

## Assessment of mineral status in subclinical hypothyroidism patients – A case control study

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### Abstract

One of the important functions of thyroid hormones is homeostasis of mineral metabolism. So thyroid disorders usually lead to disturbances in mineral metabolism.

**Objective:** To analyze serum levels of minerals like calcium, phosphorus and magnesium in patients of subclinical hypothyroidism and to correlate these parameters with TSH levels in cases.

**Materials and Methods:** The study group included 70 patients who are diagnosed with subclinical hypothyroidism and 70 healthy controls who are age and sex matched with cases. Thyroid profile which includes estimation of serum T3, T4, TSH was done. Serum calcium, phosphorus and magnesium were also estimated in both cases and controls.

**Results:** The study showed that in subclinical hypothyroidism patients serum calcium levels were significantly low with mean values of  $8.9 \pm 0.62$  and  $p < 0.05$ , whereas serum phosphorus and magnesium levels were significantly higher with mean values of  $4.6 \pm 0.65$  and  $3.03 \pm 0.58$  respectively and  $p < 0.05$  compared to controls.

**Conclusion:** The serum levels of minerals like calcium, phosphorus and magnesium levels are significantly altered in subclinical hypothyroidism. Frequent follow up and checking the levels of these minerals in SCH patients should be done. Along with the treatment of the disease, it is necessary to give mineral supplements to prevent bone complications.

**Keywords:** Calcium, Phosphorus, Magnesium, Subclinical hypothyroidism, Thyroid stimulating hormone, Thyroid hormones.

### Introduction

Deficiency of thyroid hormones cause Hypothyroidism, which is one of the most common endocrine disorder nowadays. The disease causes generalized slowing of metabolic processes.<sup>1,2</sup> 2-15% of population worldwide suffer from the disease. Incidence is higher in women compared to men.<sup>2</sup>

Subclinical hypothyroidism refers (SCH) to thyroid hormone deficiency in patients who have very less or no standard clinical features of hypothyroidism.<sup>3</sup> In SCH there is increased serum thyroid stimulating hormone (TSH) levels with almost normal thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>) concentrations.<sup>4</sup> It is the mildest form of hypothyroidism and the patients usually lack classical signs and symptoms of overt hypothyroidism. The prevalence of SCH is between 3% and 18% in the general population and higher in women than in men.<sup>5</sup> SCH patients are at risk for progression to overt hypothyroidism with an average yearly progression rate of 2% to 6% with an increased risk in females.<sup>5</sup> TSH elevation in SCH is typically between 4 – 15 mIU/L. SCH is much more common than overt hypothyroidism, therefore it should be diagnosed early to prevent occurrence of clinical hypothyroidism.<sup>3</sup>

Thyroid hormones are vital for skeletal system growth and maturation. Recent studies have shown that TSH acts as a direct regulator of bone remodelling, highlighting the importance of integrity of the hypothalamo-pituitary-thyroid axis.<sup>6</sup> Thyroid diseases have adverse effects on bone and mineral homeostasis.<sup>7</sup> Calcium, Phosphorus, and Magnesium are divalent metal ions, which are necessary for

metalloenzymes and many important metabolic pathways regulated by thyroid hormones.<sup>8</sup> Thyroid dysfunction causes disturbances in metabolism of these minerals. Thyroid hormones increase serum calcium levels by stimulating bone resorption and inhibiting parathyroid hormone (PTH) activity. Opposite effects are seen in hypothyroidism.<sup>7</sup> Magnesium stimulates cyclic 3, 5 nucleotide phosphodiesterase. Since the action of thyrotropin on the thyroid gland is mediated by cyclic AMP, the availability of magnesium could affect the response of the gland to the pituitary hormone.<sup>2</sup>

Thyroid disorders are one of the causes of secondary osteoporosis. Lesser calcium level in hypothyroidism is due to improper mobilization of calcium into the bone.<sup>9</sup> Also there is increased production of calcitonin which promotes phosphate reabsorption and calcium excretion from renal tubules.<sup>9,10</sup> Impaired metabolism of minerals like calcium and magnesium is associated with leading metabolic disorders like hypertension and cardiovascular diseases.<sup>11</sup> Many studies have been done on mineral levels in hypothyroidism, which show conflicting results. There are very less studies on mineral status in subclinical hypothyroidism. Therefore we considered this study to assess the levels of the minerals in SCH.

### Aim of the Study

1. To estimate and compare the levels of minerals like serum calcium, phosphorus and magnesium levels in subclinical hypothyroid patients and healthy controls.

2. Also to correlate the levels of serum calcium, phosphorus and magnesium with TSH levels in cases.

### Materials and Methods

Study design was of case control type. The study was undertaken in Subbaiah Institute of Medical Sciences and hospital attached to it in Shimoga. Institutional ethical committee clearance was obtained before starting the study. Informed consent was taken from study participants after explaining the procedure. 70 cases of subclinical hypothyroidism diagnosed within one year and 70 healthy controls who are age and sex matched with cases were enrolled for the study.

The diagnosis of subclinical hypothyroidism was done if the patient is having low to normal serum T3 and T4 levels and increased TSH levels in the range of 4.2-15  $\mu$  IU/ml. The normal reference range of thyroid hormones which is mentioned in the kit insert are TSH = 0.27- 4.2  $\mu$  IU/ml, T3 =70 – 204 ng/dl, T4 = 5.1 - 14.06 $\mu$ g/dl. Study duration was from June 2017- December 2017.

**Inclusion Criteria:** Patients of SCH diagnosed within one year of onset of disease, who are in the age group of 20 to 65 years of both gender were included.

### Exclusion Criteria

1. History of hepatic disease, renal disease, bone disease, diabetes mellitus, alcoholism
2. Patients on mineral supplementation or any drugs that will affect mineral metabolism

3. Pregnant women, paediatric age group, other major medical conditions

Under aseptic precautions, a sample of 4 ml venous blood was collected. Thyroid hormones were estimated by using hormone analyser. Serum calcium, phosphorus and magnesium were measured using semi auto-analyser.

1. Estimation of serum calcium by Arsenazo 3 method.
2. Estimation of serum phosphorus by Ammonium molybdate method.
3. Estimation of serum magnesium by Calmagite method.

Statistical analysis was performed using appropriate statistical tests and SPSS package version 16. Biochemical parameters were compared in both groups using Student's 't' test. p value <0.05 was considered significant.

### Results

TSH level was higher in SCH group than control, where as serum T3 and T4 levels, although still within the normal range, were towards lower side of normal, compared to controls, as shown in Table 1.

SCH group has Significant decrease in serum calcium than control (8.9 $\pm$ 0.62 vs 9.5 $\pm$ 0.87 p <0.05), meanwhile serum phosphorus and magnesium both showed significant increase in SCH group (4.6 $\pm$ 0.65 vs 4 $\pm$ 0.95, p < 0.05) and (3.03 $\pm$ 0.58 vs 1.94 $\pm$ 0.34, p <0.001) respectively, as depicted in Table 1.

**Table 1: Analysis of Age, T3, T4, TSH, serum calcium, phosphorous, magnesium in two groups**

Variables	Cases	Controls	p value
Age	44.2 $\pm$ 11.9	42.27 $\pm$ 10.3	0.21
T3(ng/dl)	113.8 $\pm$ 25.1	121.5 $\pm$ 27.7	0.14
T4( $\mu$ g/dl)	7.84 $\pm$ 2.23	8.3 $\pm$ 1.48	0.167
TSH ( $\mu$ IU/ml)	18.93 $\pm$ 27.14	2.21 $\pm$ 1.02	<0.001**
Calcium(mg/dl)	8.9 $\pm$ 0.62	9.5 $\pm$ 0.87	0.001**
Phosphorus(mg/dl)	4.6 $\pm$ 0.65	4 $\pm$ 0.95	0.001**
Magnesium (mg/dl)	3.03 $\pm$ 0.58	1.94 $\pm$ 0.34	<0.001**

\*\* p<0.05 Statistically significant

**Table 2: Pearson's Correlation between TSH with serum calcium, phosphorous and magnesium in cases**

Cases	p value	r value
TSH VS Calcium	0.006, significant	- 0.65
TSH VS Phosphorus	0.034, significant	0.49
TSH VS Magnesium	0.467, not significant	0.11

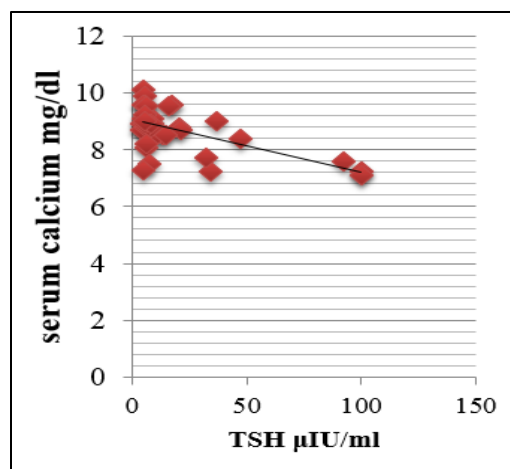


Fig. 1

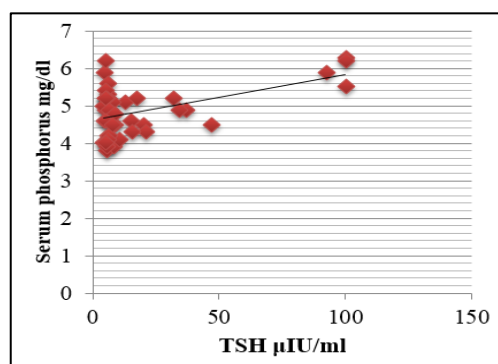


Fig. 2

## Discussion

Overt thyroid dysfunction is a risk factor of secondary osteoporosis, the effects of SCH on bone are still under discussion. Thyroid hormones are vital in maintaining renal hemodynamics, glomerular filtration, electrolyte handling and have a direct effect on calcium and magnesium resorption.<sup>12</sup> Serum calcium levels are normally regulated by T4 by releasing calcium from the cells. Therefore in hypothyroidism, where T4 is less, less calcium is released to blood.<sup>13</sup> Our study showed statistically significant decrease ( $p < 0.05$ ) in serum calcium levels in SCH patients. This is in accordance with MM Abbas et al, Kavita MM et al, Mukhesh G. Gohel et al, Murgod R et al, Shivaleela MB et al, Arvind Bharti et al<sup>3,9,11,13-15</sup> who found the same findings in their studies.

Present study showed marked elevation in serum phosphorous levels in cases of SCH when compared with healthy controls ( $p$  value  $< 0.05$ ) which is in agreement with studies by Frizel et al and Schwarz et al.<sup>16,17</sup> Many other authors<sup>3,9,10,13</sup> and Jaskiran K et al, D. Sridevi et al<sup>18,19</sup> have done similar studies in hypothyroid patients and reported that calcium is markedly reduced and magnesium and phosphorous levels are increased in cases. Suneel B et al. study showed similar results and proved that the changes in levels of calcium and phosphorus are mainly due to influence of PTH and calcitonin.<sup>10</sup> Similar results of

increased magnesium was found in study done by Frizel et al.<sup>16</sup>

The levels of calcium showed negative correlation and the levels of phosphorus showed positive correlation with TSH levels in cases. The same result was found in other studies.<sup>3,13</sup> TSH correlation with serum magnesium levels among cases was not significant in the present study which is supported by other studies conducted by Arvind Bharti et al and Frizel et al.<sup>15,16</sup>

Abedelmula M, et al.<sup>20</sup> study showed significant decrease in serum magnesium levels in SCH group which is in contrast to our study result.

## Conclusion

This study demonstrated low serum calcium, increased serum phosphorous and magnesium levels in subclinical hypothyroid patients. Hence estimation of these minerals in follow up period and supplementing the minerals, if their levels are less in blood would be more beneficial to the patients in preventing further bone complications.

**Conflict of Interest:** None.

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