EVALUATION OF THYROID FUNCTION TESTS IN POSTMENOPAUSAL OSTEOPOROTIC PATIENTS IN SULAIMANI GENERAL TEACHING HOSPITAL

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ABSTRACT

Background

Osteoporosis is a common disorder in the elderly and postmenopausal women due to loss of estrogen that increases the risk of fracture and disability. Hyperthyroidism can cause osteoporosis either due to the effect of thyroid hormones or suppressive effect of Thyroid-stimulating hormone on the bone.

Objectives

The aim of this study was to examine the association between serum thyroid-stimulating hormone levels and osteoporosis in Postmenopausal women in Sulaimani General Teaching hospital.

Patients and Methods

The study was done prospectively, we enrolled one hundred and sixty-two postmenopausal women who underwent Dual-energy X-ray absorptiometry scan in Sulaimani bone Densitometry department for routine health surveillance, thyroid function test was done for them after applying exclusion criteria.

Results

The mean thyroid stimulating hormone level (1.9 ± 1.7) vs (2.7 ± 2.30), body mass index and incidence of diabetes mellitus of the osteoporotic group is lower in comparison to those with normal bone mineral density.

Conclusion

In this study results suggest that low normal serum thyroid stimulating hormone level might be a potential risk factor for the osteoporosis in non-obese elderly women, however further prospective, large-scale, randomized controlled studies are warranted to fully establish these results.

Keywords: *Postmenopause, Osteoporosis, Thyroid, Sulaimani* .

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INTRODUCTION

Osteoporosis is a condition of decreased bone mass. This leads to fragile bones which are at an increased risk for fractures [1]. The word osteoporosis literally means "porous bones." It occurs when bones lose an excessive amount of their protein and mineral content, particularly calcium [2].

In both women and men, the balance between bone formation and resorption becomes progressively negative as they advance in age. Men, however, are less likely to develop osteoporosis than women [3].

Eighty-five percent of women in nursing homes over the age of 80 have osteoporosis, and their risk of Hip and non-vertebral fractures are 2.5 to 3.5 times more common than in the community [4].

Osteoporosis results in 1.5 million fractures per year in the United States, with the vast majority occurring in postmenopausal women [5] [5]. Furthermore, age-adjusted rates of loss in bone density at the calcaneus and total hip were associated with all-cause mortality[6].

There is a direct relationship between low levels of estrogen and the development of osteoporosis. Early menopause (before age 45) and any prolonged periods in which hormone levels are low and menstrual periods are absent can cause loss of bone mass [7] .

Many techniques are available to assess bone mineral levels, the most widely validated technique is dual energy X-ray absorptiometry (DXA) and using T-scores for the diagnosis of osteoporosis in postmenopausal women and men aged 50 years or more. It is defined as femoral neck BMD of -2.5 SD or less below the young female adult mean [8].

Hyperthyroidism is a secondary cause of osteoporosis; thyroid function test is a routine test in the evaluation of osteoporosis [9] .

The adverse effects of hyperthyroidism on the skeleton were known before the advent of satisfactory treatment for hyperthyroidism. One of the first reports of hyperthyroid bone disease was in 1891 when von Recklinghausen described the "worm-eaten" appearance of the long bones of a young woman who died from hyperthyroidism [10]. BMD (bone mineral density) was significantly decreased in patients with untreated hyperthyroidism [11] .

Thyroid hormone directly stimulates bone resorption in organ culture [12]. Higher free T4 levels within the normal reference range are associated with deterioration of trabecular microarchitecture and decreased BMD in healthy euthyroid pre and postmenopausal women [13, 14].

Increased serum interleukin-6 (IL-6) concentrations in hyperthyroid patients may also play a role in thyroid hormone-stimulated bone loss [15] .

Thyroid-stimulating hormone (TSH) may also have a direct effect on bone formation and bone resorption, mediated via the TSH receptor on osteoblast and osteoclast precursors [16, 17].

Osteoporosis appears to be independently associated with serum TSH level [18]. Low-normal serum TSH levels might be a potential risk factor for the osteoporosis of the lumbar spine in non-obese elderly women [19].

There is a laboratory difference in the reference range of TSH level. Persons with morbid obesity and persons of advanced age have higher TSH level [20, 21].

PATIENTS AND METHOD

In this cross-sectional study, 162 post-menopausal women were selected from June 2017 through December 2017, the patients were from different regions of Sulaimani governorate and they were referred to the Sulaimani bone densitometry department from different hospitals and outpatient clinics of different specialties, in order to check their BMD. The indications for checking BMD of the selected group were many, we excluded (chronic kidney disease, steroid users, malignancy, thalassemia major, chronic rheumatological diseases such as SLE (systemic lupus erythematosus), RA (Rheumatoid arthritis), Systemic sclerosis and thyroid disorders). Male and premenopausal patients were excluded as well.

In all patients, BMD was determined using dual X-ray absorptiometry (DXA, Lunar DPX-Plus), at the lumbar spine (L1–L4), wrist and at the femoral neck. BMD was measured in the radiology department of Shaheed Dr. Hemin Hospital in Sulaimani. Normal BMD or osteoporosis was calculated according to WHO criteria[22,23], based on BMD expressed as T-score indicating normal (T-score above –1 SD) and osteoporotic patients (T-score below–2.5 SD). We considered the patients osteoporotic if they showed osteoporosis in at least one site and normal if they showed normal in all three sites.

After receiving patient's informed verbal consent, thorough information was collected from the patients in a prepared data sheet regarding age, height, weight, BMI (BMI; calculated as weight in kilograms divided by the square of height in meters), and history of diabetes mellitus, and smoking. History of calcium and vitamin D intake alone or together, as well as milk and yogurt intake, was documented as well.

The blood sample was taken from the patient for assessing TSH, free T3, free T4 using the Electrochemiluminescence Immunoassay (ECLIA) on Cobas e411 and the reference range of (0.4-4.5 mIU/L) (3.1-6.8 pmol/L) (12-22 pmol/L) respectively were used.

Patients were grouped into normal, subclinical hypothyroidism, subclinical hyperthyroidism, hyperthyroidism and hypothyroidism according to this results. Table 1 [24].

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) 23, descriptive analysis was presented as mean ± standard deviation for continuous measures and absolute values (percentages) for categorical measures. A two-tailed t-test was used to compare continuous measures and an exact Fisher's test for categorical variables. The p-value of < or equal 0.05 was regarded as statistically significant.

Table 1. Classification of Thyroid Dysfunction: Biochemical Definition.

Condition	TSH Level	Thyroid Hormones	Comments
Overt hyperthyroidism	<0.1 mIU/L or undetectable	Elevated T4 or T3	
Overt hypothyroidism	>4.5 mIU/L	Low T4	
Subclinical hyperthyroidism	<0.1 mIU/L	Normal T4 and T3	Clearly low serum TSH
	0.1 to 0.4 mIU/L	Normal T4 and T3	Low but detectable
Subclinical hypothyroidism	4.5 to 10 mIU/L	Normal T4	Mildly elevated TSH
	≥10 mIU/L	Normal T4	Markedly elevated TSH

Abbreviations: T3=triiodothyronine; T4=thyroxine; TSH=thyroid-stimulating hormone.

RESULTS

The demographic characteristics of the study and thyroid function tests are presented in Table 2.

Among the one hundred and sixty-two patients enrolled in the study, one hundred and seven (66%) were having osteoporosis, the mean age for osteoporotic patients were higher than those of normal BMD 66± 8.5 and 57.4 ± 7.5 respectively (P =0.0001), in contrast, mean height and weight of normal BMD group were higher than osteoporotic (P=0.0001).

Mean BMI was lower in the osteoporotic groups than in the non-osteoporotic groups 27.1 ± 5.4 vs 33.6 ± 5.3 (P = 0.0001).

Figure 1 shows the comparison between two groups according to WHO BMI classification. Most of those with normal BMD were obese (42%), while only (27%) of osteoporotic were obese (p=0.0001).

The mean TSH level was significantly lower in the osteoporotic group (1.9 ± 1.7) vs (2.7 ± 2.30) in normal BMD group (P=0.013) Figure 2.

Biochemical classification of patients according to TSH presented in Table 3

(4.7%) of the osteoporotic group were biochemically hyperthyroid, but there was no statistically significant difference with normal BMD group (p=0.167).

Subclinical hypothyroidism, subclinical hyper-thyroidism, overt hypothyroidism were nearly the same in both groups with no statistically significant difference.

Type 2 diabetes mellitus was more common in the non-osteoporotic group (34.5%) vs (15%) and this was statistically significant (p=0.008). Smoking status was not significantly different between the two groups.

Calcium and vitamin D intake were more common in the osteoporotic group, (59.8%) of the osteoporotic group were taking both calcium and vitamin D together, and the difference was statistically significant, the results were %59.8 vs %32.7 for calcium intake and %59.8 vs %41.8 for vitamin D intake (p=0.0015) (p=0.032) respectively.

Table 2. Demographic characteristics and thyroid function among the study participants

Variables	Osteoporosis (n=107)	Normal BMD (n= 55)	P value
Age	66.7 ± 8.5	57.4 ± 7.5	0.0001
Height	152.5 ± 6.8	158.3 ± 5.2	0.0001
Weight	63 ± 13.5	84.5 ± 14.6	0.0001
BMI	27.1 ± 5.4	33.6 ± 5.3	0.0001
Underweight	6 (5.6)	-	0.096
Normal	27 (25.2)	3 (5.5)	0.0023
Overweight	47 (43.9)	10 (18.2)	0.0016
Obese	27 (25.2)	42 (76.4)	0.0001
TSH	1.9 ± 1.7	2.7 ± 2.3	0.013
Free T3	4.9 ± 1.5	4.7 ± .7	0.35
Free T4	17.4± 3.5	16.9 ± 1.9	0.321
DM	16 (15)	19 (34.5)	0.008
Hysterectomy	8 (7.5)	8 (14.5)	0.171
Smoker	8 (7.5)	2 (3.6)	0.469
Active	2 (1.9)	1 (1.8)	0.99
Ex-smoker	6 (5.6)	1 (1.8)	0.424
Ca intake	64 (59.8)	18 (32.7)	0.0015
Vit D intake	64 (59.8)	23 (41.8)	0.032
Milk intake	37 (34.6)	19 (34.5)	0.378
Yogurt intake	84 (78.5)	43 (78.2)	0.99

[a]Value given as mean ± standard deviation or number (percentage)

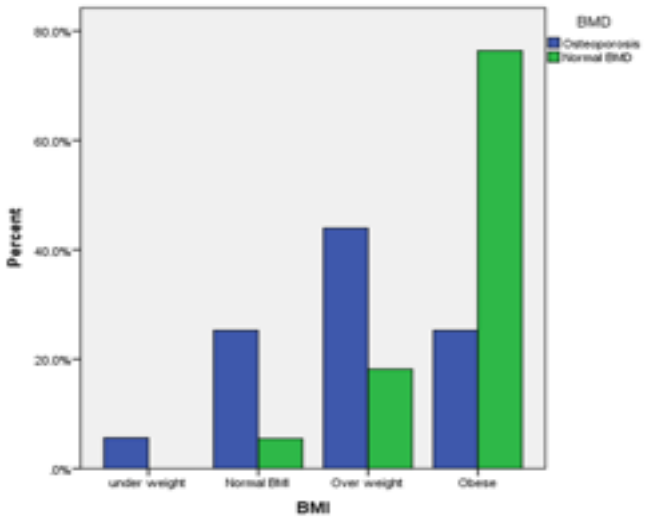

Figure 1. Bar chart showing percentage between Osteoporotic and Normal BMD according to BMI.

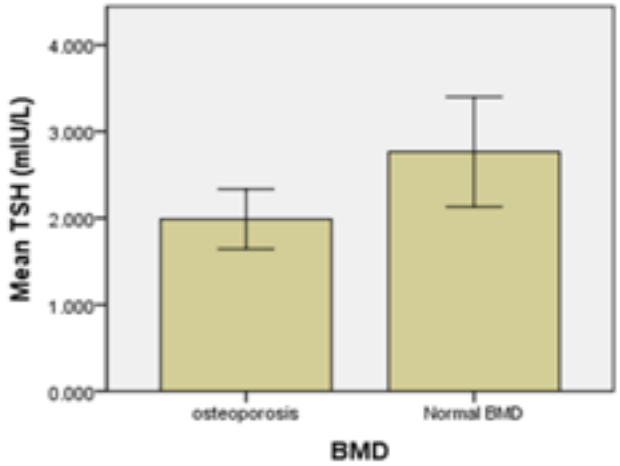

Figure 2. Bar chart showing the comparison of the mean TSH level between the two groups.

Table 3. Percentage of thyroid function status among study participants.

Thyroid status	Osteoporosis	Normal BMD	P value
Normal	91 (85%)	44 (80%)	0.504
Subclinical hyperthyroidism	2 (1.9%)	2 (3.6%)	0.605
Hyperthyroidism	5 (4.7%)	-	0.167
Subclinical hypothyroidism	9 (8.4%)	8 (14.5%)	0.28
Hypothyroidism	-	1 (1.8%)	0.34
Total	107	55	

DISCUSSION

In this study low normal TSH level is more frequent in the postmenopausal osteoporotic patients than non-osteoporotic patients, but there is no difference in the level of thyroid hormones of both groups.

This study showed a similar result regarding TSH level in the study of Acar et al., which found that TSH is lower in osteoporotic than non-osteoporotic [19], and Noh et al. which was a cross-sectional study of 756 Korean women supported a significant positive correlation between serum TSH level within the normal range and the BMD of the lumbar spine [25].

Likewise in Kim et al., low normal TSH is associated with low BMD [26], which has a similar result as in our study, also the size of our sample is small in comparison to other studies done before.

Mazziotti et al. did a study on 130 postmenopausal women, they grouped patients into three tertile according to TSH level, in their results, those in first tertile of TSH (Serum TSH 0.86 (mIU/l) (0.66–1.07) had a higher risk of fracture and their BMD is lower than those of second and third tertile [27], which gave the same result as in our study. Also, we didn't assess fracture in our patients, and we compared TSH of osteoporotic with those of normal BMD.

We assessed bone density by DEXA scan and didn't do serum biochemical marker of osteoporosis. Engler et al. did a cross-sectional study and they found patients with hyperthyroidism have their TSH suppressed even if their thyroid hormone is normal. Their Biochemical markers of bone turnover were increased [28]. This supports that suppressed TSH is an indicator of bone turn over and osteoporosis.

In Földes et al. Bone mineral density is not significantly decreased in premenopausal patients with endogenous subclinical hyperthyroidism than it does in post-menopausal women [29]. They only selected hyperthyroid patients including pre and post-menopause. All of these study cases are postmenopausal regardless of their thyroid status, and postmenopause by itself is a risk factor for osteoporosis.

In post-menopausal women, this finding might be affected by other factors that lead to osteoporosis such as lack of estrogen. Most of the cases in this study that had normal BMD were obese and their TSH was higher than those of the osteoporotic group. This may be due to the fact that obese people have higher TSH level in comparison to non-obese, as Valdés et al. showed that the prevalence of high TSH levels increases threefolds in the morbid obesity [20].

In contrary, there were studies that showed low TSH is not a risk factor for osteoporosis.

A study done by Grimnes et al. explored that within the normal range of serum TSH, serum TSH was not associated with BMD [30]. In their study subjects were divided into six different groups based on the 2.5 and 97.5 percentiles of serum TSH and they found no TSH correlation with BMD between 2.5 and 97.5 percentile, but Below 2.5 percentile of TSH there is a significant correlation between TSH and BMD, both in men and postmenopausal women.

Another study done in India supported that TSH does not affect BMD in euthyroid subjects and subjects with subclinical hypothyroidism [31], but they excluded cases above 50 years and postmenopausal women.

In this study, type 2 DM is more common in the non-osteoporotic group. This may be due to the higher incidence of obesity in the normal group which is a risk factor for type 2 DM as shown in figure 1, or due to that BMD is increased in type 2 diabetic patients. Also in diabetic patients, BMD is higher but the risk of fracture is more, this increase in BMD of type 2 diabetic patients is observed in the meta-analysis that found Despite normal BMD, patients with type 2 diabetes mellitus Are more liable for fracture [32].

In a prospective study older women with diabetes have an increased risk of fracture despite that their BMD is higher [33]. In another study diabetes may be associated with a reduction of bone strength, that is not reflected in the measurement of BMD [34].

Calcium and vitamin D intake is essential for the prevention and treatment of osteoporosis. In this study calcium and vitamin D intake was higher in the osteoporotic group, however, this may cause bias, because of the possibility of noncompliance and improper dosage intake or duration among the patients who admit taking it.

In conclusion, this study supports low normal reference range of TSH as a risk factor for osteoporosis, so in treating patients with hypothyroid achieving a higher level of TSH may decrease the risk of osteoporosis in the elderly women, and in the evaluation of osteoporosis thyroid function may be of value affecting the intended management.

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