Role of reduced thyroid hormone status on bone mineral metabolism

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Abstract

Background: The most common endocrine disorder is hypothyroidism which accounts to 11%. Thyroid hormones have a wide array of functions such as physiological growth and development of skeletal system, maintenance of basal metabolic rate and regulation of various metabolisms, including mineral metabolism. Nowadays due to its direct action on bone turn over, thyroid hormones are considered to have an important role on bone mineral metabolism. Thyroid disorders are important cause for secondary osteoporosis. So the present study was done to know the levels of bone minerals, calcium and phosphorus in hypothyroidism and its relation with thyroid hormone levels. Methods: A case-control study was conducted on 30 hypothyroid patients and 30 euthyroid healthy controls in the age group of 20-60 years. Blood samples were collected from all the study population. Serum total triiodothyronine, total thyroxine and TSH by Enzyme-Linked Immunosorbent Assay, Serum calcium by Arsenazo III method, phosphorous by ammonium molybdate method were estimated. Results: Serum calcium levels in cases was found to significantly reduced when compared to controls (p<0.001). Serum phosphorous levels also showed considerable elevation in cases when compared to controls (p<0.001). There was a significant negative correlation between TSH and serum calcium in cases. Conclusion: The present study indicated the important role of reduced thyroid hormone status on bone mineral metabolism. This study concludes that serum calcium was significantly reduced and phosphorus levels were significantly increased in hypothyroid patients when compared to euthyroid control subjects. So frequent monitoring of serum calcium and phosphorus in hypothyroid patients would reduce the burden of bone pathologies.

Keywords: Hypothyroidism, calcium, phosphorous

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INTRODUCTION

Thyroid diseases are common and their incidence and prevalence were considered to increase with age¹. In India, hypothyroidism is most common, among the 42 million people suffering from thyroid diseases.² Thyroid gland

produces the hormones T3 and T4 which play a crucial role in cell differentiation during development and help to maintain thermogenic, metabolic homeostasis like carbohydrate, protein, lipid and mineral metabolism in adult.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 hormones⁴. So any disorder of thyroid hormone also affects the bone mineral metabolism which is considered to be an important cause of secondary osteoporosis. Thyroid hormones exert its effects on osteoblasts via nuclear receptors to stimulate osteoclastic bone resorption.^{3,5} In the commonly occurring thyroid dysfunction, hypothyroidism, bone turnover is reduced, which leads to decreased blood calcium level⁶. Literature has revealed conflicting results on serum calcium and phosphorus levels in hypothyroidism. Hence,

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this study was done to evaluate serum calcium and phosphorus in hypothyroid patients and its correlation with thyroid profile T3, T4, and thyroid-stimulating hormone (TSH) levels in these patients and to know the importance to examine their levels in hypothyroid disorders. So the aim of this study to evaluate the effect of reduced thyroid hormone status on bone mineral metabolism. The objectives are 1) To analyse the levels of calcium and phosphorous in hypothyroid patients, 2) To compare the level of the above analytes with that of the normal control population. 3) To correlate the levels of serum calcium and phosphorus with TSH levels in cases.

METHODS

This comparative study was done at Govt. Kilpauk Medical College over a period of 3 months (from December 2019- February 2020) after getting the Institutional Ethical Committee clearance. The study population include two groups:

Group 1(cases): consists of already diagnosed hypothyroid patients

Inclusion criteria: cases in the age group of 18-60years with TSH $> 5.5 \ \mu$ IU/ml

Group 2(controls): Age and gender matched normal subjects with no history of thyroid disorders.

Exclusion criteria: Patients suffering with renal diseases, hepatic diseases, diabetes mellitus, hypertension and pregnant women were excluded from the study.

Under strict aseptic precautions, 5 ml fasting venous blood was collected after getting proper informed and written consent from the study population. The blood was centrifuged, serum separated and used for biochemical estimation.

Laboratory tests done:

- 1. Serum TSH, T3 and T4 were measured by enzyme linked immunoassay by using Benesphera kits.
- 2. Serum calcium was estimated by Arsenazo III method and
- 3. Serum phosphorous by ammonium molybdate method on semiautoanalyser.

Statistical Analysis:

Statistical analysis was done using SPSS version 21 package. Statistical results were expressed as mean \pm SD. To correlate the parameters among the cases Pearson's correlation test was applied. P- value < 0.05 was considered statistically significant.

RESULTS

The age of the subjects in both groups were matched with mean age of 36.16 ± 11.48 among cases and 37.80 ± 11.50 among controls with p value of 0.584

There was a significant increase of TSH, in cases with p value < 0.001. Significant decrease in T4 was noted (p < 0.05) in cases as given in Table 1.

Table 1	: Comparison o	f serum TSH, T	3 an	d T4 in Cases	and Control s	ubjects
	VARIABLES	CASES		CONTROLS	P VALUE	
	TSH(μIU/dl)	19.54±13.6	7	3.22±1.31	0.001	
	T4(ng/dl)	8.92±3.42		10.14±1.78	0.007	
	T3(µg/dl)	1.23±0.40		1.66±1.27	0.136	

Among the minerals, there was a significant increase in phosphorous and magnesium serum levels and a significant decrease in that of calcium levels as shown in Table 2

Table 2:	Comparison of serum	Calcium and Pho	osphorus in Case	s and Control	subjects
	VARIABLES	CASES	CONTROLS	P VALUE	
	Calcium(mg/dl)	8.07±0.72	10.49±0.38	0.001	
	Phosphorus(mg/dl)	4.78±0.87	2.78±0.46	0.001	

In our study analysis when TSH levels were compared with serum calcium and phosphorus among the hypothyroid patients, it showed a statistically significant negative correlation between TSH and serum calcium. However there was no significant correlation of TSH with serum phosphorous and magnesium as given in Table 3.

Table 3: Pearson correlation coefficient between TSH and Calcium, Phosphorous among the hypothyroid patients

CASES	P Value	R Value	Significance
TSH Vs Calcium	0.026	-0.66	SIGNIFICANT
TSH Vs Phosphorus	0.545	0.128	NON SIGNIFICANT

DISCUSSION

Thyroid dysfunction is one of the important causes for secondary osteoporosis. Hence the bone minerals like Serum calcium and phosphorous levels can be fairly used as index of bone resorption^{3,7}. The present study was done to assess the levels of serum calcium and phosphorus in hypothyroid patients. In this study there was a significant decrease (p<0.0001) in serum calcium levels in hypothyroid patients (8.07 ± 0.72) when compared with the control subjects (10.49±0.38). As thyroid hormones are most essential for normal growth and maturation of the skeletal system, their reduced level causes depressed bone turnover, leading to reduced blood calcium⁶. Thyroxine normally regulates blood calcium levels by releasing calcium extra cellular. In hypothyroidism, less thyroxine in the bloodstream and thus less thyroxine entry into the cells leading to decreased extra cellular calcium release^{1,8}. Our results are in accordance with the other studies done by Shivallela et al.9., Kavitha MM et al.10., Roopa and Soans et al.¹¹., and Abbas. et al.¹² In our study there was a statistically significant increase in phosphorous levels (4.78±0.87 vs 2.78±0.46) in hypothyroid patients when compared to control group. In hypothyroidism there is increased production of calcitonin which promotes the tubular reabsorption of phosphate and favour the tubular excretion of calcium, leading to hypocalcemia and hyperphosphatemia.^{1,13} When serum TSH levels were compared with serum Calcium and Phosphorus it showed a strong negative correlation between serum calcium and TSH values among hypothyroid patients (r = -0.66). TSH is considered an antiresorptive hormone, which through distinct unrelated mechanisms and inhibits osteoclastogenesis and osteoblastogenesis¹⁴. Kumar and Prasad et al. substantiated the same in an animal study which revealed increased excretion of calcium in rats with high TSH¹⁵.

However there was a significant increase in serum phosphorus levels in hypothyroid patients there was no statistical significance in the correlation of serum phosphorous and TSH levels among hypothyroid patients. But the studies conducted by Kavitha *et al.* and Susanna TY *et al.* showed increase in serum phosphorous and also a strong positive correlation with TSH level in hypothyroids^{4,10}.

CONCLUSION

Our study concludes that in hypothyroid patients, the serum calcium level was decreased and serum phosphorus level was increased when compared to euthyroid control subjects. Also there was a strong negative correlation between serum TSH and serum calcium levels were observed among hypothyroid individuals. It is therefore recommended for the regular evaluation of these minerals in hypothyroid patients which would improve their bone health and quality of life.

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