IBBJ
Spring 2016, Vol 2, No 2

Original Article

Correlation between Thyroid Function and Bone Mineral Density in Elderly People

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Submitted 03 Sep 2016; Accepted 18 Oct 2016; Published 24 Nov 2016

Investigations regarding the relationship between bone mineral density (BMD) and thyroid function tests even in the normal range are limited. Therefore, the present study was conducted to investigate the relationship between BMD with thyroid function tests in elderly people. This study is a part of a prospective study about health status of the elderly people in Amirkola city (AHAP) which is ongoing from 2011. A total of 1178 people (655 men (55.6%) and 523 women (44.4%)) were enrolled in this study and the TSH, T4 and T3 levels were measured by ELISA method. BMD was assessed by Dual X-ray Energy Absorptiometry (DEXA). Our results demonstrated a significant positive correlation between total T3 and TSH levels with femur density in women (r= 0.068, P= 0.019 and r= 0.122, P= 0.005, respectively). There was also a negative correlation between T4 levels and femur density in men (P=0.034, r= -0.083). Obtained results showed a significant direct correlation between normal levels of TSH and femoral density in elderly females but not in normal elderly males. In addition, there was no significant correlation between normal TSH levels and density of lumbar region in both males and females.

Keywords: Thyroid function, osteoporosis, TSH, elderly people, bone mineral density

Osteoporosis is known as an important health problem leading to physical, psychological and economic consequences. Osteoporosis is also the most common metabolic disorder of bone which increases with age in both men and women. Thyroid hormones are significant factors in bone metabolism

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and bone mass. A comparison of thyroid-stimulating hormone (TSH) levels in its reference range with bone status in postmenauposal women revealed that bone mineral density (BMD) increases in line with TSH levels, and osteopenia or osteoporosis are more present in women with lower limits of TSH.

However, no relationship was found between BMD and total T4 levels (1). Another study also showed that BMD is inversely related to free T4 (FT4) levels and positively related to TSH levels, but its association with FT4 levels is stronger (2). The above relationships demonstrate that the effect of TSH on bone formation is independent of peripheral hormones. TSH may act on bone remodeling via its receptor which is present on osteoblasts and osteoclasts (3). Furthermore, unlike the femur, a relationship between lumbar spine density and TSH levels was suggested in men and women with postmenopausal euthyroid, showing the different impact of TSH on trabecular and cortical bones (4). A study on euthyroid men showed that upon adjustment for height and weight, changes in TSH levels within the normal range have a direct correlation with BMD of the lumbar spine but not with femoral neck BMD (5). Relatively, upon age and BMI adjustment in postmenopausal women, significant correlation was found between TSH levels within the normal range and lumbar BMD (6). However, there are controversial reports on the relationship between TSH levels and BMD in euthyroid women. For example, Loida et al. found that there was no relationship between the levels of TSH, BMD, vertebral and non-vertebral fractures in menopaused women (7). Also, Lin et al. reported no significant relationship between TSH levels in the normal range with wrist density among the middle-aged population (8). Conflicting results among these studies could be due to the polymorphism of the together, changes in TSH levels within normal range may have a relationship with BMD of the lumbar spine and femoral neck. Since this relationship was controversial among elderly populations and also ost previous studies were performed on postmenopausal women, the aim of this study was to investigate the relationship between TSH levels in the normal range and femoral and lumbar BMD on the basis of gender in the elderly population of Amirkola, Iran.

Materials and methods

Study population

This cross-sectional study is a part of the Amirkola health and ageing project (AHAP) (research No. 892,917). AHAP Cohort study mainly considered geriatric medical problems such as falling, bone fragility and fractures, cognitive impairment and dementia, poor mobility and functional dependence. People with age of 60 years and over were invited to participate in this study through posters distributed throughout the city and were assessed by a broad range of biochemical and hormonal tests measured at baseline and follow-up. In total, 1616 elderly people participated in this study (72.3% response rate). Four patients were excluded because they did not went through evaluation for cognitive impairment. Therefore, a total of 1612 subjects were entered in this study. Among them, 881 (54.7%) were males and 731 (45.3%) females. Table 1 shows the demographic characteristics of the participants. All participants signed a written informed consent. In addition, The AHAP cohort study was approved by the medical ethics committee of Babol university of medical sciences. A detailed discussion of the AHAP sample has been described previously (10).

Thyroid hormone measurements

TSH, T3 and FT4 were measured by ELISA (Diametra kit) and TSH levels between 0.5- 5 milliinternational units per liter (mIU/L) were

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Table 1. Demographic characteristics of studied population

Variables		N (%)	Variables		N (%)
Gender	Male	655 (55.6)	T3 (ng.dl)	<70	19 (1.6)
	Female	523 (44.4)		70-190	1137 (96.5)
Age group (years)	60-64	468 (39.7)		>190	22 (1.9)
	65-69	260 (22.1)	T4 (µg/dl)	<4.5	27 (2.3)
	70-74	197 (16.7)		4.5-12	1127 (95.7)
	75-79	158 (13.4)		>12	24 (2)
	80-84	67 (5.7)	TSH (mIU/L)	<0.5	20 (1.7)
	85-99	28 (2.4)		0.5-5	980 (83.2)
Hyperthyroidism	No	1166 (99)		>5	178 (15.1)
	Yes	12 (1)	Renal diseases	No	1171 (99.4)
Hypothyroidism	No	1132 (96.1)		Yes	7 (0.6)
	Yes	46 (3.9)	Diabetes Mellitus	No	787 (66.8)
Lumbar densitometry	Normal	367 (31.2)		Yes	365 (31)
	Osteopenia	464 (39.4)		Unknown	26 (2.2)
	Osteoporosis	347 (29.5)	Hypertension	No	441 (37.4)
Femur densitometry	Normal	410 (34.8)		Yes	711 (60.3)
				Unknown	26 (2.2)
	Osteopenia	553 (46.9)	Vitamin D (ng/ml)	<20	438 (37.2)
	Osteoporosis	215 (18.3)		20-29.9	358 (30.4)
Lumbar or femur densitometry	Normal	239 (20.3)		>=3	382 (32.4)
	Osteopenia	533 (45.2)	Smoking now	No	1099 (93.3)
	Osteoporosis	406 (34.5)		Yes	79 (6.7)

considered as normal reference range.

Measurement of bone density

BMD was measured using dual energy X-ray absorptiometry (DEXA) using Lexxos densitometer 2008 model (made in France) in the left femoral neck and lumbar bone L2-L4 and the results were expressed based on T-Score. T-Score ≤-2.5 SD was considered as osteoporosis, -2.5< T-Score ≤-1 as osteopenia and T-Score >-1 was considered as normal (11).

Statistical analysis

Data analysis was performed using SPSS18 software version 18. ANOVA, Pearson correlation coefficient and linear regression were used for quantitative variables, and chi-square test for qualitative variables; P value ≤ 0.05 was considered as the level of significance.

Results

This study was conducted on 1178 elderly subjects whose demographic characteristics are presented in Table 1. The 60 to 64 year-old age group was the most presented one with the frequency of 39.7%. Hyperthyroidism and hypothyroidism were detected in 1% and 3.9% of participants, respectively. T3, T4, TSH values were normal in 96.5%, 95.7% and 83.2%, respectively of the studied population. T3 level was less than 70 ng/dl in 1.6% and above 190 ng/dl in 1.9% of participants. T4 level was less than 4.5 µg/dl in 2.3% and above 12 mg/dl in 2% in the studied population. The level of TSH was less than 0.5 mIU/L in 1.7% and above 5 mIU/L in 15.1% of studied population. There was a significant negative correlation between T4 levels and femur density in men (P= 0.034 and r= -0.083). In addition, there was a significant correlation between lumbar and femur densitometry (Table 2).

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Table 2. The correlation between densitometry results and thyroid function, age, and physical activity scales results in older men

	density	density	T3	T4	TSH	T3uptake	Age	Activity
Femur density	r= 0.592							
	P= 0.000							
T3	r= -0.01	r= 0.044						
	P= 0.807	P= 0.259						
T4	r= -0.037	r= -0.083	r= 0.249					
	P= 0.35	P= 0.034	P= 0.000					
TSH	r= -0.005	r= 0.048	r= -0.092	r= -0.19				
	P= 0.899	P= 0.22	P= 0.019	P= 0.000				
T3uptake	r= - 0.004	r= -0.013	r= -0.036	r= -0.18	r= -0.059			
	P= 0.909	P= 0.743	P= 0.358	P= 0.000	P= 0.132			
Age	r= -0.122	r= -0.326	r= -0.071	r= 0.043	r= 0.066	r= 0.037		
	P= 0.002	P= 0.000	P= 0.655	P= 0.27	r= 0.09	P= 0.345		
BMI	r= 0.353	r= 0.542	r= 0.056	r= -0.091	r= 0.046	r= -0.077	r= -0.196	r= 0.043
	P= 0.000	P= 0.000	P= 0.149	P= 0.02	P= 0.236	P= 0.048	P= 0.000	P= 0.403

As shown in Table 3, there was a significant positive correlation between TSH levels and femur density in women (P= 0.005 and r= 0.122). In addition, mean T3 levels were significantly different among the study population according to the densitometry results (P= 0.009). Moreover, mean T3 levels in people with normal densitometry were significantly higher than that of those with osteope-nia and osteoporosis (Table 4).

As shown in Table 5, there was no significant correlation between the results of densitometry and TSH levels in the elderly studied subjects.

Table 3. The correlation between densitometry results and thyroid function, age, and physical activity scales results in older women

	Lumbar Density	Femur Density	T3	T4	TSH	T3uPtake	Age	Activity
Femur density	r=0.605							
	P=0.000							
T3	r=-0.016	r=0.0306						
	P=0.709	P=0.408						
T4	r=0.019	r=-0.033-	r=0.388					
	P=0.655	P=0.453	P=0.000					
TSH	r=0.08	r=0.122	r=-0.057	r=-0.258				
	P=0.069	P=0.005	P=0.193	P=0.000				
T3uptake	r=-0.021	r=0.001	r=0.17	r=0.011	r=-0.107			
	P=0.63	P=0.958	P=0.000	P=0.804	P=0.014			
Age	r=-0.227	r=-0.404	r=-0.04	P=-0.04	r= -0.01	r=-0.43		
	P=0.000	P=0.000	P=0.36	P=0.000	P=0.815	P=0.328		
BMI	r=0.314	r=0.396	r=0.081	r=-0.035	r=0.127	r=-0.051	r=-0.27	r=-0.054
	P=0.000	P=0.000	P=0.064	P=0.427	P=0.004	P=0.248	P=0.000	P=0.232

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Table 4. Mean and standard deviation of thyroid function test results and some quantitative parameters according to the densitometry results in elderly people

	Group	Number	Mean± SD	P- value	Post hoc		
					P1-2	P1-3	P2-3
T3	normal	410	127.1± 34.5	0.009	0.004	0.022	0.932
	osteopenia	553	121.1± 29.4				
	osteoporosis	215	121± 32.2				
T4	normal	410	7.6± 1.8	0.219	0.502	0.082	0.201
	osteopenia	553	7.7± 1.8				
	osteoporosis	215	7.9± 1.8				
TSH	normal	410	5 ± 3.8	0.402	0.181	0.45	0.769
	osteopenia	553	4.6± 3.4				
	osteoporosis	215	3.9± 3.5				
T3 uptake	normal	410	33.3± 2.8	0.624	0.955	0.399	0.353
	osteopenia	553	33.3 ± 3.7				
	osteoporosis	215	33± 2.9				
Age	normal	410	66.2± 5.8	0.000	0.000	0.000	0.000
	osteopenia	553	68.6± 7				
	osteoporosis	215	68.4± 7.3				
Diseases	normal	409	2.5± 1.7	0.000	0.231	0.000	0.000
	osteopenia	553	2 .6± 2				
	osteoporosis	215	3.2 ± 2				
BMI	normal	410	29.2± 3.9	0.000	0.000	0.000	0.000
	osteopenia	553	26.6± 4.4				
	osteoporosis	215	25.2± 4.9				

Discussion

The results of this study on elderly subjects showed that there is an inverse correlation between T4 levels and the femoral density in men, and also a direct correlation between TSH levels and the femoral density in women. Also, T3 levels in men with normal densitometry was significantly higher than people with osteopenia and osteoporosis, but T4 and TSH levels had no significant difference. Although some studies regarding the TSH levels and BMD revealed different results, the findings of the present study were consistent with those of some previous reports. Correspondingly, Morris et al. showed that in postmenopausal women the femoral BMD increases alongside with increase of TSH levels within normal range, while low TSH levels was mostly present in women with osteopenia and osteoporosis (1, 11). Furthermore, the study of Kim et al. in Korea on postmenopausal women showed that after adjusting for age and body mass index, BMD was lower in women with low normal TSH levels compared to those with higher normal limit of TSH levels, but no relationship was observed between the FT4 levels and BMD (12) showing that the effect of thyroid hormone on bone is independent of TSH levels. The reason for stronger association between thyroid hormones and femoral density compared to the lumbar bone may be due to the catabolic effect of thyroid hormones on cortical bone. Since the cortical bone is more present in the femur, this could explain the above association (3).

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In some of the previous studies, this association was significant in the lumbar region, but not in the femur. For instance, the study of Noh et al. on euthyroid postmenopausal Korean women after adjusting for age and body mass index, showed a significant relationship between TSH levels in the normal range and lumbar densitometry (6). Also, the study of Beomjun et al. in South Korea on euthyroid men after adjustment for body mass index showed that the changes in TSH levels in the normal range have a direct relationship with BMD of the lumbar spine and no relationship with femoral neck BMD (5). Another study performed on postmenopausal women in Puerto Rico, as well as the study of Bauer et al. in USA revealed no relationship between increased TSH levels and hip BMD (7, 14). The above controversies may be due to TSH receptor polymorphism in different people as well as gender and age differences, which may lead to different BMD scores (9); or can be due to the difference in the geographical location of people and the position of measured BMD (femoral or lower back). According to the NHANES III 1992-2002 analysis, TSH levels in people without thyroid disease increases with age, and patient's age should be taken in account to interpret the results of thyroid function tests (15).

Taken together, the present study showed a significant relationship between TSH levels and femoral densitometry in women, and also an inverse relationship between FT4 levels and femoral density in men, but there was no association between thyroid hormones levels and lumbar density. The cross-sectional nature, lack of follow-up, lack of consideration of some of comorbidities in people, as well as the neglect of nutritional status (vitamin D and calcium) which can affect samples selection, are some limitations of this study which can be negligible due to the large sample size. Moreover, the strengths of this study can be the high sample size and being population based with inclusion of both sexes. This study could provide an important opportunity for a better understanding of the relationship between thyroid function and bone mineral density, but further investigations are needed to recognize all factors affecting this relationship.

Acknowledgement

The authors would like to thank the Deputy for Research at Babol University of Medical Sciences for financial support given to this project (grant no.899917).

Conflict of interest

The authors declared no conflict of interest.

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