http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i12.27

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original article

Evaluation of Bone Mineral Density Level in Overt Hyperthyroidism

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Abstract

Hyperthyroidism is convoyed by osteoporosis or osteopenia with increased rates of bone formation and predominance with bone resorption. Thyroid disease is a common and important health problem in Bangladesh. Thyroid hormones are necessary for normal skeletal growth, maturation, basic metabolism, and bone turnover. There is inadequate awareness about the hyperthyroid bone disease which further reduce quality of life. Therefore there is a great need to evaluate bone mineral density in hyperthyroid patient, so that early diagnosis of low bone mass or osteoporosis can be made. So this study would be beneficial to find out the profile of bone involvement in overt hyperthyroidism by BMD measurement and thereby reducing or avoiding bone pain and osteoporotic fracture risk in hyperthyroidism.

Objective: *This study aimed to assess the profile of bone involvement in overt hyperthyroidism by measuring bone mineral density in respective of age and sex.*

Study Design: *Observational study.*

Place of study: *Medicine department of Khulna Medical College Hospital.*

Period of study: *The study was conducted among the indoor patients of medicine wards Khulna Medical College Hospital, Bangladesh from June, 2013 to December, 2013.*

Study Population: *35 patients, diagnosed as Hyperthyroidism both clinically and biochemically.*

Method and Materials: *This was an observational study. The patients had been treated with radioiodine and antithyroid drug were excluded. All other secondary causes of low BMD like type-I diabetes mellitus, liver and kidney disease, history of drug intake like long term steroid intake were also excluded. The age of the patients ranged from 25 to 40 years. Both male and female were included. BMD of each study population was measured by Lunar DXA scanner at both lumbar spine and femoral neck regions. Low BMD was defined according to World Health Organization (WHO) criteria. The T-score was considered as BMD parameter and was expressed as either osteoporosis or osteopenia with the rest being in normal group.*

Result: *Among total patients 35, 13 (37.1%) were male and 22 (62.9%) were female. Ratio was 1:1.9. Majority were in older age (31-40 years) compared to younger age (25-30 years), percentage being 71.4% vs. 28.6%. BMD was expressed in absolute value (gm/cm^2) and T score. Low BMD was found at both femoral neck (16/35, 45.7%) and lumbar spine (24/35, 68.6%). According to WHO classification, 3 (23.1%) male and 6 (27.3%) female had osteoporosis, whereas 5 (38.5%) male and 10(45.5%) female had osteopenia in lumbar spine. At femoral neck, 2 (15.4 %) male and 3 (13.6%) had osteoporosis, whereas 5 (38.5%) male and 6 (27.3%) female were osteopenia. These difference between male and female was not statistically significant at any site of measurement (p value >0.05). In this study, younger age group had more bone loss compared to older age group at both lumbar spine and femur neck. Low BMD level at neck femur region was statistically significant in younger age group (p value < 0.05%). Considering T-Score, 80% of younger population had either osteoporosis or osteopenia (osteoporosis-40% and osteopenia-40%) at lumbar spine compared to 64.0% in older age group (osteoporosis 20% and osteopenia 44%). At femoral neck, 60% of younger study population and 40% of older population had bone involvement (younger group: osteoporosis vs. osteopenia = 30% vs. 30%; older group: osteoporosis vs. osteopenia = 08% vs. 32%). T-score at femoral neck of male (-1.22±1.19) indicate higher incidence of osteopenia compared to female (-0.79±1.17).On the other hand, osteopenia was found to be more severe in female patients compared to the male at lumbar spine (T-score: male vs. female =-1.43± 1.23 vs. -1.65±1.46). This observation also was not statistically significant.*

Conclusion: *Hyperthyroidism has more impact on younger age when the peak bone mass is achieved and femur neck region may be more affected area. Bone loss is occurred in both spine and hip irrespective of sex. BMD measurement should be a routine procedure in hyperthyroid patients*.

Introduction

Thyroid disorders have been reported in over 110 countries of world with 1.6 billion people at risk and major disorders of thyroid gland are hyperthyroidism and hypothyroidism[1].

Hyperthyroidism is caused by excess synthesis and secretion of the thyroid hormone[2]. About 1 % of the U.S population has hyperthyroidism. Women are affected five to ten times more than men[3]. Major causes of hyperthyroidism are Graves' disease, toxic multinodular goiter and toxic thyroid nodule[4]. Graves' disease is a common endocrine disorder and patients in active state have wide spread systemic manifestations involving all organ system such as CNS, respiratory, cardiovascular, reproductive, gastrointestinal and skeletal system. The effects are due to the metabolic actions of excess thyroid hormone[5]. A representative, cross-sectional sample of the UK population followed up for 20 years provides incidence and prevalence data on overt hyperthyroidism showing prevalence of 19 per 1000 women and 2 per 1000 men[6] [7]Though thyroid hormones are necessary for normal skeletal growth, maturation, basic metabolism and bone turnover[8], thyroid hormones also have direct catabolic effect on bone mineral homeostasis leading to increase bone mineral resorption and calcium loss through kidneys[9]. These effects eventually may cause osteopenia or more serious effect as osteoporosis and also higher incidence of fracture rates[10,11]. With the introduction of antithyroid drugs and radioiodine therapy in 1940's clinically apparent hyperthyroid bone disease has become less common[5]. With invention of new diagnostic tools such as osteodensitometry and biochemical bone markers, important change in bone mineral metabolism in hyperthyroidism has been able to be diagnosed[12]. In past, conventional radiography was used to assess bone mineral content. During 1970-80s single photon absorptiometry (SPA) and dual photon absorptiometry (DPA) were used to quantify bone mineral density at various sites. From 1991 onwards dual energy X-ray absorptiometry (DXA) is available for bone mineral density measurements[5]. Because of advantages of high precision, short scan times, low radiation dose and stable calibration, DXA has proven to be appropriate in meeting the need for scanning equipment to assist in the diagnosis of osteoporosis and aid decision about treatment[13].

Bone mineral densitometry means measurement of bone mineral content and this test is single most valuable method to determine bone health. Bone mineral density (BMD) is measured by dividing bone mineral content by the area or volume of bone. There are various techniques for determining bone mineral density but the areal bone mineral density (a BMD in gram per square centimeter) from proximal femur obtained by DXA still remains the gold standard and this is also promulgated by the World Health Organization (WHO) guidelines for diagnosis of bone fragility[13]. Bone mineral densitometry is the single best approach for establishing the diagnosis of osteoporosis, detecting low bone mass before the disease develops (osteopenia) and for predicting risk for future fractures, compared to the conventional plain X-rays which can reveal osteoporosis only after 30% bone has been lost[14]. Primary osteoporosis is bone loss that occurs during the normal human aging process. Secondary osteoporosis is defined as bone loss that results from specific well defined clinical disorders. It may be due to a large and diverse group of medical disorders which include thyroid and other endocrine disorders, adverse effects of medication, immobilization, and disorders of gastrointestinal or biliary tract, renal disease and cancer[15].In 1994, a WHO study group recommended a definition of osteoporosis that was based on a BMD measurement of spine, hip or forearm expressed as T-Scores. The T-Score is defined as the number of standard deviations (SD) above or below the mean bone mineral density of young healthy adult of 25-35 years of age. WHO report also proposed creating an intermediate category characterized by low bone mass between the normal and osteoporotic states and referred to 'osteopenia'. T-Score of 2.5 SD or more below the young adult mean (>-2.5 SD) is classified as having osteoporosis, a T-score between -1 and -2.5 is classified as osteopenia and a T-Score ≥-1 is regarded as healthy. A fourth category of "established osteoporosis" was also proposed to denote osteoporosis associated with presence of one or more documented fragility fractures, usually of wrist, spine or hip[16]. A decrease in T-Scores by 1 unit, increase fracture risk by a factor of 2.5[13]. Early diagnosis of hyperthyroidism and proper treatment may reduce possibility of bony involvement and thereby reduce fracture risk. Bone mineral density of hyperthyroid patient is not well evaluated in Bangladesh so far. Therefore studies are necessary to validate the findings in Bangladeshi context.

Method and Materials

This observational study was done at medicine department of Khulna Medical College Hospital, Khulna from July 2013 to December 2013. A total of 35 patients diagnosed to have hyperthyroidism clinically and proven by thyroid function test, were included in this study. Patients had been treated with radioiodine and antithyroid drug were excluded from this study. All other secondary causes of low BMD like type-I diabetes mellitus, liver and kidney disease, history of drug intake like long term steroid intake were also excluded. The age of the study population ranged from 25 to 40 years. Both male and female were included in the study. BMD of each study population was measured by Lunar DXA scanner at both lumbar spine and femoral neck regions. Low BMD was defined according to World Health Organization (WHO) criteria. The T-score was considered as BMD parameter and was expressed as either osteoporosis or osteopenia with the rest being in normal group.

Result and Observations

The age of study population ranged from 25 to 40 years. The lowest and highest ages in the study population were 25 and 40 year. ≤30 years aged group was considered as younger age group and >30 years aged group was considered as older group.

The findings derived from data analysis are presented below-

Gender distribution

Table I shows sex distribution of the study population. The number of male and female was 13 (37.1%) and 22 (62.9 %). Male to female ratio was 1: 1.9

Table I: Sex distribution of study population (n=35)

Sex	Frequency	%	Male: Female
Male	13	37.1	1:1.9
Female	22	62.9	
Total	**35**	**100.0**	

Age Distribution

Table II shows, among thirty five (35) study population 10 (28.6%) were ≤30 years age and 25 (71.4%) were >30 year age. Mean age ± SD was 34.46 ± 5.69.

Table II: Distribution of age among study population

Age (in year)	Frequency	%
≤30	10	28.6
>30	25	71.4
Total	**35**	**100.0**

Mean ± SD (Range) = 34.46 ± 5.69 (25-40)

Distribution of frequency of low BMD at lumbar spine

Table III shows the frequency of low BMD in the term of osteoporosis and osteopenia at lumbar spine 24 (68.6 %). Among them 9 (25.7%) was osteoporotic and 15 (42.9%) was osteopenic.

Table III: Distribution of frequency of low BMD at lumbar spine in the term of osteoporosis and osteopenia.

BMD T-Score	Frequency	%
Osteoporosis	9	25.7
Osteopenia	15	42.9
Normal	11	31.4
Total	**35**	**100.0**

Distribution of frequency of low BMD at femoral neck

Table IV shows frequency of distribution of low BMD according to T-score as osteoporosis and osteopenia at femoral neck of study population. A total 16 (45.7%) of study population had low BMD at femoral neck. Among these 5 (14.3%) study population were osteoporotic and 11 (31.4%) were osteopenic

Table IV: Frequency of low BMD at femoral neck in the term of osteoporosis and osteopenia

BMD T-Score	Frequency	%
Osteoporosis	5	14.3
Osteopenia	11	31.4
Normal	19	54.3
Total	**35**	**100.0**

Distribution of mean (± SD) of BMD value in respective of sex

Table V show the distribution of BMD value in both lumbar spine and femoral neck in respective of sex. There was no significant difference of BMD value between male and female at any site. According to T-score, male were found to be more osteopenic in femoral neck compared to female. At lumbar spine female showed to be more osteopenic than male.

Table V: Distribution of mean (± SD) of BMD value in respective of sex.

BMD	Sex		P value*
	Male	Female	
Lumbar Spine			
Absolute (g/cm^3)	1.05 ± 0.14	0.98 ± 0.17	0.260
T-Score (mean)	-1.43 ± 1.23	-1.65 ± 1.46	0.653
Femoral Neck			
Absolute (g/cm^3)	0.92 ± 0.17	0.91 ± 0.15	0.900
T-Score (mean)	-1.22±1.19	-0.79 ± 1.17	0.310

*t test was done to measure the level of significant.
Data was expressed as Mean ± SD.

Distribution of frequency of osteoporosis and osteopenia at lumbar spine in respective of sex:

Table VI shows frequency of osteoporosis and osteopenia at lumbar spines between male and female. In male 3 (23.1%) were osteoporotic compared to female 6 (27.3%). Considering osteopenia 5 (38.5%) male were osteopenic compared to female 10 (45.5%). There was no statistical significant difference between male and female regarding distribution of osteoporosis or osteopenia.

Table VI: Distribution of frequency of osteoporosis and osteopenia at lumbar spine in respective of sex

T-score	Sex		P value*
	Male n=13	Female n=22	
Lumbar Spine			
Osteoporosis	3 (23.1)	6 (27.3)	0.789
Osteopenia	5 (38.5)	10 (45.5)	
Normal	5 (38.5)	6 (27.3)	
Total	**13**	**22**	

*Chi-Square test was done to measure the level of significant.
Figure within parentheses indicated in percentage.

Distribution frequency of osteoporosis & osteopenia at femoral neck in respective of sex

Table VII shows frequency of osteoporosis and osteopenia between male and female at femoral neck**.** In male 2 (15.4%) were osteoporotic compared to female 3 (13.6%), whereas 5 (38.5%) male were osteopenic compared to female 6 (27.3%).

There was no statistically significant difference in distribution of osteoporosis or osteopenia between male and female at femoral neck.

Table VII: Distribution of frequency of osteoporosis and osteopenia at femoral nec between male and female.

T-score	Sex		P value*
	Male n=13	Female n=22	
Femoral Neck			
Osteoporosis	2 (15.4)	3 (13.6)	0.743
Osteopenia	5 (38.5)	6 (27.3)	
Normal	6 (46.2)	13 (59.1)	
Total	**13**	**22**	

*Chi-Square test was done to measure the level of significant.
Figure within parentheses indicated in percentage.

Distribution of mean (±SD) BMD value and T-score in respective of age

Table VIII shows BMD value is lower in younger age group (≤30 years age group) compared to older age group (>30 years age group) in both femoral neck and lumbar spine. Younger age group was more osteopenic than older age group at both sites. This difference was statistically significant at femoral neck.

Table VIII: Distribution of mean (±SD) BMD value and T-score in respective of age

BMD	Age (in year)		P value*
	≤30	>30	
Lumbar Spine			
Absolute (g/cm^3)	0.94 ± 0.14	1.03 ± 0.17	0.150
T-Score (SD)	-2.01 ± 1.21	-1.39 ± 1.40	0.231
Femoral Neck			
Absolute (g/cm^3)	0.84 ± 0.14	0.95 ± 0.15	0.049
T-Score (SD)	-1.39 ± 1.18	-0.77 ± 1.15	0.164

*t test was done to measure the level of significant.
Data was expressed as Mean ± SD.

Table IX shows 4 (40.0%) of study population of younger age were osteoporotic compared to 5 (20.0%) of older study population, whereas 4 (40.0%) of younger study population was osteopenic compared to 11 (44.0%) of older study population at lumbar spine. These differences were not statistically significant.

Table IX: Distribution of frequency of osteoporosis and osteopenia at lumbar spine in younger and older age group:

T-score	Age (in year)		P value*
	≤30	>30	
Lumbar Spine			
Osteoporosis	4 (40.0)	5 (20.0)	0.423
Osteopenia	4 (40.0)	11 (44.0)	
Normal	2 (20.0)	9 (36.0)	
Total	**10**	**25**	

*Chi-Square test was done to measure the level of significant.
Figure within parentheses indicated in percentage.

Distribution of frequency of osteoporosis and osteopenia at femoral neck in younger and older age group:

Table X shows 3(30.0%) of younger study population were osteoporotic compared to 2 (8.0%) of older study population, whereas 3 (30.0%) of younger study population were osteopenic compared to 8 (32.0%) of older study population at femoral neck.

Table X: Distribution of frequency of osteoporosis and osteopenia at femoral neck in younger and older age group

T-score	Age (in year)		P value*
	≤30	>30	
Femoral Neck			
Osteoporosis	3 (30.0)	2 (8.0)	0.228
Osteopenia	3 (30.0)	8 (32.0)	
Normal	4 (40.0)	15 (60.0)	
Total	**10**	**25**	

Discussion

Hyperthyroidism is a common disorder in Bangladesh. Wide spread systemic manifestations involving all organ system such as CNS, respiratory, cardiovascular, reproductive, gastrointestinal system are noted in hyperthyroidism[5]. Marcocci et al. (1997) had shown that suppressed TSH may also result in a potentially serious health problem at bone level[21]. Evaluation of bone mineral density of a hyperthyroid patient is therefore necessary to avoid extra burden by taking appropriate measures. In the present study a total of 35 patients were selected by inclusion and exclusion criteria from hyperthyroid patient attending the center for radioiodine therapy. Their bone mineral density was evaluated measuring T-score at lower lumbar spines and neck femur. Effects of hyperthyroidism on T-score value were evaluated considering different factors like age and sex. Among them, 22 (62%) were female and 13 (37.1%) were male. The ratio was 1:1.9 (Table-I). This finding showed that hyperthyroidism was more common in female patients compared to the male. Hussain et al. (2010)[16] and Udayakumar et al. (2006)[11] had shown increased incidence of female hyperthyroid patients than male, male female ratio being 1:1.2.Age of the patient range 25 to 40 with mean (±SD) age being of 34.46 (±5.69). Udayakumar et al. (2006)[11] in their study demonstrated mean age of 29.4 in 50 hyperthyroid patients. In the present study the population was divided into two age groups. The age of ≤30 years (ranging from 25 to 30 years) and of >30 years (31-40 years) were considered as younger and older group respectively. The study showed that higher frequency of hyperthyroidism in older age group (25 patients) than the younger group (10 patients), percentage being 71.4% vs. 28.6% respectively (Table II).These results showed that hyperthyroidism was more common in older patients than the younger group which correlates well with other report (59% vs. 41%)[55]Many investigators had made conclusion that bone mineral density was reduced in hyperthyroid patient causing osteopenia or osteoporosis[17,18]. Though bone mineral density measurement at proximal femoral neck is considered gold standard[13], BMD of both lumbar spine and femoral neck were measured in this study for better evaluation. BMD values were expressed in absolute value and T-score were measured in the term of osteoporosis and osteopenia. In this study, low BMD was observed at both femoral neck (16/35, 45.7%) and lumbar spine region (24/35, 68.6%). Frequency of osteoporosis and osteopenia at femoral neck was 14.3% and 31.4% respectively, whereas at lumbar spine the frequency was 25.7% vs. 42.9% (Table III and Table IV). Udayakumar et al. (2006)[11] found 46 out of 50 patients (92%) had bone involvement with frequency of osteoporosis and osteopenia 60% and 32% respectively. In their study, BMD was measured only at lumbar spine. Present study made an inference on effect of disease in respective of sex. No statistical significant difference was observed between male and female patients considering bone mineral density which being decreased in both male and female. At lumbar spine, frequency of osteoporosis and osteopenia in male and female was 23.1% vs 27.3% and 38.5% vs. 45.5% respectively. Frequency of osteoporosis and osteopenia at femoral neck in male and female was 15.4% vs. 13.6% and 38.45% vs. 27.3% respectively (Table V, VI, VII). This observation could not be compared with any other established studies. The present study showed that younger age group had more bone mineral loss than older group at both lumbar and neck femur region. Low BMD level at neck femur region of younger age group was statistically significant ($p<0.05$) (Table VIII). Karga et al. (2004)[17] showed that untreated female hyperthyroid patients, who were affected at a younger age (13-30 years), had more pronounced loss of bone mineral compared to older age group (31-50 years). Their study was not powered enough to give relative risk. However, present study was well correlated with the observation reported by Karga et al. (2004)[17]. Considering the

T-score at lumbar spine, 80 % of younger population had either osteoporosis or osteopenia (osteoporosis-40.0%, osteopenia-40.0%) compared to 64.0% in older group (osteoporosis 20.0% and osteopenia 44.0%) (Table IX). In case of T-score at femoral neck, 60% of younger group and 40% of older group had bone involvement (younger group: osteoporosis vs. osteopenia = 30% vs. 30%; older group: osteoporosis vs. osteopenia = 08% vs. 32%) (Table X).These findings support the reported result by Karga et al. (2004)[17]. Present study also showed that cortical bone (femoral neck) was more affected than trabecular bone (lumbar spine) in young age group. Greenspan & Greenspan (1999)[19] had shown in their study that thyroid hormone had a greater impact on cortical bone than trabecular bone. This observation was well correlated with present study. In the present study, the mean T-score at femoral neck was -1.22±1.19 in male population and in female (T-score -0.79 ± 1.17) indicating higher incidence of osteopenia among the male than female. This finding of low T-score in male population compared to female, may be due to severe decrease in femoral neck T-score (-3.6) in a (1) patient when compared to lumbar spine T-score (-2.6) in the same patient (Appendix-VII, Patient no-8). This unusual finding of low T-score value could not be explained or it may be due to technical error. Similarly by eliminating this patient (Appendix VII, Patient no-8) and another 2 female patient's T-score values (Appendix VII, Patient no-7 and 20), the obtained result showed that male and female had almost normal value of T-Score (Male vs. Female: -1.01±0.99 vs. -0.56±0.92 respectively) in femoral neck (Appendix VIII). On the other hand, osteopenia was found to be more severe in female patients compared to the male when T-score at lumbar spine was considered (Male vs. female: -1.43±1.23 vs. -1.65±1.46) (Table V). Though low BMD was found in lumbar spine of both male and female, there was no statistically significant difference in BMD value between male and female. Jodar et al. (1997)[20] showed in their study that no significant difference was found between different sites of measurement in active hyperthyroid patients, which suggested a generalized reduction of bone mass in axial skeleton in both male and female. This observation was similar with the results of the present study.

Conclusion

Hyperthyroidism is a risk factor for low bone mass with increasing probability of developing osteopenia and osteoporosis. The present study showed significant impact of hyperthyroid state on bone health which correlates well with the findings of several studies done elsewhere. These observations would be beneficial to the patients diagnosed as having overt hyperthyroidism to adopt proper measures well ahead before involving the skeletal system.

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