Study of Serum Calcium, Magnesium And Phosphorous Levels In Patients With Thyroid Disorders

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ABSTRACT  
Thyroid disorders are most common and prevalent conditions in India, incidence being 42 million. Thyroid hormones are central regulator of body’s haemodynamics, thermoregulation and metabolism. They also determine the mineral pool in the blood. The aim of the study was to study Serum calcium, magnesium and phosphorous levels in patients with thyroid disorders. In this study we included 30 diagnosed cases of Hypothyroidism, 30 diagnosed cases of Hyperthyroidism and 30 healthy controls in the similar age group from whom 3 ml of blood was drawn under aseptic precautions to measure Serum calcium, magnesium and phosphorous levels by spectrophotometry method. Serum Ca\(^{2+}\) and PO\(^{4-}\) levels were significantly elevated in hyperthyroid and significantly decreased in hypothyroid patients compared to healthy controls. Serum Mg\(^{2+}\) level was significantly decreased in hyperthyroid and significantly elevated in hypothyroid patients compared to healthy controls. There was a significant negative correlation between serum TSH and Ca\(^{2+}\) level. The study indicates the profound influence of thyroid hormone on mineral metabolism. A patient with thyroid disorder may also manifest the symptoms that reflect altered mineral levels. Hence it is necessary to evaluate the serum levels of calcium, magnesium and phosphorous in patients with thyroid disorder in order to prevent further bone complications.  

Key words: Thyroid hormones, calcium, magnesium, phosphorous.

How to Cite this Article  
INTRODUCTION
The thyroid gland produces two related hormones, Thyroxin (T₄) and triiodothyronine (T₃). Acting through thyroid hormone receptors α and β, these hormones play a critical role in cell differentiation during development and helps to maintain thermogenic and metabolic homeostasis in adults (Fauci AS et al, 2008). The term hyperthyroidism is reserved for disorders that result from sustained overproduction of hormone by the thyroid gland itself. Reduced production of thyroid hormone is the central feature of the clinical state termed hypothyroidism. Thyroid hormone is essential for normal growth and maturation of the skeleton. Before puberty, thyroid hormone plays a major role in the maturation of bone (Kronenberg HM et al, 2008). In India, 42 million people are suffering from thyroid diseases; hypothyroidism being the commonest thyroid disorder (Murgod R and Soans G, 2012). The mean annual incidence of hypothyroidism is up to 4 in 1000 females, 1 in 1000 males and 1 in 4000 newborns (Suneel B et al, 2011; Suneel B et al, 2012). Calcium (Ca²⁺) and phosphorous (PO₄⁻) are the principal constituents of bone and together they comprise 65% of its weight. The quantitatively minor amounts of each of these ions in the extracellular fluid and within cells play crucial roles in normal physiology (Kronenberg HM et al, 2008). The majority of the total body stores of Ca²⁺ and PO₄⁻ are located in bone in the form of hydroxyapatite. Magnesium (Mg²⁺) is the second most abundant intracellular cation in the body after potassium (Moe MS, 2008). Most of the total body Mg²⁺ (67%) are found in bones and soft tissues (Gilroy CV et al, 2006). Thyroid hormone determines the mineral pool in the blood by influencing mobilization of minerals like Ca²⁺ and PO₄⁻ into the blood and also by influencing their clearance through urinary excretion due to its effect on glomerular filtration rate (GFR) or renal plasma flow (RPF) (Suneel B et al, 2011; Suneel B et al, 2012).

Previous studies done on serum Ca²⁺, PO₄⁻ and Mg²⁺ levels in thyroid disorders have shown conflicting results. Even though thyroid disorders are most common and prevalent conditions in India, studies focusing on blood levels of minerals are sparse (Murgod R and Soans G, 2012; Suneel B et al, 2011; Suneel B et al, 2012; Shivaleela MB et al, 2012).

AIMS AND OBJECTIVES
The present study was undertaken to assess the serum levels of Ca²⁺, PO₄⁻ and Mg²⁺...
levels in thyroid disorders. We also investigated the correlation of serum TSH with Ca\(^{2+}\), Mg\(^{2+}\) and PO\(^{4-}\) levels in hypo and hyperthyroidism.

**MATERIALS AND METHODS**

**Study design**

A case control study was carried out and the study group was selected from patients attending Medicine OPD of S.S.Hospital attached to S. S. Institute of Medical Sciences & Research Centre (SSIMS & RC), Davangere. The study was approved by the institutional ethical committee. Written informed consent was taken from each subject.

**Inclusion criteria**

The study population included cases and healthy controls in the age group of 18-60 years attending the medicine outpatient department of SS hospital attached to SSIMS & RC. Both males and females were included in the study. They were divided into 3 groups:

a) Group 1 included 30 newly diagnosed and untreated cases of hypothyroidism. The diagnosis was based on decreased serum T\(_3\) and T\(_4\) levels associated with increased TSH levels.

b) Group 2 included 30 newly diagnosed and untreated cases of hyperthyroidism. All patients suffering from thyroid disorders were diagnosed and confirmed by the physician based on T\(_3\) (Normal: 0.7-2.0 ng/mL), T\(_4\) (Normal: 4.5-11.0 μg/dL) and TSH (Normal: 0.4-4.2 μIU/mL) levels of the patients.

c) Group 3 included 30 healthy controls in the similar age group having normal thyroid profile.

**Exclusion criteria**

Paediatric age group (<18 yrs), elderly age group (>60 yrs), renal disorders, hepatic disorders, bone disorders, diabetes, hypertension or any other systemic illness that may affect the mineral status, patients on mineral supplementation, drugs for treatment of thyroid disorders or any other medications that might affect serum mineral concentration.

**Method of sample collection**

About 3 ml of venous blood was drawn using a disposable syringe under aseptic conditions in a sterile bulb from selected subjects. Blood was allowed to clot and serum was separated after 30-45 min by Remicentrifuge machine at 3000 rpm, serial no: LMC-9375.
Analytical methods
The serum was used for the analysis of calcium, magnesium and phosphorous by the spectrophotometric method on semi autoanalyzer using commercially available kits (Burtis and Ashwood, 2001).

RESULTS
Results of the present study are shown below.

Table 1: Age and sex distribution in cases and healthy controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypothyroid</th>
<th>Hyperthyroid</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs)</td>
<td>35.4 ± 11.0</td>
<td>38.9 ± 10.4</td>
<td>37.3 ± 10.7</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>05/25</td>
<td>08/22</td>
<td>07/23</td>
</tr>
</tbody>
</table>

The values are expressed as Mean ± SD
* p value <0.05 - significant compared with controls
** P value <0.001 - highly significant compared with controls

Table 2: Comparison of serum calcium, magnesium and phosphorous levels in cases and healthy controls

<table>
<thead>
<tr>
<th>Group 1 (N=30) Hypothyroid</th>
<th>Group 2 (N=30) Hyperthyroid</th>
<th>Group 3 (N=30) Healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 (ng/ml)</td>
<td>0.79 ± 0.39**</td>
<td>3.34 ± 2.46 **</td>
</tr>
<tr>
<td>T4 (μg/dl)</td>
<td>4.73 ± 2.51 **</td>
<td>14.6 ± 2.76 **</td>
</tr>
<tr>
<td>TSH (μIU/ml)</td>
<td>28.58 ± 24.96 **</td>
<td>0.15 ± 0.22</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>6.35 ± 1.20 **</td>
<td>14.48 ± 1.93 **</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>4.92 ± 1.02 **</td>
<td>1.23 ± 0.29 **</td>
</tr>
<tr>
<td>Phosphorous (mg/dl)</td>
<td>1.59 ± 0.42 **</td>
<td>5.75 ± 0.69 **</td>
</tr>
</tbody>
</table>

The values are expressed as Mean ± SD; n= number of subjects
* p value <0.05 - significant compared with controls
** P value <0.001 - highly significant compared with controls

STATISTICAL ANALYSIS
The data was expressed in terms of mean and standard deviation. The comparison among the groups was done using one way analysis of variance (ANOVA) and post hoc.
Serum Ca\(^{2+}\) and PO\(^{-4}\) levels were significantly elevated in hyperthyroid (14.48 ± 1.93 and 5.75 ± 0.69, respectively, p<0.001) and significantly decreased in hypothyroid patients (6.35 ± 1.20 and 1.59 ± 0.42, respectively, p<0.001) compared to healthy controls (9.97 ± 0.63 and 3.63 ± 0.57, respectively). Serum Mg\(^{2+}\) levels were significantly decreased (1.23 ± 0.29) in hyperthyroid and significantly elevated (4.92 ± 1.02) in hypothyroid patients compared to healthy controls (2.04 ± 0.21).

**Fig. 1**: Graph showing the comparison of Serum calcium, magnesium and phosphorous levels in groups 1 (Hypothyroid), 2 (Hyperthyroid) and 3 (Healthy controls).

### Table 3: Correlation of serum TSH with Calcium, Phosphorous and Magnesium

<table>
<thead>
<tr>
<th>Relation between</th>
<th>Hypothyroid</th>
<th>Hyperthyroid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r value</td>
<td>p value</td>
</tr>
<tr>
<td>TSH &amp; Calcium</td>
<td>-0.36</td>
<td>0.04*</td>
</tr>
<tr>
<td>TSH &amp; Phosphorous</td>
<td>0.03</td>
<td>0.87</td>
</tr>
<tr>
<td>TSH &amp; Magnesium</td>
<td>0.04</td>
<td>0.83</td>
</tr>
</tbody>
</table>
There was significant negative correlation between serum TSH and calcium in hypothyroid cases. No other significant correlation was found in hypo and hyperthyroid cases.

**Fig. 2: Scatter plot showing correlation of serum TSH with Calcium in Hypothyroid cases**

**DISCUSSION**

The present study was taken to study the effect of thyroid hormones on mineral status (Ca$^+$, PO$_4$$^{2-}$ and Mg$^{2+}$). Taking the age, the peak incidence of thyroid disorder was observed between 25- 38 years. Taking sex incidence, women had higher incidence when compared to men.

Previous studies done on serum calcium, phosphorous and magnesium levels in thyroid disorders have shown variable results. Most of the studies have shown hypercalcemia in hyperthyroidism and hypocalcemia in hypothyroidism (Murgod R and Soans G, 2012; Suneel B et al, 2011; Suneel B et al, 2012; Shivaleela MB et al 2012) which is consistent with the present study. Hyperthyroidism is characterized by accelerated bone turnover, which is caused from direct stimulation of bone cells by high thyroid hormone concentration leading to hypercalcemia (Shivaleela MB et al, 2012; Schwarz C et al, 2012; Pantazi H and Papapetrou PD, 2000). Thyroid hormones exert its effect on osteoblasts via nuclear receptors to stimulate osteoclastic bone resorption (Shivaleela MB et al, 2012). Patients with hyperthyroidism have a significantly decreased bone mineral density (BMD) (Feigerlova E et al, 2012). Thus hyperthyroidism is one of the major
causes of secondary osteoporosis (Shivaleela MB et al, 2012; Dhanwal DK, 2011). In hypothyroidism, there is depressed bone turnover due to impaired mobilization of calcium in to the bone that leads to decrease in the blood calcium level (Suneel B et al, 2011). Reduced bone turnover impairs bone formation and mineralization with a subsequent risk of bone fragility and increased fracture (Feigerlova E et al, 2012). Associated vitamin D deficiency may be the cause for hypocalcaemia in Indian hyperthyroid patients (Shivaleela MB et al, 2012; Dhanwal DK, 2011). There are variable reports on serum phosphorous levels in patients with thyroid disorders. Some studies reported hyperphosphatemia in hyperthyroidism and vice versa which is consistent with the present study (Shivaleela MB et al, 2012). The changes are due to suppressed parathyroid hormone (PTH) levels as well as direct effects of thyroid hormones on tissue $\text{PO}_4^{-4}$ metabolism and renal $\text{PO}_4^{-4}$ handling (Dhanwal DK, 2011). Thyroid hormones stimulate bone resorption directly thereby increasing serum $\text{Ca}^+$ and $\text{PO}_4^{-4}$ levels and suppressing PTH. Opposite effects are seen in hypothyroidism (Shivaleela MB et al, 2012). Some studies reported hypophosphatemia in hyperthyroidism and vice versa (Murgod R and Soans G, 2012; Suneel B et al, 2011; Suneel B et al, 2012; Schwarz C et al, 2012). In hypothyroidism, increased production of thyroid calcitonin can promote the tubular reabsorption of phosphate. In hyperthyroidism, decreased production of thyroid calcitonin promotes the tubular excretion of phosphate (Suneel B et al, 2011; Suneel B et al, 2012).

Studies regarding serum magnesium in thyroid disorders are also conflicting. Some studies reported hypermagnesaemia in hypothyroidism and vice versa which is consistent with the present study (Murgod R and Soans G, 2012; Schwarz C et al, 2012; Jones JE et al, 1966). Thyroid hormone has direct effect on the tubule, which if chronically absent, results in renal retention of magnesium (Murgod R and Soans G, 2012; Mc Caffrey C and Quamme GA, 1984). Hyperthyroidism can increase renal excretion of magnesium, thus leading to hypomagnesemia (Gilroy CV et al, 2006). Increased thyroid activity causes more magnesium to be consumed by the tissue, thus favouring hypomagnesaemia (Swaminathan S et al, 2010). Some studies reported hypomagnesaemia in hypothyroidism and vice versa. In hypothyroidism there is increased renal plasma flow (RPF) leading
to high clearance of magnesium from kidneys leading to hypomagnesaemia. In hyperthyroidism there is hypermagnesaemia because of low clearance of magnesium from renal tubules (Suneel B et al, 2011; Suneel B et al, 2012).

CONCLUSION

The present study indicates the profound influence of thyroid hormone on mineral metabolism and changes in these minerals may eventually lead to complications like decreased bone mineral density and secondary osteoporosis. Therefore, it is necessary to evaluate the serum levels of these minerals in all patients with thyroid disorders.

REFERENCES


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Conflict of Interest: None declared