

ORIGINAL RESEARCH

Study of thyroid disorders in relation to bone biochemical parameters

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ABSTRACT

Background: Thyroid hormones are essential for normal skeletal development and normal bone metabolism in adults but can have detrimental effects on bone structures in states of thyroid dysfunction. Present study was aimed to study thyroid disorders in relation to bone biochemical parameters (Serum calcium, Serum phosphorus, serum ALP & vitamin D) at a tertiary care hospital.

Material and Methods: Present study was single-center, cross sectional, observational study, conducted in patients with thyroid disorders, 18-70 years age, visiting Medicine OPD for their regular thyroid check-up, underwent estimation of thyroid hormones profile (TSH, T4, T3, serum calcium, serum phosphorus, serum ALP & vitamin D).

Results: In present study 300 patients, majority were from 36-45 years (47.67 %), female (71 %) and had co-morbidities as diabetes mellites (18 %), hypertension (29.67 %). Majority were euthyroid (38 %) while others were Hypothyroid (28 %), Subclinical Hypothyroid (20 %) & Hyperthyroid (14 %). Serum calcium levels in euthyroid patients (8.634 ± 0.711 mg/dl) were more than that of hypothyroid patients (8.125 ± 0.838 mg/dl), Subclinical Hypothyroid patients (7.760 ± 0.81 mg /dl) & Hyperthyroid patients (8.10 ± 1.213 mg/ dl), difference was statistically highly significant (p- 0.001). Serum phosphorus levels in euthyroid patients (3.634 ± 0.421 mg/dl) were less than that in Hypothyroid patients (3.80 ± 0.854 mg /dl), Subclinical Hypothyroid patients (3.690 ± 0.422 mg/ dl) & Hyperthyroid patients (4.021 ± 0.698 g /dl), difference was statistically significant (p- 0.004). Serum ALP levels in euthyroid patients (112 ± 39.806 mg/dl) were less than that of hypothyroid patients (138.143 ± 86.695 mg /dl) & more than levels in Subclinical Hypothyroid patients (94.90 ± 15.442 mg/dl) & Hyperthyroid patients (106.143 ± 31.749 mg/dl), difference was statistically highly significant (p- 0.001). **Conclusion:** All patients with various thyroid disorders should be periodically evaluated for bone biochemical parameters (Serum calcium, Serum phosphorus, serum ALP & vitamin D) for early diagnosis of bone related disorders and to decide treatment protocol.

Keywords: Thyroid disorders, bone biochemical parameters, serum calcium, serum phosphorus, serum ALP, vitamin D

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INTRODUCTION

Thyroid disorders are one of the most common endocrine disorders. The spectrum of thyroid dysfunction ranges from hypothyroidism (under production) to hyperthyroidism (over production). Thyroid disorders may affect individuals belonging to any age and gender, but its occurrence is different in different geographical areas and in different age and sex groups.¹

Thyroid hormones are essential for normal skeletal development and normal bone metabolism in adults but can have detrimental effects on bone structures in states of thyroid dysfunction.² Bone constitutes the skeletal structure that supports the human body and regulates calcium and phosphorus homeostasis.³ Calcium (Ca²⁺) and phosphorus (PO₄²⁻) are all divalent metal ions, which are necessary for metalloenzymes and various crucial metabolic pathways directly or indirectly regulated by thyroid hormones.⁴

Calcium and phosphorus imbalance are the most common metabolic disturbances seen in thyroid dysfunction.⁵ Studies on hypothyroid subjects have shown contradictory findings where the levels of serum calcium and phosphorus were low in patients with overt hypothyroidism. Some studies show a normal serum calcium and phosphorus levels⁵ while others have observed a low serum calcium and magnesium levels and an increase in serum phosphorus levels in patients with hypothyroidism.^{6,7} Present study was aimed to study thyroid disorders in relation to bone biochemical parameters (Serum calcium, Serum phosphorus, serum ALP & vitamin D) at a tertiary care hospital.

MATERIAL AND METHODS

Present study was single-center, cross sectional, observational study, conducted in department of General Medicine & Department of Biochemistry, at Rohilkhand Medical College & Hospital, Bareilly, UP, India. Study approval was obtained from institutional ethical committee.

Inclusion criteria:

- Patients with thyroid disorders, 40-70 years age, visiting Medicine OPD for their regular thyroid check-up, willing to participate in present study

Exclusion criteria:

- Subjects suffering from diseases like cirrhosis, congestive cardiac failure, tuberculosis, and renal diseases.
- History of drug intake like steroids, anti-epileptics, antipsychotics, oral contraceptive pills.
- Pregnant or lactating women.

The patients visiting Medicine OPD for their regular thyroid check-up were considered for study. Study was explained to patients & a written informed consent was taken for participation. Demographic details, clinical history was collected.

5 ml of venous blood samples were drawn from every participant in plain blood collection tubes, using sterile syringes and centrifuged (3000 r.p.m) for five minutes to obtain serum for analysis of thyroid hormones profile (TSH, T₄, T₃, Serum calcium, Serum phosphorus, serum ALP & vitamin D, measured by Cobas c501 automated analyzer, employing standard reagents and procedures. However, hormonal assay was performed by ELISA technique.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were also tested using chi-square test or Fisher exact test as applicable. P value less than 0.05 was considered as statistically significant.

RESULTS

In present study 300 patients, majority were from 36-45 years (47.67 %), female (71 %) & had co-morbidities as diabetes mellitus (18 %), hypertension (29.67 %).

Table 1: Demographic characteristics and thyroid related history of the study population

Characteristics	Frequency (n=300)	Percentage
Age-group (years)		
18-35	24	8.00%
36-45	143	47.67%
46-54	94	31.33%
55-70	39	13.00%
Mean \pm SD	45.85 \pm 14.68	
Gender		
Female	213	71.00%
Male	87	29.00%
Comorbidities		
Diabetes mellitus	54	18.00%
Hypertension	89	29.67%

In present study, majority were euthyroid (38 %) while others were Hypothyroid (28 %), Subclinical Hypothyroid (20 %) & Hyperthyroid (14 %).

Table 2: Thyroid status

Thyroid status	Frequency (n=300)	Percentage
Euthyroid	114	38.00%
Hypothyroid	84	28.00%
Subclinical Hypothyroid	60	20.00%
Hyperthyroid	42	14.00%

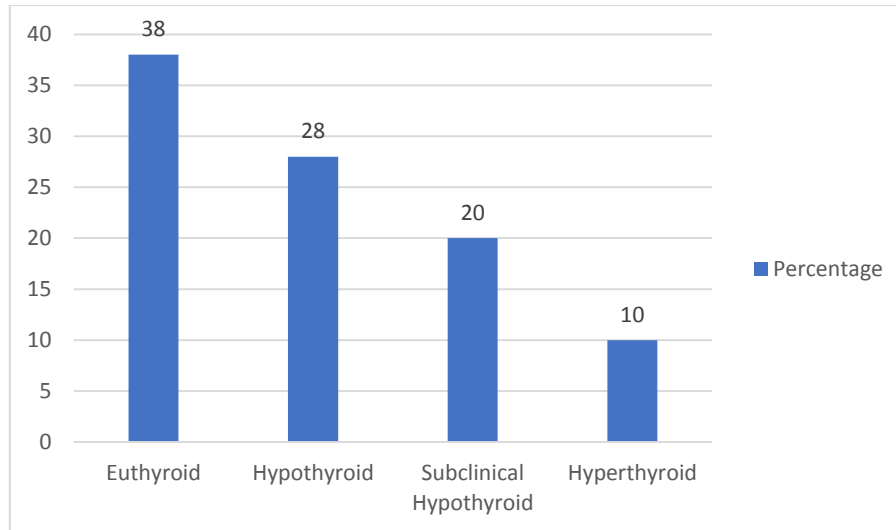


Figure 1: Thyroid status

In present study, serum calcium levels in euthyroid patients (8.634 ± 0.711 mg/dl) were more than hypothyroid patients (8.125 ± 0.838 mg/dl), Subclinical hypothyroid patients (7.760 ± 0.811 mg/dl) & hyperthyroid patients (8.10 ± 1.213 mg /dl), difference was statistically highly significant (p- 0.001).

Serum phosphorus levels in euthyroid subjects (3.634 ± 0.421 mg/dl) were less than that of hypothyroid patients (3.80 ± 0.854 mg/dl), Subclinical hypothyroid patients (3.690 ± 0.422 mg/dl) and hyperthyroid patients (4.021 ± 0.698 mg /dl), difference was statistically significant (p- 0.004).

Serum ALP levels in euthyroid subjects (112 ± 39.806 mg/dl) were less than that of hypothyroid patients (138.143 ± 86.695 mg/dl) , and more than levels in Subclinical Hypothyroid patients (94.90 ± 15.442 mg /dl) & hyperthyroid patients (106.143 ± 31.749 mg/dl), difference was statistically highly significant (p- 0.001).

Vitamin D levels in euthyroid subjects (35.43 ± 23.783 mg/dl) were more than hypothyroid patients (20.724 ± 13.068 mg/dl) , Subclinical hypothyroid patients (28.807 ± 23.917 mg /dl) & Hyperthyroid patients (23.689 ± 17.814 mg /dl), difference was statistically highly significant (p- 0.001).

Table 3: Comparison between various groups of thyroid patients showing biochemical and bone health parameters

Parameters	Euthyroid	Hypothyroid	Subclinical Hypothyroid	Hyperthyroid	P value*
Serum calcium (mg/dl)	8.634 ± 0.711	8.125 ± 0.838	7.760 ± 0.811	8.10 ± 1.213	0.001
Serum phosphorus (mg/dl)	3.634 ± 0.421	3.80 ± 0.854	3.690 ± 0.422	4.021 ± 0.698	0.004
serum ALP (IU/L)	112 ± 39.806	138.143 ± 86.695	94.90 ± 15.442	106.143 ± 31.749	0.001
vitamin D (ng/mL)	35.43 ± 23.783	20.724 ± 13.068	28.807 ± 23.917	23.689 ± 17.814	0.001

DISCUSSION

Thyroid hormones exert their effects on osteoblasts via nuclear receptors to stimulate bone resorption.⁸ In hypothyroidism there is a depressed turn over due to impaired mobilization of calcium into bone that leads to decrease in blood calcium level. In hypothyroidism increased production of calcitonin can promote tubular reabsorption of phosphate and tubular excretion of calcium.⁹ Serum magnesium and phosphorus levels are increased in hypothyroidism.¹⁰

Overt hypothyroidism is known to lower bone turnover by reducing both osteoclastic bone resorption and osteoblastic activity. These changes in bone metabolism would result in an increase in bone mineralization. Decreased T3 and T4 leads to hypocalcaemia, which in-turn triggers overproduction of calcitonin. Calcitonin is responsible for the reabsorption of phosphate in tubules, leading to hyperphosphatemia. The disturbance in calcium and phosphorus levels in blood affects the bone metabolism. There is a decreased bone turnover in hypothyroidism leading to osteoporosis. This in-turn makes the individuals more prone to fracture especially in the older ages, when left untreated.¹¹

A study conducted by Kavitha MM et al.,⁷ also shows hypocalcaemia and hyperphosphatemia in hypothyroidism. Padhiary M et al.,¹² compared overt hypothyroidism patients with healthy controls, levels of serum sodium, potassium and calcium were significantly decreased in cases than the controls. Serum magnesium and phosphorus were significantly elevated in cases than controls.

In hyperthyroidism patients, accelerated bone remodeling leads to escalate bone resorption, thus increasing release of calcium into systemic circulation. The elevated calcium levels in turn inhibit the Parathyroid Hormone (PTH) secretion and generate a negative calcium imbalance. As a protective response against hypercalcemia, the reduction in PTH levels causes hypercalciuria.¹³

Sarah H M et al.¹⁴ noted that in hyperthyroidism patients, significant difference was observed in serum levels of Osteocalcin (p-value <0.0001), ALP (p-value <0.0001) and calcium (p-value=0.0004) levels in hyperthyroid patients and control group, while no significant (p-value=0.17) difference was observed in serum phosphorus levels. Elevated serum Osteocalcin, ALP and calcium were significantly associated with the elevated thyroid hormones (total T3 and total T4).

Suneel B et al.,¹⁵ observed a significant increase in the serum phosphorus levels that may be due to increased production of thyroid calcitonin which promotes the tubular reabsorption of phosphate and tubular excretion of calcium, resulting in hyperphosphatemia and hypocalcemia, respectively.

Adult hypothyroid patients tend to exhibit higher than normal bone density. It is usually associated with normal or low alkaline phosphatase (ALP) together with normal serum calcium and phosphorus concentrations. Hypothyroid patients have a reduced tolerance to oral calcium and may develop hypercalcaemia when given calcium. The defect appears to be retarded disposition of calcium, rather than excess absorption.¹¹

An impaired mobilization of calcium into the bone can cause a depressed turnover in hypothyroidism, and this can often lead to a decrease in the blood calcium level. A reduced mobilization of calcium prevails in hyperthyroidism, and this can lead to an increase in the blood calcium level.¹⁷

A direct correlation between serum thyroxine concentration and serum alkaline phosphatase levels has been found by several workers. The raised levels of serum alkaline phosphatase levels could be either of hepatic or of bone origin. Following treatment, serum alkaline phosphatase levels remain elevated for several months suggesting increased bone turnover continues even after restoration of a normal metabolic rate.¹⁸

CONCLUSION

Thyroid hormones in more than one ways may play a crucial role in regulating various bone biochemical parameters. Thus, all patients with various thyroid disorders should be periodically evaluated for bone biochemical parameters (Serum calcium, Serum phosphorus, serum ALP and vitamin D) for early diagnosis of bone related disorders to decide treatment protocol and to ensure better medical management.

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