

# A Cross-Sectional Study on the Association of TSH Levels and Bone Mineral Densitometry of Postmenopausal Women at Makati Medical Center

Milldeanna de Guzman, M.D.\*; Monica Therese Cating-Cabral, M.D.\*; Andres Ebison Jr, M.D.\*; and Joie DJ Isip, M.D.\*

## Abstract

**Introduction:** Thyroid stimulating hormone (TSH) acts on the thyroid gland to induce thyroid hormone synthesis and maintain trophic thyroid cell integrity. Earlier studies determined the role of thyroid hormones on bone metabolism, skeletal development and establishment of peak bone mass, but had conflicting results. This study aims to determine the association of TSH levels with bone mineral density (BMD) scores on healthy postmenopausal women.

**Methodology:** This is a cross-sectional study involving healthy postmenopausal women seen at the Makati Medical Center (MMC). Linear correlation of TSH and BMD scores was determined by Pearson correlation analysis. Odds ratio (OR) for osteoporosis and/or osteopenia in range-based categories of TSH was computed using binary logistic regression.

**Results:** TSH levels were found to have weak inverse

correlation with lowest BMD scores, spine and femur (p-value 0.959, 0.491 and 0.715 respectively). OR for osteoporosis has no statistical significance for each range-based categories of TSH. Women with TSH levels of 2.50-3.49 mU/l has lower OR (p value 0.032, OR 0.23, 95% CI) of having osteoporosis or osteopenia than in women in the reference category but was not significant after adjustment with other variables (p-value 0.107).

**Conclusion:** There is no significant association between TSH levels and BMD scores amongst healthy postmenopausal woman. Odds of having osteoporosis and/or osteopenia have no statistical significant correlation with any given range of TSH levels. Age, amongst other variables, remained a significant factor in having osteoporosis and/or osteopenia.

**Keywords:** TSH, BMD, Postmenopausal women, osteoporosis

## Introduction

Thyroid stimulating hormone (TSH), which is produced by thyrotrophs in the anterior pituitary gland, acts on the thyroid gland causing the two established main function of the hormone: to induce thyroid hormone synthesis and to maintain trophic thyroid cell integrity. It acts through the TSH G protein-coupled receptor located on the thyrocyte plasma membrane.<sup>1</sup> However, TSH receptors (TSHR) were found, not only in thyroid gland, but also in lymphocytes, pituitary, thymus, fibroblasts, kidneys and adipose tissues which leads to studies on different biological actions of TSH.

A study by Etsuko, Abe et al, provided evidence for direct effects of TSH on bone remodelling using cellular and molecular approaches through TSHR null mice. With the use of high-resolution dual photon confocal imaging and immunostaining, the study showed that bone cell precursors express TSH receptors, and that the expression

of these receptors is maximal during the early and mid phase of osteoclast and osteoblast formation. The study has shown that TSH inhibits osteoclast formation and survival and osteoblast differentiation and type 1 collagen expression, defining its role on both bone formation and resorption.<sup>3</sup>

Several studies, therefore, came out these recent years with the aim of determining the clinical role of TSH on bone formation, bone remodelling, and its association with osteoporosis. Earlier studies determined the role of thyroid hormones on bone metabolism, skeletal development and establishment of peak bone mass. However, little is known if TSH has direct effects of bone metabolism as well.

A prospective study in Europe was done by Murphy et al, associating the thyroid function with bone mineral density and risk on nonvertebral fractures in healthy euthyroid postmenopausal women. Higher FT4 and FT3 were associated with lower bone mineral density (BMD) and increased risk in nonvertebral fracture. Higher TSH on the other hand turned out to be protective and nonvertebral fracture risk was decreased.<sup>4</sup>

On the other hand, a study by Kim et al. on the association of TSH levels and BMD scores in healthy euthyroid men, showed results suggesting that serum TSH

\*Makati Medical Center, Department of Medicine, Section of Endocrinology, Diabetes and Metabolism

Corresponding Author: Milldeanna L. de Guzman, M.D., Makati Medical Center, Makati City, Philippines  
Email: milldeguzmanmd@gmail.com

levels within the low end of reference range may be associated with low BMD in men.<sup>5</sup>

TSH was not recommended for routine screening of postmenopausal women with osteoporosis with no known thyroid illness, unless with high index of clinical suspicion.<sup>6</sup> Since recent investigations on the possible association of TSH and bone mineral density and the possible role of TSH in bone remodeling have conflicting results, this study, using a cross-sectional design, aims to determine the association of TSH levels and BMD scores in healthy Filipino postmenopausal women who underwent executive check-up from year 2012-2015. Data was collected from the patient records, which includes BMD scores at the lumbar spine and femoral neck using dual energy X-absorptiometry (DEXA) and TSH concentrations measured through Immunoradiometric assay (IRMA). The association of TSH levels and BMD scores was determined using Pearson correlation analysis.

## OBJECTIVES

**General objective:** To determine the association of TSH levels with BMD scores.

### Specific objectives:

1. To determine the association of serum TSH levels with BMD scores in healthy postmenopausal women who underwent executive check-up in Makati Medical Center from year 2012-2015.

2. To determine the odds of having osteopenia and osteoporosis in relation to TSH levels of healthy postmenopausal women who underwent executive check-up in Makati Medical Center from year 2012-2015.

3. To determine the association of other variables such as age, body mass index (BMI) and smoking history with BMD scores in healthy postmenopausal women who underwent executive check-up in Makati Medical Center from year 2012-2015.

## Methodology

This is a single center cross-sectional study which involved healthy Filipino women, age 40 years old and above, in menopause (defined as cessation of menses for at least 12 consecutive months), who had an executive check-up at Makati Medical Center from 2012 to 2015. Women who have thyroid disease, cancer, chronic kidney disease, parathyroid disease, acromegaly, hypercortisolism, porphyria, anorexia, myeloma, as well as patients who are taking medications affecting thyroid function and bone mineral density such as levothyroxine, anti-thyroid

medications, lithium, anti-epileptics, bisphosphonates, chemotherapy and on any form of dialysis were excluded. Records were reviewed by the investigator, and demographic data was collected which includes: age, height, weight, BMI, co-morbidities and medications, past medical history, smoking history, serum TSH levels and BMD scores.

A minimum of 67 subjects were required for this study based on a level of significance of 5.0%, a power of 80%, and an odd of having osteoporosis when BMD at the lumbar spine increased with TSH level based on Kim DJ, et al.<sup>7</sup> Given that the approximate population for this study was 100 subjects, adjustment for small sample size was used.

## STATISTICAL ANALYSIS

Descriptive statistics was used to summarize the clinical characteristics of the patients. Frequency and proportion were used for nominal variables, median and IQR for ordinal variables, and mean and SD for interval/ratio variables. In data analyses, the association of serum TSH levels with T-scores measured by BMD-DEXA scores of the spine or femoral neck was determined using Pearson correlation analysis. To determine which of the independent variables: TSH level, age, BMI, and smoking history, is associated with the risk of having osteoporosis or osteopenia, binary logistic regression was used. Odds ratios (OR) with 95% confidence interval (CI), of 1) Osteoporosis alone (defined as T-score of -2.5 or below), or 2) Osteoporosis and osteopenia (defined as T-score of -1 or below), within different range-based categories of TSH compared with reference range category (TSH 0.50-1.49 mU/IU) was estimated in logistic regression model. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at 0.05  $\alpha$ -level of significance. STATA 12.0 was used for data analysis.

## ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Institutional Review Board (IRB) of Makati Medical Center. It was conducted in accordance with the ethical principles set out in relevant guidelines (Declaration of Helsinki 2008, WHO Operational Guidelines, ICH-GCP and National Ethics Guidelines for Health Research). All precautions were made to maintain privacy of the patient's data involved in this study. A special research code number was assigned to medical record information and personal identifiers (name, medical record number) were removed. Information linking the research code number to the name and other personal identifiers was stored in a separate secured location which can only be accessed by the investigator.

## Results

A total of 149 records listed under the postmenopausal package from the year 2012 to 2015 were reviewed. Thirteen of them were taking thyroid medications and ten of them were taking medications for osteoporosis. Thirty-eight of them have missing records resulting in exclusion of 61 subjects, obtaining a total inclusion of 88 subjects in the study.

Characteristics of subjects were given at Table I. The study population comprises of post-menopausal women with a mean age of 57 years old and an average BMI of

**Table I. Demographic profile of patients (n=88)**

|                          | Frequency (%); Mean + SD |
|--------------------------|--------------------------|
| Age (yrs)                | 56.80 ± 7.35             |
| Height (cm)              | 154.79 ± 7.95            |
| Weight (kg)              | 62.51 ± 11.35            |
| BMI (kg/m <sup>2</sup> ) | 26.26 ± 5.50             |
| Comorbidities            |                          |
| Hypertensive             | 37 (42.05)               |
| Diabetic                 | 13 (14.77)               |
| Liver disease            | 63 (71.59)               |
| Dyslipidemia             | 64 (72.73)               |
| Smoker                   | 12 (13.64)               |
| TSH (mIU/L)              | 1.68 + 0.92              |

26 kg/m<sup>2</sup>. Majority of them belong to obese 1 classification (39.78%, n=35). The mean (±SD) TSH level was 1.68 ± 0.92 mIU/L, all are euthyroid. Eighty-four percent of them have co-morbidities, either hypertension, diabetes, dyslipidemia, liver disease and kidney disease. Dyslipidemia and liver disease were prevalent in roughly seven out of 10 women. Twenty-two percent of the study population has osteoporosis while 55% has osteopenia.

Using Pearson correlation analysis, TSH concentrations were found to have weak inverse correlation with BMD scores at spine and femur (Table II).

The odds of having osteoporosis between the reference category and other TSH categories did not show any statistical significant difference. Adjustment with other variables (age, BMI, and smoking history) was done and showed the same results (Table III).

While the rest of TSH level categories showed no significant difference in the odds ratio of having a T-score lower than -1, the TSH level category of 2.50-3.49 mIU/L showed a significant decrease on the OR compared with the reference range. After adjustment with other variables, the difference between the OR did no longer show statistical significance (Table IV).

Supplemental analysis on determining the association of TSH, age, BMI and smoking history, with the odds of having osteoporosis was done using logistic regression analysis. It showed that with per unit increase in BMI, there was a 13% decrease in odds of having osteoporosis (Table V). Additional regression was done analyzing this association and showed no statistical significance (Table VI).

When cases of osteoporosis and osteopenia were combined, analyses showed that age was significantly associated with increased odds of having a T-score lower than -1. In contrast to the previous finding, BMI had no significant association with osteoporosis (Table VII).

**Table II. Correlation between TSH levels with BMD scores**

|                             | Correlation Coefficient | Degree of Association | P-value |
|-----------------------------|-------------------------|-----------------------|---------|
| BMD spine                   | -0.0745                 | Negatively weak       | 0.4905  |
| BMD femur                   | -0.0395                 | Negatively weak       | 0.7150  |
| Lowest BMD (spine or femur) | -0.0056                 | Negatively weak       | 0.9590  |

Statistical method used was Pearson correlation analysis.

The correlation coefficient is interpreted as follows:  $p < 0.300$  = weak;  $0.500 - 0.300$  = moderate,  $p > 0.500$  = strong.

**Table III.** Odds ratio of osteoporosis from BMD measured in spine or femur in association with different TSH levels

| TSH levels (mU/L) | Osteoporosis <sup>a</sup> | Non-cases <sup>b</sup> | OR (95% CI)          | Adjusted OR (95% CI) |
|-------------------|---------------------------|------------------------|----------------------|----------------------|
|                   | Frequency (%)             |                        |                      |                      |
| spine             | (n=12)                    | (n=76)                 |                      |                      |
| < 0.50            | 0                         | 2 (2.63)               | 1                    | 1                    |
| <b>0.50-1.49</b>  | 7 (58.33)                 | 41 (53.95)             | (reference)          | (reference)          |
| 1.50-2.49         | 4 (33.33)                 | 17 (22.37)             | 1.38 (0.36 to 5.33)  | 2.48 (0.54 to 11.49) |
| 2.50-3.49         | 0                         | 13 (17.11)             | 1                    | 1                    |
| 3.50 and above    | 1 (8.33)                  | 3 (3.95)               | 1.95 (0.18 to 21.54) | 1.08 (0.05 to 23.59) |
| femur             | (n=13)                    | (n=75)                 |                      |                      |
| < 0.50            | 0                         | 2 (2.67)               | 1                    | 1                    |
| <b>0.50-1.49</b>  | 7 (53.85)                 | 41 (54.67)             | (reference)          | (reference)          |
| 1.50-2.49         | 5 (38.46)                 | 16 (21.33)             | 1.83 (0.51 to 6.62)  | 3.09 (0.72 to 13.32) |
| 2.50-3.49         | 0                         | 13 (17.33)             | 1                    | 1                    |
| 3.50 and above    | 1 (7.69)                  | 3 (4)                  | 1.95 (0.18 to 21.54) | 1.42 (0.11 to 18.75) |
| Lowest BMD        | (n=19)                    | (n=69)                 |                      |                      |
| < 0.50            | 0                         | 2 (2.90)               | 1                    | 1                    |
| <b>0.50-1.49</b>  | 11 (57.89)                | 37 (53.62)             | (reference)          | (reference)          |
| 1.50-2.49         | 7 (36.84)                 | 14 (20.29)             | 1.68 (0.54 to 5.20)  | 3.28 (0.84 to 12.74) |
| 2.50-3.49         | 0                         | 13 (18.84)             | 1                    | 1                    |
| 3.50 and above    | 1 (5.26)                  | 3 (4.35)               | 1.12 (0.11 to 11.89) | 0.69 (0.05 to 10.02) |

<sup>a</sup> Osteoporosis defined as T-score of < -2.5 in BMD measurement<sup>b</sup> Non-cases defined as T-score of > -2.5 in BMD measurement**Table IV.** Odds ratio of Osteoporosis and Osteopenia combined from BMD measured in spine or femur in association with different TSH levels.

| TSH levels (mU/L) | Osteoporosis and Osteopenia <sup>a</sup> | Non-cases <sup>b</sup> | OR (95% CI)                      | Adjusted OR (95% CI) |
|-------------------|------------------------------------------|------------------------|----------------------------------|----------------------|
|                   | Frequency (%)                            |                        |                                  |                      |
| spine             | (n=47)                                   | (n=41)                 |                                  |                      |
| < 0.50            | 0                                        | 2 (4.88)               | 1                                | 1                    |
| <b>0.50-1.49</b>  | 26 (55.32)                               | 22 (53.66)             | (reference)                      | (reference)          |
| 1.50-2.49         | 13 (27.66)                               | 8 (19.51)              | 1.38 (0.48 to 3.92)              | 1.79 (0.56 to 5.73)  |
| 2.50-3.49         | 5 (10.64)                                | 8 (19.51)              | 0.53 (0.15 to 1.85)              | 0.41 (0.09 to 1.84)  |
| 3.50 and above    | 3 (6.38)                                 | 1 (2.44)               | 2.54 (0.25 to 26.18)             | 2.72 (0.21 to 34.63) |
| femur             | (n=65)                                   | (n=23)                 |                                  |                      |
| < 0.50            | 0                                        | 2 (8.70)               | 1                                | 1                    |
| <b>0.50-1.49</b>  | 39 (60)                                  | 9 (39.13)              | (reference)                      | (reference)          |
| 1.50-2.49         | 16 (24.62)                               | 5 (21.74)              | 0.74 (0.21 to 2.55)              | 1.08 (0.24 to 4.79)  |
| 2.50-3.49         | 7 (10.77)                                | 6 (26.09)              | 0.27 (0.07 to 1.00) <sup>c</sup> | 0.24 (0.04 to 1.40)  |
| 3.50 and above    | 3 (4.62)                                 | 1 (4.35)               | 0.69 (0.06 to 7.45)              | 0.79 (0.05 to 13.43) |
| Lowest BMD        | (n=67)                                   | (n=21)                 |                                  |                      |
| < 0.50            | 0                                        | 2 (9.52)               | 1                                | 1                    |
| <b>0.50-1.49</b>  | 40 (59.70)                               | 8 (38.10)              | (reference)                      | (reference)          |
| 1.50-2.49         | 17 (25.37)                               | 4 (19.05)              | 0.85 (0.23 to 3.21)              | 1.39 (0.27 to 7.04)  |
| 2.50-3.49         | 7 (10.45)                                | 6 (28.57)              | 0.23 (0.06 to 0.88) <sup>d</sup> | 0.19 (0.03 to 1.19)  |
| 3.50 and above    | 3 (4.48)                                 | 1 (4.76)               | 0.6 (0.06 to 6.53)               | 0.64 (0.03 to 11.57) |

<sup>a</sup> Osteoporosis and Osteopenia defined as T-score of < -1.0 in BMD measurement<sup>b</sup> Non-cases defined as T-score of > -1.0 in BMD measurement<sup>c</sup> - *P*-Value = 0.050; <sup>d</sup> - *P*-Value = 0.032

**Table V.** Association of TSH, Age, BMI, and Smoking history with Osteoporosis defined by lowest T-score as measured by BMD of either spine or femur using logistic regression analysis.

| TSH levels (mU/L) | Osteoporosis <sup>a</sup><br>(n=19) | Non-cases <sup>b</sup><br>(n=69) | OR (95% CI)         | P-value |
|-------------------|-------------------------------------|----------------------------------|---------------------|---------|
|                   | Frequency (%); Mean + SD            |                                  |                     |         |
| TSH               | 1.60 ± 0.99                         | 1.70 ± 0.90                      | 0.84 (0.47 to 1.53) | 0.575   |
| Age               | 58.58 ± 5.96                        | 56.30 ± 7.65                     | 1.04 (0.97 to 1.12) | 0.242   |
| BMI               | 24.48 ± 4.21                        | 26.75 ± 5.73                     | 0.87 (0.75 to 1.00) | 0.049   |
| Smoker            | 0                                   | 12 (17.39)                       | 1                   | -       |

*P-Value = 0.0726; R<sup>2</sup> = 8.16%*

<sup>a</sup> Osteoporosis defined as T-score of < -2.5 in BMD measurement

<sup>b</sup> Non-cases defined as T-score of > -2.5 in BMD measurement

**Table VI.** Association of BMI with Osteoporosis defined by lowest T-score as measured by BMD of either spine or femur using logistic regression analysis.

|     | Odds Ratio | 95% CI           | P-Value |
|-----|------------|------------------|---------|
| BMI | 0.9044     | 0.8004 to 1.0219 | 0.107   |

*P-Value = 0.0793; R<sup>2</sup> = 3.35%*

**Table VII.** Association of TSH, Age, BMI, and Smoking history with Osteoporosis and Osteopenia combined, defined by lowest T-score as measured by BMD of either spine or femur using logistic regression analysis.

| Variables | Osteoporosis and Osteopenia <sup>a</sup><br>(n=67) | Non-cases <sup>b</sup><br>(n=21) | OR (95% CI)         | P-value          |
|-----------|----------------------------------------------------|----------------------------------|---------------------|------------------|
|           | Frequency (%); Mean + SD                           |                                  |                     |                  |
| TSH       | 1.68 ± 0.92                                        | 1.70 + 0.92                      | 1.06 (0.53 to 2.13) | 0.862            |
| Age       | 58.58 + 7.10                                       | 51.74 + 5.55                     | 1.22 (1.10 to 1.37) | <b>&lt;0.001</b> |
| BMI       | 25.83 + 5.73                                       | 27.50 + 4.70                     | 0.93 (0.84 to 1.03) | 0.145            |
| Smoker    | 8 (12.31)                                          | 4 (17.39)                        | 0.40 (0.08 to 2.07) | 0.274            |

*P-Value = 0.0003; R<sup>2</sup> = 22.13%*

<sup>a</sup> Osteoporosis and Osteopenia defined as T-score of < -1.0 in BMD measurement

<sup>b</sup> Non-cases defined as T-score of > -1.0 in BMD measurement

## Discussion

While there were many recent studies showing significant positive association between TSH and BMD, this cross-sectional study involving 88 healthy postmenopausal women showed that TSH levels had a weak inverse correlation with T-scores measured by BMD-DEXA of the spine and femur. A cross-sectional hospital-based study done last 2006 involving 959 healthy Korean postmenopausal women showed a significant positive correlation of BMD measured at the lumbar spine and femoral neck with TSH levels ( $p$  for trend  $<0.001$  at both sites). TSH levels were also categorized to quintiles to find any difference in BMD scores among quintiles. They found that those with high normal TSH levels (2.8-5.0 mU/L) had significantly higher BMDs measured at both lumbar spine and femoral neck with a  $p$  value of 0.004 and 0.006 respectively.<sup>7</sup> Same finding has been showed by a cross-sectional data based on the National Health and Nutrition Examination Survey III (NHANES III) data, involving postmenopausal American women, where BMD increased significantly as TSH increased over its reference range.<sup>9</sup> Baqi et al. also found highly significant association of TSH on BMD scores measured on the lumbar spine and femur, independent of age, BMI as well as FT4 levels ( $p$ -value  $<0.001$ ) on linear multiple regression and Pearson's correlation coefficient.<sup>10</sup> Marwaha et al. did a cross-sectional study involving 1290 Indian men and pre-menopausal women aged less than 50 years old (mean age of 30 years old) with normal thyroid function and subclinical hypothyroidism, to evaluate the correlation of thyroid function with BMD at different sites (lumbar spine, femur and forearm). The study showed no significant correlation between TSH and BMD at any sites in all subjects. In addition, they hypothesized that TSH values above 0.1 mU/L may play a permissive role in maintaining BMD explaining their finding of lack of association of TSH with BMD in both euthyroid and subclinical hypothyroid subjects.<sup>11</sup> Their speculation was based on a population-based study by Svare et al, wherein they demonstrated that BMD at radius was lower in subjects with TSH  $<0.1$  mU/L, but has a little change with increasing TSH levels.

A cross-sectional study was done by Noh et al. examining the correlation between TSH levels and osteoporosis of the lumbar spine in healthy women with normal thyroid function. The study showed significantly higher multivariate-adjusted odds ratios (ORs) for osteoporosis of the lumbar spine in 1st and 2nd quartiles of serum TSH levels as compared with the 4th quartile (OR 2.169, 95% CI 1.128-4.171; and OR 2.122, 95% CI 1.123-4.007, respectively) amongst non-obese elderly women. This was not the case however in obese women, where there was no significant increased risk of osteoporosis with any TSH levels.<sup>12</sup> In our study, the 4th quintile (TSH level category 2.50-3.49 mU/L) showed a significant decrease on the odds ratio of having either osteoporosis or osteopenia

compared with the reference range, but this was no longer seen after adjustment with other variables. This can be explained by a difference in the profile of subjects included in the 4th quintile wherein they have significant higher BMI compared with the reference range ( $p$  value= 0.032; mean BMI: 1st quintile  $25.19 \pm 3.69$ , 2nd quintile  $25.27 \pm 4.08$ , 3rd quintile  $27.58 \pm 8.04$ , 4th quintile-  $28.35 \pm 5.7$ ; 5th quintile  $25.03 \pm 0.88$ ). Using logistic regression analysis, it had also been shown that there was a decrease in the OR of having osteoporosis per unit increase on BMI in this study. This may reflect the study by Noh et al, wherein the correlation of osteoporosis and lower TSH levels found in non-obese elderly woman was not found in obese elderly woman. An inverse association of BMI and BMD status had been shown by a study done by Asomaning et al, where they demonstrated that the odds of bone loss was decreased by 12% for every unit increase in BMI (OR = 0.88, 95% CI 0.85-0.91).<sup>13</sup>

## LIMITATIONS AND RECOMMENDATIONS

The data was limited on the facts recorded on the charts that were available in medical records. An observation of BMD changes in relation to thyroid function over a period of time cannot be assessed as well. Study population was also limited. The results of the study therefore were only suggestive and not conclusive.

For further studies, we recommend to broaden the age of the study population and also apply the study in men. The association of other variables such as thyroid hormones (FT4 and FT3) to BMD scores can be considered.

## Conclusion

TSH levels within normal thyroid status were not significantly correlated with bone mineral density in this specific study population of healthy Filipino postmenopausal women seen at MMC Executive check-up department. This finding was further supplemented by insignificant odds ratio of osteoporosis and osteopenia in any given range of TSH levels. At this point, the findings supports the recommendation of not including TSH in initial screening of healthy Filipino postmenopausal women with osteoporosis who has no known thyroid disease, unless with clinical suspicion. Further investigations are still needed. Age, amongst other variables, remained a significant factor in having a T-score of less than or equal to -1.

## References

1. **Melmed S, Polonsky K, Larsen PR, Kronenberg H:** William's Textbook of Endocrinology-12th edition. Philadelphia: Elsevier Saunders, 2011.
2. **Davies T, Marians R, Latif R:** The TSH receptor reveals itself. *J Clin Invest*, 110(2): 161-164, 2002.

3. Abe E, Marians RC, Yu W, Wu XB, Ando T, Li Y, Iqbal J, Eldeiry L, Rajendren G, Blair HC, Davies TF, Zaidi M: TSH is a negative regulator of skeletal remodeling. *Cell*, 115:151–62, 2003.
4. Murphy E, Glüer CC, Reid DM, Felsenberg D, Roux C, Eastell R, Williams GR: Thyroid function within the upper normal range is associated with reduced bone mineral density and an increased risk of nonvertebral fractures in healthy euthyroid postmenopausal women. *J Clin Endocrinol Metab*, 95:3173–81, 2010.
5. Kim BJ, Lee SH, Bae SJ, Kim HK, Choe JW, Kim HY, Koh JM, Kim GS: The Association between serum thyrotropin (TSH) levels and bone mineral density in healthy euthyroid men. *Clin Endocrinol (Oxf)*, 73(3):396-403, 2010.
6. Watts N, Bilezikian J, Camacho P, Greenspan S, Harris S, Hodgson S, Kleerekoper M, Luckey M, McClung M, Pollack RP, Petak S: AACE Postmenopausal Osteoporosis Guidelines, *Endocr Pract*, 16(Suppl 3):17-19, 2010.
7. Kim DJ, Khang YH, Koh JM, Shong YK, Kim GS: Low normal TSH levels are associated with low bone mineral density in healthy postmenopausal women. *Clin Endocrinol (Oxf)*, 64:86–90, 2006.
8. Svare A, Nilsen TIL, Bjoro T, Forsmo S, Schei B, Langhammer A: Hyperthyroid levels of TSH correlate with low bone mineral density: the HUNT 2 Study. *Eur J Endocrinol*, 161: 779-786, 2009.
9. Morris MS: The association between thyroid-stimulating hormone in its reference range and bone status in postmenopausal American. *Bone*, 002040:1128–34, 2007.
10. Baqi L, Payer J, Killinger Z, Susienkova K, Jackuliak P, Cierny D, Langer P: The level of TSH appeared favourable in maintaining bone mineral density in postmenopausal women. *Endocr Regul*, 44:9–15, 2010.
11. Marwaha RK, Garg MK, Tandon N, Kanwar R, Narang A, Sastry A, Bhadra K: Thyroid Function and Bone Mineral Density among Indian Subjects. *Indian J Endocrinol Metab*, 16(4): 575–579, 2012.
12. Noh HM, Park YS, Lee J, Lee W: A cross-sectional study to examine the correlation between serum TSH levels and the osteoporosis of the lumbar spine in healthy women with normal thyroid function. *Osteoporos Int*, 26(3):997-1003, 2015.
13. Asomaning K, Bertone-Johnson ER, Nasca PC, Hooven F, Pekow PS: The association between body mass index and osteoporosis in patients referred for a bone mineral density examination. *J Womens Health (Larchmt)*, 15(9):1028-34, 2006.