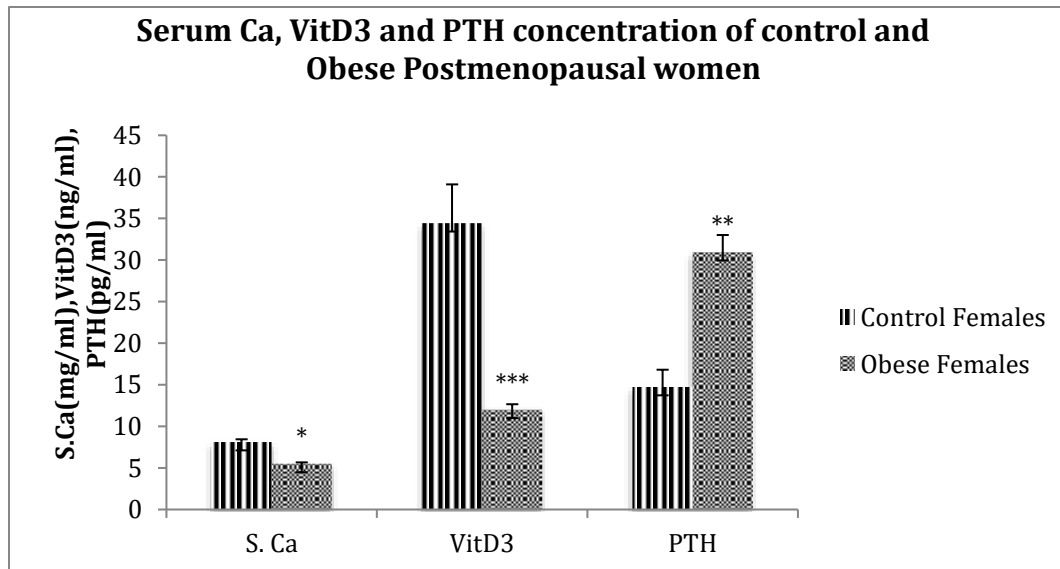


Fig 1. Serum Ca, VitD3 and PTH concentration of control and Obese Postmenopausal women

In the present experiment serum calcium, vitamin D3 status and parathyroid hormone was evaluated in normal weight and obese postmenopausal women. BMI criteria for Asian population was used to grouped the females into normal weight ($BMI = 18.5-22.9 \text{ Kg/m}^2$) and obese ($BMI > 25 \text{ Kg/m}^2$) (Low *et al.*, 2009). Our findings suggested lower serum Vitamin D as well as calcium level however higher concentration of serum PTH in obese group. Serum 25-hydroxy vitamin D deficiency is defined as when its concentration is less than 10 ng/ml, when its range is 10-20 ng/ml it's called insufficiency and sufficient when > 21 ng/ml (Suresh & Naidu, 2006). In the present study, the 25hydroxy vitamin D levels in postmenopausal women were found to be between 10 and 20 ng/ml, which indicate vitamin D insufficiency. This finding is in line with study conducted by Yikilkan *et al.* (2013), authors reported Vit D3 insufficiency and raised concentration of PTH in women with ceased menstruation for at least 1 year and had body mass index ($BMI < 25 \text{ kg/m}^2$) (Yikilkan *et al.*, 2013). Several studies have shown that low serum calcium levels, hypovitaminosis D and hyperparathyroidism are the top most risk elements for

developing osteoporosis (Sosa *et al.*, 2009; Atik, 2008; Boonen *et al.*, 2004).

Hypovitaminosis D is mainly caused by poor diet, limited exposure to sunlight, hydroxylation of vitamin D through kidneys, and a reduced synthesis of vitamin D in the skin. Natural food sources of vitamin D are very few; therefore, vitamin D main source is sunlight exposure. Studies showed that clothing pattern and sunlight exposure are the principal aspects for vitamin D insufficiency in Pakistani women signifying a high rate of 25(OH) D deficiency in these women (Lowe *et al.*, 2011; Fahim, 2005). Most of the women in this study did not utilize the dairy products on a regular basis, so they were deprived of proper dietary calcium intake. Our findings coincide with the previous study conducted by Lowe *et al.* (2011) in the rural community of Peshawar, Pakistan, authors also reported a low calcium diet consumption by these women, coupled with low vitamin D status, result in a very low rate of calcium absorption (Lowe *et al.*, 2011). Clothing trends like wearing a full burqa when outside, sedentary lifestyle, housing structure in urban population (Karachi) less exposure to daylight are major factors for the low vitamin D and ultimately low calcium levels.

Several studies observed that in menopause obesity may increase the risk factors for severe menopausal symptoms (Thurston *et al.*, 2008; Da Fonseca *et al.*, 2013). Khokhar *et al.* (2010) also demonstrated the higher incidence of overweight and obesity in menopause as compared to premenopause (Khokhar *et al.*, 2010). Overweight and obesity is increased with the age as well as sedentary lifestyle of women in our society, this outcome is confirmed by the study conducted by the Nazli *et al.* (2015), authors observed a significant association between obesity and age, which, according to the authors, could be credited to a decreased physical activity with increasing age. They also discussed that social restriction predominant in our society that reserves women to reside at home and refrain from going outside for walk or outdoor activities (Nazli *et al.*, 2015).

As we have compared the different parameters of normal weight with obese postmenopausal women, so both the studied groups were postmenopausal. Not much work has been done to study the prevalence of obesity related altered vitamin D, calcium and PTH hormone concentration among normal weight and postmenopausal women at national and international level. Most of the studies performed to study the pre and postmenopausal comparison. Although studies are there which show the relationship between increase in obesity at menopause and occurrence of

obesity related morbidities like diabetes, hypertension.

Large-scale studies evaluated the positive correlation of obesity with lower 25D concentrations, high PTH concentrations (Parikh *et al.*, 2004; Lagunova *et al.*, 2009). However, Arunabh *et al.* (2003) demonstrated inverse relation of serum 25D concentration to body fat contents (Arunabh *et al.*, 2003). Another study also described that weight gain leads to lower level of Vitamin D3 (Vimeswaran *et al.*, 2013). The relation between decreased vitamin D3 levels and obesity is thus well documented

CONCLUSION

Vitamin D insufficiency, low calcium status as well as raised PTH concentration was very common in obese postmenopausal population and are the most important risk factors of osteoporosis after menopause. Future studies are suggested to spread awareness about the significance of calcium and vitamin D intake to prevent bone loss and weight management through exercise or daily walk after menopause.

REFERENCES

- Arunabh, S., Pollack, S., Yeh, J., & Aloia, J. F. (2003). Body fat content and 25-hydroxyvitamin D levels in healthy women. *The Journal of Clinical Endocrinology & Metabolism* 88(1): 157-161.
- Atik O.S. (200). Osteoporotic fracture risk assessment. *Joint Dis Rel Surg*, 19: 100.
- Bilezikian, J. P., Marcus, R., Levine, M. A., Marcocci, C., Silverberg, S. J., & Potts, J. T. (Eds.). (2014). *The parathyroids: basic and clinical concepts*. academic Press.
- Blum, M., Dolnikowski, G., Seyoum, E., Harris, S. S., Booth, S. L., Peterson, J. & Dawson-Hughes, B. (2008). Vitamin D 3 in fat tissue. *Endocrine* 33(1): 90-94.
- Bolland, M. J., Grey, A. B., Ames, R. W., Horne, A. M., Gamble, G. D., & Reid, I. R. (2006). Fat mass is an important predictor of parathyroid hormone levels in postmenopausal women. *Bone*, 38(3): 317-321.
- Boonen, S., Rizzoli, R., Meunier, P. J., Stone, M., Nuki, G., Syversen, U., ... & Reginster, J. Y. (2004). The need for clinical guidance in the use of calcium and vitamin D in the management of osteoporosis: a consensus report. *Osteoporosis international*, 15(7): 511-519.

- Maggio Da Fonseca, A., Bagnoli, V. R., Souza, M. A., Azevedo, R. S., Couto Junior, E. D. B., Soares Junior, J. M., & Baracat, E. C. (2013). Impact of age and body mass on the intensity of menopausal symptoms in 5968 Brazilian women. *Gynecological Endocrinology* 29(2): 116-118.
- Fahim, F. (2005). The magnitude of low bone mineral [corrected] density in middle and old age women. *JPM. The Journal of the Pakistan Medical Association* 55(11): 500-502.
- Forrest, K. Y., & Stuhldreher, W. L. (2011). Prevalence and correlates of vitamin D deficiency in US adults. *Nutrition research* 31(1): 48-54.
- García-Pérez, M. A., Moreno-Mercer, J., Tarin, J. J., & Cano, A. (2004). Bone turnover markers and PTH levels in surgical versus natural menopause. *Calcified tissue international* 74(2): 143-149.
- Garneo P, Delmas PD. Bone turnover markers. *Encyclopedia of Endocrine Diseases* (2004). Eds Martin L. California: Elsevier Inc; 401-13.
- Guyton, A. C., & Hall, J. E. (2006). Textbook of medical physiology, 11th. *WB Saunders Company, Philadelphia*.
- Habiba, U., Ahmad, S., & Hassan, L. (2002). Predisposition to osteoporosis in postmenopausal women. *Journal-College of Physicians and Surgeons of Pakistan* 12: 297-301.
- Holick, M. F. (2005). The vitamin D epidemic and its health consequences. *The Journal of nutrition* 135(11): 2739S-2748S.
- Holick, M. F., Binkley, N. C., Bischoff-Ferrari, H. A., Gordon, C. M., Hanley, D. A., Heaney, R. P. & Weaver, C. M. (2011). Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *The Journal of clinical endocrinology & metabolism* 96(7): 1911-1930.
- Khan, A. H., Iqbal, R., Naureen, G., Dar, F. J., & Ahmed, F. N. (2012). Prevalence of vitamin D deficiency and its correlates: results of a community-based study conducted in Karachi, Pakistan. *Archives of osteoporosis* 7(1): 275-282.
- Khokhar, K. K., Kaur, G., & Sidhu, S. (2010). Prevalence of obesity in working premenopausal and postmenopausal women of Jalandhar District, Punjab. *Journal of Human Ecology* 29(1): 57-62.
- Lagunova, Z., Porojnicu, A. C., Lindberg, F., Hexeberg, S., & Moan, J. (2009). The dependency of vitamin D status on body mass index, gender, age and season. *Anticancer research* 29(9): 3713-3720.

- Low, S., Chin, M. C., Ma, S., Heng, D., & Deurenberg-Yap, M. (2009). Rationale for redefining obesity in Asians. *Annals Academy of Medicine Singapore* 38(1): 66.
- Lowe, N. M., Ellahi, B., Bano, Q., Bangash, S. A., Mitra, S. R., & Zaman, M. (2011). Dietary calcium intake, vitamin D status, and bone health in postmenopausal women in rural Pakistan. *Journal of health, population, and nutrition* 29(5): 465.
- Nazli, R., Akhtar, T., Lutfullah, G., Khan, M. A., Lutfullah, G., & Haider, J. (2015). Prevalence of obesity and associated risk factor in a female population of rural Peshawar-Pakistan. *Khyber Med Univ Journal* 7(1): 19-24.
- Nordin, B. C., Need, A. G., Morris, H. A., O'Loughlin, P. D., & Horowitz, M. (2004). Effect of age on calcium absorption in postmenopausal women. *The American journal of clinical nutrition* 80(4): 998-1002.
- Parikh, S. J., Edelman, M., Uwaifo, G. I., Freedman, R. J., Semega-Janneh, M., Reynolds, J., & Yanovski, J. A. (2004). The relationship between obesity and serum 1, 25-dihydroxy vitamin D concentrations in healthy adults. *The Journal of Clinical Endocrinology & Metabolism* 89(3): 1196-1199.
- Qureshi, H. J., Hussain, G., Jafary, Z. A., Bashir, M. U., Latif, N., & Riaz, Z. (2010). Calcium status in premenopausal and postmenopausal women. *Journal of Ayub Medical College Abbottabad* 22(2): 143-145.
- Ross, A. C. (2011). The 2011 report on dietary reference intakes for calcium and vitamin D. *Public health nutrition* 14(5): 938-939.
- Sheweita, S. A., & Khoshhal, K. I. (2007). Calcium metabolism and oxidative stress in bone fractures: role of antioxidants. *Current drug metabolism*; 8(5): 519-525.
- Shirazi, L., Almquist, M., Malm, J., Wirfält, E., & Manjer, J. (2013). Determinants of serum levels of vitamin D: a study of life-style, menopausal status, dietary intake, serum calcium, and PTH. *BMC women's health* 13(1): 1-13.
- Snijder, M. B., van Dam, R. M., Visser, M., Deeg, D. J., Dekker, J. M., Bouter, L. M. & Lips, P. (2005). Adiposity in relation to vitamin D status and parathyroid hormone levels: a population-based study in older men and women. *The Journal of Clinical Endocrinology & Metabolism* 90(7): 4119-4123.
- Sosa Henriquez M, Gomez de Tejada Romero M.J. (2009). Evidenced based medicine and drugs approved for the treatment of osteoporosis. Role of calcium and vitamin D. *Rev Clin Esp*; 209: 25-36.
- Suresh M, Naidu DM (2006). Influence of years since menopause on bone mineral metabolism in South Indian women. *Indian journal of medical sciences*; 60(5): 190-198.

- Thurston, R. C., Sowers, M. R., Chang, Y., Sternfeld, B., Gold, E. B., Johnston, J. M., & Matthews, K. A. (2008). Adiposity and reporting of vasomotor symptoms among midlife women: the study of women's health across the nation. *American journal of epidemiology* 167(1): 78-85.
- Vimaleswaran, K. S., Berry, D. J., Lu, C., Tikkanen, E., Pilz, S., Hiraki, L. T. & Hyppönen, E. (2013). Causal relationship between obesity and vitamin D status: bi-directional Mendelian randomization analysis of multiple cohorts. *PLoS medicine* 10(2): e1001383.
- Weaver, C. M., Gordon, C. M., Janz, K. F., Kalkwarf, H. J., Lappe, J. M., Lewis, R. & Zemel, B. S. (2016). The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. *Osteoporosis international* 27(4): 1281-1386.
- Yikilkan, H., Aypak, C., Görpeliöglu, S., Dicle, M., & Önder, Ö. (2013). Parathyroid hormone and optimal vitamin D status in postmenopausal women. *Turkish Journal of Medical Sciences* 43(6): 990-994.