

## Effect of thyroid hormones on serum calcium and phosphorous

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### Abstract

**Introduction:** Calcium and phosphorous are the two important minerals whose abnormalities are most ignored in the developing countries. The impact of calcium abnormalities ranges from abdominal pain, muscle spasms, psychiatric disorders to cardiac arrest. Other than the known regulators of calcium and phosphorous, thyroid hormones may affect the levels of calcium and phosphorous. The aim of our study is to estimate serum calcium, phosphorous and thyroid profile and to see the effect of thyroid hormones on serum calcium and phosphorous.

**Materials and Methods:** 40 hyperthyroid and 40 hypothyroid patients were taken as cases. 40 healthy individuals were taken as controls. Thyroid profile, serum calcium and phosphorous were estimated in cases and controls. Serum calcium and phosphorous levels were compared with thyroid hormones among cases and controls. Correlation of thyroid hormones with serum calcium and phosphorous were done.

**Result:** The mean serum calcium and phosphorous levels in hyperthyroid patients are  $12.7 \pm 0.89$  mg/dl and  $5.1 \pm 0.68$  mg/dl respectively which are increased (p value < 0.05) compared to controls. The mean serum calcium and phosphorous levels are  $6.9 \pm 0.93$  mg/dl and  $2.3 \pm 1.1$  mg/dl respectively in hypothyroid patients which are decreased (p value < 0.05) compare to controls. Strong correlations of all thyroid hormones with serum calcium and phosphorous in hyperthyroidism and hypothyroidism is seen (p value < 0.05).

**Conclusion:** Hyperthyroidism and hypothyroidism may lead to hypercalcemia and hypocalcemia respectively, which are the cause of many disorders and disabilities. The concentration of serum calcium and phosphorous should be checked regularly in those patients.

**Keywords:** Hyperthyroidism, Hypothyroidism, Serum calcium, Serum phosphorous.

### Introduction

Calcium and phosphorous are very important minerals in our body, which are regulated by various mechanisms in our body. Alteration in the homeostasis of these minerals will lead to hazardous effects in the body. The adverse effects of hypercalcemia are anorexia, confusion, psychosis, renal stones etc. The symptoms of hypocalcemia are muscle cramps, paresthesia, tetany, seizures etc.<sup>1</sup>

Other than the usual regulators of calcium and phosphorous like vitamin D, calcitonin and parathyroid hormones, it is said that thyroid hormones also play a role in the regulation of calcium and phosphorous in our body.<sup>1,2</sup>

Thyroid hormones which include T3, T4 and TSH play a major role in the cellular development, thermogenic maintenance and mineral and metabolic processes in our body.<sup>3</sup> On one hand hyperthyroidism is responsible for decreased bone mineral density, increased osteoporotic fractures and increase serum calcium and phosphorous levels, on the other hand hypothyroidism is known to decrease serum calcium and phosphorous levels.<sup>4-7</sup>

In hyperthyroidism there is accelerated bone turn over and poor mobilization of calcium that leads to increase serum calcium and phosphorous concentration. While in hypothyroidism opposite effect takes place.<sup>2,4</sup>

Previous studies done on calcium and phosphorous in thyroid disorders had conflicting results. Some studies had shown normal levels of calcium and phosphorous in thyroid disorders, while others had shown altered levels.<sup>8</sup>

The aim of our study was to determine the serum calcium and phosphorous levels in the hyperthyroid and hypothyroid patients and to compare them with the healthy controls to determine the effect of thyroid hormones on serum calcium and phosphorous.

### Materials and Methods

The study was conducted in the Department of Biochemistry, Pacific Medical College and Hospital, Udaipur between August 2016 to March 2018. Institutional ethics committee clearance had been taken before starting the study. 40 patients with hypothyroidism and 40 patients with hyperthyroidism were enrolled in the study as cases along with 40 healthy individuals were taken as control group. Clinical and laboratory diagnosis had been done to determine the cases and controls.

Individuals with any hepatic, renal and cardiac disease, chronic infection, any medication to treat thyroid disorders or affect thyroid hormones and calcium and phosphorous concentration, alcoholism, on mineral supplements were excluded from the study.

After taking informed consent, 2 ml of venous blood was withdrawn from the study group in the plain vacutainer. Blood was allowed to clot, and centrifuge was done to separate serum. Serum thus separated was stored at 4-8° c temperature till the analysis was done. Estimation of serum T3, T4 and TSH were done by fully automated analyzer cobas e411 and serum calcium and phosphorous were analyzed by fully automated analyzer cobas c311.

### Statistical Analysis

The results are expressed as mean  $\pm$  SD. Unpaired student 't' test was applied to compare the different parameters between cases and controls. 'p' value <0.05 was considered as statistically significant. Pearson's correlation coefficient was applied to see the correlation between thyroid profile and serum calcium and phosphorous. 'p' value < 0.05 was considered as statistically significant in Pearson's correlation coefficient.

### Result

As shown in Table 1, there is no significant difference in the gender and age between cases and controls. Also, there is clear increase in the Serum T3, T4 and decrease in the TSH levels. There is significant difference in the serum calcium and phosphorous between hyperthyroidism and control group with the p value < 0.05. The concentration of both serum calcium

and phosphorous are increased in the hyperthyroid patients compare to control group.

As shown in Table 2, there is no difference in gender and age between cases and controls. Also, there is clear decrease in the concentration of T3, T4 and increase in TSH levels. There is decrease concentration of serum calcium and phosphorous in the hypothyroid patients compared to normal control group. The difference is statistically significant with p value < 0.05.

As shown in Table 3 there is significant positive correlation of serum T3 with serum calcium in both hyperthyroid and hypothyroid patient. The r value is +0.85 and +0.82 respectively (p value < 0.05 in both). There is also strong positive correlation of serum T4 with serum calcium in hyperthyroid and hypothyroid patient (r value + 0.79 and +0.88 respectively and p value < 0.05 in both). There strong positive correlation between serum T3 and T4 with serum phosphorous in hyperthyroid and hypothyroid patients (r value +0.74, +0.76, +0.68 and +0.65 respectively and p value < 0.05 in all). There is strong negative correlation between TSH and serum calcium levels in both hyperthyroid and hypothyroid patients (r value -0.73 and -0.69 respectively and p value <0.05 in both). There is also strong negative correlation between TSH and serum phosphorous levels in hyperthyroid and hypothyroid patients (r value -0.62 and -0.69 respectively and p value < 0.05 in both).

**Table 1: Shows the comparison of demographic details, thyroid profile, serum calcium and phosphorous levels in hyperthyroid cases with normal healthy controls**

	Hyperthyroidism	Control	
Gender (Female/male)	30/10	28/12	Not Significant
Age (years)	35.3 $\pm$ 5.6	34.7 $\pm$ 6.1	No Significant
Serum T3(ng/ml)	3.1 $\pm$ 0.15	1.4 $\pm$ 0.18	p value < 0.05
Serum T4( $\mu$ g/dl)	15.3 $\pm$ 1.1	9.7 $\pm$ 2.4	p value < 0.05
Serum TSH( $\mu$ IU/ml)	0.09 $\pm$ 0.03	2.67 $\pm$ 0.45	p value < 0.05
Serum Calcium (mg/dl)	12.7 $\pm$ 0.89	9.5 $\pm$ 1.2	p value < 0.05
Serum Phosphorous(mg/dl)	5.1 $\pm$ 0.68	3.6 $\pm$ 0.79	p value < 0.05

**Table 2. Shows the comparison of demographic details, thyroid profile. Serum calcium and phosphorous levels in hypothyroid cases with normal healthy controls**

	Hypothyroidism	Control	
Gender (Female/Male)	29/11	28/12	Not Significant
Age (Years)	33.6 $\pm$ 4.7	34.7 $\pm$ 6.1	Not Significant
Serum T3(ng/ml)	0.4 $\pm$ 0.02	1.4 $\pm$ 0.18	p value < 0.05
Serum T4( $\mu$ g/dl)	2.7 $\pm$ 0.59	9.7 $\pm$ 2.4	p value < 0.05
Serum TSH( $\mu$ IU/ml)	6.1 $\pm$ 1.6	2.67 $\pm$ 0.45	p value < 0.05
Serum Calcium (mg/dl)	6.9 $\pm$ 0.93	9.5 $\pm$ 1.2	p value < 0.05
Serum Phosphorous(mg/dl)	2.3 $\pm$ 1.1	3.6 $\pm$ 0.79	p value < 0.05

**Table 3: Shows the correlation of thyroid profile with serum calcium and phosphorous in hyperthyroidism and hypothyroidism**

Correlation between	Hyperthyroidism	Hypothyroidism
Serum T3 and Serum Calcium	r value = +0.85 p value < 0.05	r value = +0.82 p value < 0.05
Serum T4 and Serum Calcium	r value = +0.79 p value < 0.05	r value = +0.88 p value < 0.05
Serum TSH and Serum Calcium	r value = -0.73 p value < 0.05	r value = -0.69 p value < 0.05
Serum T3 and Serum Phosphorous	r value = +0.74 p value < 0.05	r value = +0.76 p value < 0.05
Serum T4 and Serum Phosphorous	r value = +0.68 p value < 0.05	r value = +0.65 p value < 0.05
Serum TSH and Serum Phosphorous	r value = -0.62 p value < 0.05	r value = -0.69 p value < 0.05

### Discussion

The thyroid gland secretes two most important hormones i.e. T3 and T4. They influence almost all metabolisms like carbohydrate, lipid and protein metabolism. They also maintain water and electrolyte homeostasis. Recently thyroid hormones are having greater attention because of their effects on mineral metabolism.<sup>13</sup>

In our study we have divided cases into two groups. Based on clinical and laboratory diagnosis, one group is having hyperthyroidism, and another group is having hypothyroidism. The concentration of serum calcium and phosphorous have been compared between these groups and healthy controls.

As per our study, there is significant increase in the concentration of serum calcium and phosphorous between hyperthyroid patient and healthy controls. Our results are consistent with the research done by Indrajit Nath et al.,<sup>3</sup> Shivleela MB et al.,<sup>9</sup> Abdelgayoum A.,<sup>5</sup> Mosekilde et al.<sup>14</sup> and Manicort et al.<sup>15</sup>

As per our study, there is significant decrease in the concentration of serum calcium and phosphorous between hypothyroid patients and control group. Similar results have been found in the studies done by D. Sridevi et al.,<sup>16</sup> Malamos et al.<sup>17</sup> and Gamage et al.<sup>18</sup>

As per our study there is strong positive correlation of Serum T3 and T4 with Serum calcium (p value <0.05) and strong negative correlation of Serum TSH with Serum Calcium (p value <0.05) in hyperthyroidism which suggests that Serum calcium level will increase as there is increase in the severity of hyperthyroidism. There is also strong positive correlation of Serum T3 and T4 with Serum calcium and strong negative correlation of Serum TSH with Serum calcium (p value <0.05) in hypothyroidism which also suggests that as the severity of hypothyroidism increases Serum Calcium concentration decreases. Same effects are also seen in the serum Phosphorous levels. These results are consistent with the research by Indrajit Nath et al.,<sup>3</sup> Abdelgayoum A.,<sup>5</sup> Mosekilde et al.,<sup>14</sup> Malamos et al.,<sup>17</sup> Gamage et al.<sup>18</sup>

The increase in the serum calcium and phosphorous levels in the hyperthyroid patient is because of effect of thyroid hormones on osteoblast to stimulate osteoclastic bone resorption via nuclear receptors, which increases bone turnover. PTH suppression as well as direct effect of thyroid hormone on tissue phosphate metabolism and renal phosphate will lead to the changes occurring in the phosphate concentration. The molecular mechanism behind the effect of thyroid hormones on serum calcium and phosphorous is multifactorial. The hyperthyroid state increases sensitivity of beta adrenergic receptors to catecholamines. Thyroid hormones especially T3 increase sensitivity of IL-6 to bones, which increases osteoclastic differentiation by increasing the expression of the receptor of nuclear factor  $\kappa$ B ligand. These all leads to increase concentration of serum calcium and phosphorous. While in hypothyroidism opposite effect will occur.<sup>3,19,20,21</sup>

In hypothyroid patients, there may be increase production of calcitonin with decrease availability of thyroxine inside the cell which will lead to increase tubular excretion of calcium and decrease extracellular calcium release, ultimately will lead to decrease concentration of serum calcium.<sup>16</sup>

### Conclusion

Hypercalcemia and hypocalcemia are two abnormalities which are very much neglected in India. They can lead to various abnormalities and disabilities. In our study we found that serum calcium and phosphorous are affected by the thyroid hormones. Whenever there are any thyroid hormone disturbances, alterations in the levels of serum calcium and phosphorous should be looked for to prevent any abnormalities from occurring.

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