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Original Research Article

An Observational Assessment of Bone Minerals, Calcium and Phosphorus in Hypothyroidism and its Relation with Thyroid Hormone Levels

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Abstract

Aim: The aim of the present study was to assess the levels of bone minerals, calcium and phosphorus in hypothyroidism and its relation with thyroid hormone levels.

Methods: The cross-sectional and observational study was done at department of Biochemistry, NMCH, Jamuhar, Sasaram, Bihar over a period of 12 months (August 2022 to July 2023)

Results: 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. Among the minerals, there was a significant increase in phosphorous and magnesium serum levels and a significant decrease in that of calcium levels. 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.

Conclusion: The study concluded 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.

Keywords: Hypothyroidism, calcium, phosphorous

Introduction

Thyroid hormones (TH), vitamin D (VD) and steroids belong to a special group of endocrine molecules which produce their effects by signaling in nuclear receptors (NR) [1]. Typically they are pleiotropic hormones, affecting a significant range of cell types in most tissues and in various systems. In common TH, steroids and VD also have intense effect on bone strength and on mineral and energy metabolism. While glucocorticoids and gonadal steroids, respectively, lead to a loss and an increase in bone mass, TH have a more complex effect depending on age, circumstances.[1]Recently, Dhanwal et al [2] have reported hypovitaminosis D and its impact on bone mineral homeostasis and bone density. Patients with Graves' disease in India have steatorrhea and marked proximal muscle weakness due to skeletal muscle myopathy. [3] Majority of patients have increased skin pigmentation during thyrotoxic state. [4] Thyroid hormones have direct catabolic effect on bone mineral homeostasis, leading to increased bone mineral resorption and calcium loss through kidneys. [5] Increased skin pigmentation and related vitamin D deficiency coupled with excessive urinary calcium loss, caused by thyrotoxicosis, may well be responsible for causing significant abnormalities in bone mineral homeostasis in thyrotoxic patients in India. Negative calcium balance due to catabolically induced increase in bone resorption may also be operative in Indian thyrotoxic patients.

Bone mineral homeostasis is predominantly controlled by three hormones, i.e. parathyroid hormone (PTH), 1,25(OH)2D and calcitonin. [6] These hormones act on three target tissues, i.e. bone, intestine and kidney. There is a close interaction among PTH, 1,25(OH)2D and calcitonin to regulate serum calcium, phosphorous, and magnesium levels through actions on target tissues. In skin, ultraviolet light (wavelength of 290–315 nm) converts 7-dehydrocholestrol, a precursor of cholesterol, to vitamin D3. Vitamin D3 is metabolized in the liver

to 25(OH)D by 25-hydroxylase enzyme and then in kidneys to its active form 1,25(OH)2D by 1-αhydroxylase enzyme. Serum 25(OH)D has a longer half-life of 21 days and is a measure of vitamin D nutritional status. 1,25(OH)2D stimulates calcium absorption in gut and also regulates bone turnover and renal excretion of calcium and phosphorous. [7] The net effect of 1,25(OH)2D is to raise serum calcium while decreasing PTH. Serum calcium and 1,25(OH)2D levels regulate PTH secretion from parathyroid gland. PTH stimulates bone turnover and renal phosphorous excretion by inhibiting phosphorous reabsorption in proximal and distal tubules and renal calcium reabsorption at distal tubule. The net effect of PTH is to raise serum Ca and 1,25 (OH)2D while decreasing serum phosphorous levels.

The aim of the present study was to assess the levels of bone minerals, calcium and phosphorus in hypothyroidism and its relation with thyroid hormone levels.

Materials and Methods

The cross-sectional and observational study was done at Department of Biochemistry, NMCH, Jamuhar, Sasaram, Bihar over a period of 12 months (August 2022 to July 2023). The study population included 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 µIU/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 ± SD. To correlate the parameters among the cases Pearson's correlation test was applied. P- value < 0.05 was considered statistically significant.

Results

Table 1: Comparison of serum TSH, T3 and T4 in Cases and Control subjects

Variables	Cases	Controls	P Value
TSH(µIU/dl)	19.52±12.68	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	0.128

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.

Table 2: Comparison of serum Calcium and Phosphorus in Cases 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

Among the minerals, there was a significant increase in phosphorous and magnesium serum levels and a significant decrease in that of calcium levels.

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

CASES	PValue	RValue
TSHVsCalcium	0.032	-0.62
TSHVsPhosphorus	0.525	0.132

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.

Discussion

Thyroid diseases are common and their incidence and prevalence were considered to increase with age. [8] In India, hypothyroidism is most common, among the 42 million people suffering from thyroid diseases. [9] 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. [10] Calcium (Ca^{2+}) and phosphorus (PO_4^{2-}) are all divalent metal ions, which are necessary for metalloenzymes and various crucial metabolic pathways directly or indirectly regulated by thyroid hormones. [11]

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 calcium. [12] 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. [13] 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. Among the minerals, there was a significant increase in phosphorous and magnesium serum levels and a significant decrease in that of calcium levels. 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. Our results are in accordance with the other studies done by Shivallela et al [14], Kavitha MM et al [15], Roopa and Soans et al [16], and Abbas et al. [17]

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 and unrelated mechanisms inhibits osteoclastogenesis and osteoblastogenesis. [18] Kumar and Prasad et al [19] substantiated the same in an animal study which revealed increased excretion of calcium in rats with high TSH. However there was a significant increase in serumphosphorus 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 [20] and Susanna TY et al[19] showed increase in serum phosphorous and also a strong positive correlation with TSH level in hypothyroids.

Conclusion

The study concluded 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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