ORIGINAL ARTICLE

Comparison of Various Bone and Biochemical Parameters at Various Stages of Thyroid Disease

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ABSTRACT

Background: A normal level of thyroid hormone is essential for appropriate skeletal development and mineralization. In patients of hyperthyroidism, it has been established that there is an increased bone resorption due to increased osteoclastic activity resulting in bone loss, but little is known about subclinical hyperthyroid patients. In Pakistan, subclinical and hyperthyroid conditions have a prevalence of 5.1% and 5.8% respectively and both have a higher incidence in females. The fluctuations in the level of thyroid hormone increase the risk of osteoporosis, resulting in vertebral and hip fracture

Aim: To assess the difference in various parameters of bone function between euthyroid, hyperthyroid and subclinical hyperthyroid patients.

Methods: All patients included in this study were recruited from INMOL hospital Lahore according to inclusion and exclusion parameters. After taking informed consent, a detailed history and clinical examination was carried out. Thyroid profile including FT_3, FT_4 and TSH were done . Ad S o S and Bone transmission time were calculated using DBM Ultrasonographic bone profiler. The measurements were done by using two transducers each of 12mm, which were placed on a highly accurate calliper. This measurement was done at the medial and lateral side of each finger. The emitter probe generated an ultrasound wave while the receiver calculated the arriving signals through the phalanx.

Results: A total of 84 patients were included in the study with a mean age of 26-32 years. All of them agreed to participate in the study. Serum FT_3 and FT_4 and TSH were determined to identify the three thyroid groups. Bone profile and Biochemical parameters were then measured in relation to different functional levels of thyroid hormone.

Conclusion: The results indicate a visible difference between patients with normal functioning thyroid gland and hyperthyroid and subclinical hyperthyroid patients.

Keywords: Bone transmission time, Hyperthyroidism, Subclinical hyperthyroidism, Euthyroid

INTRODUCTION

A normal level of thyroid hormone is essential for appropriate skeletal development and mineralization (Allain and McGregor, 1993). In patients of hyperthyroidism, it has been established that there is an increased bone resorption due to increased osteoclastic activity resulting in bone loss, but little is known about subclinical hyperthyroid patients.(Abu et al., 1997, Britto et al., 2005**)**. In Pakistan, both of these conditions have a prevalence of 5.1% and 5.8% respectively and both have a higher incidence in females. (Alam Khan et al 2002). These fluctuations in the level of thyroid hormone increase the risk of osteoporosis, resulting in vertebral and hip fractures (Udayakumar et al., 2006). This is due to shortening of bone remodeling cycle and increased osteoclastic resorption of bone (Bassett and Williams, 2003, Al-Shoumer et al., 2006). In order to better understand the changes in bone architecture it was decided to conduct a comparative study to assess the difference in various parameters between euthyroid, hyperthyroid and subclinical hyperthyroid patients.

MATERIALS AND METHODS

All patients included in our study were taken from INMOL hospital Lahore. After taking informed consent, a detailed history and clinical examination was carried out. Thyroid profile including FT_3,FT_4 and TSH were done through Radioimmunoassay (RIA) (Melmed et al 2011). AdSoS and Bone transmission time were calculated using DBM Ultrasonographic bone profiler (Alexandersen et al., 2005).DBM relies on passage of ultrasound through distal end of first phalanx diaphysis in close proximity of condyles of first four fingers of hand. The area was chosen as it contained more trabecular and cortical bone. The measurement was done by two transducers each of 12mm which were placed on a highly accurate calliper to calculate the area between two probes. This measurement was done at the medial and lateral side of each finger. The emitter probe generated an ultrasound wave while the receiver calculated the arriving signals through the phalanx. The speed of sound(SoS) through the phalanx was calculated by dividing the thickness of finger measured divided by the time of passage. Serum calcium, phosphate and alkaline phosphatase were assessed by colorimetric method (Bassett, and Williams,2003)

Statistical analysis: Patients were recruited for purposive consecutive sampling according to the inclusion criteria of the study. Data distribution were assessed for normality by Shapiro Wilk test. For non-normal data median with Interquartile range (IQR) was given. Means of different parameters were compared by single factor ANOVA followed by Post hoc Tukey test (SPSS version 18).

RESULTS

A total of 84 patients were included in the study with a mean age of 26-32 years. All of them agreed to participate in the study. Serum FT_3 and FT_4 and TSH were determined

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to identify the three thyroid groups. Bone profile and different functional levels of thyroid hormone. Biochemical parameters were then measured in relation to

Table 1: Details of various parameters determined, based on functional thyroid status. Values given are mean ±SD. Statistics according to single factor ANOVA. - Anthropometric measures

Parameters	Euthyroid (n=28)	Hyperthyroid (n=28)	Subclinical hyperthyroid (n=28)	p-value
Age (years)	26.28 ± 6.52	31.23 ± 9.61	35.23 ± 10.15	0.003
Height	159 ± 9.13	161.58 ± 9.93	157.03 ± 6.89	0.124
Weight	56 ± 12.62	55.81 ± 12.53	59.73 ± 12.35	0.417
BMI	22.34 ± 5.22	21.33 ± 4.25	24.24 ± 4.92	0.04

Table 2: Details of PostHoc Tukey Test between groups

Comparison of age	p value
Euthyroid VS Hyperthyroid	0.123 (NS)
Euthyroid VS Subclinical Hyperthyroid	0.002
Subclinical Hyperthyroid VS Hyperthyroid	0.232(NS)
Comparison of Ad SoS	**p value**
Euthyroid VS Hyperthyroid	0.002
Euthyroid VS Subclinical Hyperthyroid	0.003
Subclinical Hyperthyroid VS Hyperthyroid	0.999(**NS**)
Comparison of T-Score	
Euthyroid VS Hyperthyroid	0.001
Euthyroid VS Subclinical Hyperthyroid	0.001
Subclinical Hyperthyroid VS Hyperthyroid	0.997(**NS**)
Comparison of BTT	
Euthyroid VS Hyperthyroid	0.005
Euthyroid VS Subclinical Hyperthyroid	0.016
Subclinical Hyperthyroid VS Hyperthyroid	0.924(**NS**)
Comparison of UBPI	
Euthyroid VS Hyperthyroid	0.115(**NS**)
Euthyroid VS Subclinical Hyperthyroid	0.077(**NS**)
Subclinical Hyperthyroid VS Hyperthyroid	0.977(**NS**)
Comparison of BMI	
Euthyroid VS Hyperthyroid	0.722 (**NS**)
Euthyroid VS Subclinical Hyperthyroid	0.206 (**NS**)
Subclinical Hyperthyroid VS Hyperthyroid	0.035
Comparison of Z-score	
Euthyroid VS Hyperthyroid	0.002
Euthyroid VS Subclinical Hyperthyroid	<0.001
Subclinical Hyperthyroid VS Hyperthyroid	0.598 (**NS**)
Comparison of FT3	
Euthyroid VS Hyperthyroid	<0.001
Euthyroid VS Subclinical Hyperthyroid	0.285(**NS**)
Subclinical Hyperthyroid VS Hyperthyroid	<0.001
Comparison of FT4	
Euthyroid VS Hyperthyroid	<0.001
Euthyroid VS Subclinical Hyperthyroid	0.495(**NS**)
Subclinical Hyperthyroid VS Hyperthyroid	<0.001
Comparison of TSH	
Euthyroid VS Hyperthyroid	<0.001
Euthyroid VS Subclinical Hyperthyroid	<0.001
Subclinical Hyperthyroid VS Hyperthyroid	0.474 (**NS**)
Comparison of Phosphate	
Euthyroid VS Hyperthyroid	0.080 (**NS**)
Euthyroid VS Subclinical Hyperthyroid	0.466 (**NS**)
Subclinical Hyperthyroid VS Hyperthyroid	0.003
Comparison of Alkaline Phosphatase	
Euthyroid VS Hyperthyroid	<0.001
Euthyroid VS Subclinical Hyperthyroid	0.025
Subclinical Hyperthyroid VS Hyperthyroid	0.263(**NS**)

Table 3: Bone Profile Parameters

Parameters	Euthyroid (n=28)	Hyperthyroid (n=28)	Subclinical (n=28)	p-value
Ad S o S(m/s)	2159.68 ± 97.37	2060.58 ± 136.33	2061.87 ± 85.36	0.001
T-score	0.60 ± 1.41	-0.8572 ± 1.96	-0.89 ± 1.22	<0.001
Z-score	1.10(0.66-2.13)	-0.51 ± 2.09	-0.09 ± 1.15	0.001
Ultrasound Bone Profile Index	0.71 ± 0.15	0.59 ± 0 .27	1.5190 ± 0.26467	0.058
Bone transmission time	1.71 ± 0.30	1.4926 ± 0.26810	1.5190 ± 0.26467	0.003

Table 4: Serum Parameters

Parameters	Euthyroid	Hyperthyroid	Subclinical	p-value
FreeT_3	4.39 ± 0.62	16.45(9.19-32.61)	4.70(3.80-5.01)	<0.001
FreeT_4	16.63±1.68	41.35±13.72	18.45(13.45-20.08)	<0.001
Thyroid stimulating Hormone	1.18(1.02-2.14)	0.02(0.02-0.05)	0.02(0.02-0.05)	<0.001
Calcium	6.72 ± 0.64	6.98± 0.43	6.59(6.36-7.26)	0.252
Inorganic phosphate	4.03 ± 0.77	4.40 ± 0.66	3.82 ± 0.52	0.004
Alkaline phosphatase	185.00(155.00-243.00)	330.00(230.00-384.00)	289.00(178.00-354.00)	0.002

DISCUSSION

Problems with thyroid result in bone changes. 84 patients were included in the study, 28 each from subclinical, hyperthyroid and euthyroid group. Age group of the patients that were selected were between 20-40 years. Patients included both male and female but were mostly female. All the patients belonged to middle class. Patients were evaluated for various parameters which included A d S o S and biochemical analysis of calcium, phosphate and alkaline phosphatase.

It was observed that there was a difference in different parameters between patients of all the three groups. When these parameters were compared by Post hoc Tukey test it was seen that the fluctuations in levels of thyroid hormone has led to change in structure of bone, which were seen when euthyroid patients were compared with hyperthyroid and subclinical hyperthyroid patients (Table 1)

Amplitude dependent speed of sound showed that patient with normal functioning thyroid differed from hyperthyroid and subclinical hyperthyroid groups($p < 0.05$) showing that when patients were euthyroid due to treatment /or otherwise bone related parameters were lower than hyperthyroid but higher than subclinical hyperthyroid. It was also seen that there was no difference in AdSoS values between hyper and subclinical hyperthyroid patients ($p= 0.999$), thus showing that AdSoS values are not affected by slight fluctuations in thyroid hormone. Since QUS is unable to estimate the presence of fragility in cancellous bone in the absence of major changes in the bone, that is why the resultant increase in fragility was not detected by QUS. This shows that although changes did occur in hyperthyroid and subclinical groups but these changes were only seen when they were compared together. However, when these patients were assessed for T-score it was observed that patients having a normal level of thyroid hormone differed from those having high or subnormal levels of TSH ($p < 0.001$), but no significant difference was observed between subclinical and hyperthyroid patients**.**

CONCLUSIONS

1. There was a difference in QUS bone profile between hyperthyroid, subclinical and euthyroid patients.
2. Patients with normal functioning thyroid did differ from both hyperthyroid and subclinical hyperthyroid patients in their bone profile.
3. Patients of subclinical hyperthyroidism had low phosphate levels which showed that there were some early changes in the bone suggesting demineralization. Since phosphate is water soluble its loss through the kidney might have contributed to low serum phosphate levels.

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