

A comparative study of the ionic and total calcium levels in women with thyroid dysfunction

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Abstract

Background: Thyroid hormones play an important role in the homeostasis of calcium and phosphorous levels. A person with thyroid dysfunction may exhibit symptoms that are owing to the alteration in calcium levels.

Objective: To evaluate the effect of thyroid function on the total and ionic calcium levels in women with thyroid dysfunction.

Materials and Methods: The study group included three groups: group I (clinically proven healthy controls), group II (hyperthyroidism), and group III (hypothyroidism) with 45 subjects in each group. Estimation of the biochemical parameters was done by standard methods, and the level of ionic calcium was calculated using a formula.

Result: Serum total calcium and ionic calcium were significantly decreased in hypothyroidism group subjects when compared with hyperthyroidism and healthy control subjects. In groups II and III, the total calcium was inversely correlated with the thyroid stimulating hormone level.

Conclusion: Our study showed that there is an association between the serum calcium levels and thyroid function. However, there is no marked difference between the total and ionic calcium levels in thyroid dysfunction.

KEY WORDS: Total calcium, ionic calcium, hyperthyroidism, hypothyroidism

Introduction

Thyroid disorders are one of the most common endocrine disorders. Bone remodeling is affected by the direct or indirect effect of the thyroid hormones on the bone cells.^[1] The bone is affected by the interaction of the thyroid stimulating hormone (TSH) with the TSH receptors that are expressed on the precursors of osteoblasts and osteoclasts.^[2] In the early life, a deficiency of the thyroid hormone can lead to a delay in the bone development. An impaired mobilization of calcium into

the bone can cause a depressed turnover in hypothyroidism, and this can often lead to a decrease in the blood calcium level. A reduced mobilization of calcium prevails in hyperthyroidism, and this can lead to an increase in the blood calcium level.^[3] The plasma contains calcium that occurs in three physiochemical states. Ionized calcium, which is also termed as free calcium constitutes, approximately, 50%, remaining 40% is bound to the plasma proteins, and the rest 10% is complexed with small anions. All plasma or serum calcium is ionized, regardless of its association with proteins or small anions; hence, the term ionized calcium is inaccurate. Because the free or ionized calcium is biologically active and tightly regulated, it is the best indicator for calcium status.^[4] Despite the measurement of free calcium being clinically more useful, it has not replaced the measurement of total calcium.

Previous studies have been carried out on serum calcium levels in thyroid disorders. Some of the studies revealed conflicting results. Normal values were obtained in some,^[5] while decreased serum calcium levels in hypothyroidism were

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obtained in others.^[6] Hyperthyroid patients have been reported with hypercalcemia,^[7] while there are also reports of hypocalcemia in hyperthyroid patients, with 26% of hyperthyroid patients in India showing hypocalcemia.^[8]

To overcome this, we decided to focus on the serum levels of total calcium and free (ionized) calcium in both the hypo- and hyperthyroid cases in order to determine whether free calcium is a better indicator for calcium levels than total calcium.

Materials and Methods

This study was conducted in the Clinical Biochemistry laboratory at the RL Jalappa Hospital, the attached hospital of Sri Devaraj Urs Medical College, Kolar, Karnataka, India, over a period of 4 months from September to December 2014. The Institutional Ethical clearance was obtained for the study. The study group included a total of 135 subjects in the age group of 18 to 55 years.

- group I: forty-five age-matched healthy individuals;
- group II: forty-five clinically proven cases of hyperthyroidism; and
- group III: forty-five clinically proven cases of hypothyroidism.

Women aged above 55 years, those with hepatic, renal, and cardiovascular diseases, those with parathyroid disorders, those on mineral supplementation, those on treatment for thyroid disorders, and those on medications that can affect the calcium levels were excluded from our study.

After 8 h of overnight fasting, 2 mL of venous blood was drawn from both the control and study groups under aseptic conditions. The serum was separated by centrifugation and stored at -20°C until estimation. The serum total T3, T4, and TSH were estimated by chemiluminescence method,^[9] using Vitros 250 ECI Johnson and Johnson analyzer. Serum total calcium and serum albumin were analyzed in Vitros 250 Dry chemistry analyzer by O-Arsenazo method^[10] and Bromocresol green dye binding method,^[11] respectively. Ionic or free calcium was calculated using the formula^[12]:

Ionized calcium = $0.25 \times [0.9 + (0.55 \times \text{total calcium}) - (0.3 \times \text{albumin})]$.

Statistical Analysis

Statistical analyses were performed using SPSS software, version 20 (Armonk, NY, USA). Results were expressed as mean \pm SD. ANOVA test was used for testing the significance between the groups, followed by Post hoc test using Bonferroni criterion. Correlation of parameters was done by Pearson's correlation formula. A p value of < 0.05 was considered statistically significant.

Result

Table 1 shows the comparison of the biochemical parameters between the groups I, II, and III. ANOVA test showed that the serum total T3, T4, TSH, serum albumin, serum

total calcium, and ionic calcium were highly significant with $p < 0.001$. When groups I and II were compared [Table 2] using Post hoc test, T3 and T4 showed a highly significant p value < 0.001 , whereas albumin, total calcium, and ionic calcium showed a significant p value < 0.05 . When the groups I and III were compared [Table 2], T4, TSH, albumin, total calcium, and ionic calcium were highly significant with a p value < 0.001 . On comparison of group II vs. group III, only T3, T4, and TSH showed a highly significant p value of < 0.001 [Table 2].

Correlation of Total Calcium with TSH in Hyperthyroidism

When the total calcium with TSH was correlated in hyperthyroidism group, a negative correlation was observed with r value = 0.021 [Figure 1].

Correlation of Total Calcium with TSH in Hypothyroidism

In hypothyroidism group, a negative correlation of total calcium with TSH ($r = 0.013$) was observed [Figure 2].

Discussion

Our study showed that serum total calcium and ionic calcium were significantly decreased in hypothyroidism group when compared with hyperthyroidism subjects and healthy control subjects. In both the groups II and III, total calcium was inversely correlated with the TSH level. Thyroid disease is a pathological condition, which affects the calcium and phosphorous metabolism. Abnormalities in the calcium and phosphorous homeostasis are known as disorders of the mineral metabolism. Thyroid hormone is essential for the normal growth and maturation of skeleton. Thyroid disease has widespread systemic manifestations including their effect on bone resorption.^[13] Serum calcium levels have been used as an index of bone resorption.^[14]

In cases of hyperthyroidism, there will be a direct stimulation of bone cells by high thyroid hormone concentrations.^[15] Hypercalcemia has been reported in about 23% cases of hyperthyroidism.^[16] The percentage of hypercalcemia in hyperthyroidism cases increased to 50% when ionized calcium was measured instead of total serum calcium.^[17]

Our study showed that when cases of hyperthyroidism were compared with controls, the results were highly significant for both the measured total calcium and ionic calcium, with a significant p value of < 0.001 . This is in accordance with the findings of Manicourt *et al.*,^[18] but in contrast to Dhanwal *et al.*^[8] However, the changes in the serum calcium level do not appear to be an acute problem for these patients, although it may lead to problems on a long-term basis. Studies conducted by Szabo Ritzl^[19] have shown elevated ionized calcium levels in patients older than 60 years of age. The linear correlation between the ionized calcium levels and the different parameters of thyroid function is highly significant in the older age group.

In hypothyroidism, there can be decrease in the blood calcium levels because of impaired mobilization of calcium

Table 1: Comparison of the biochemical parameters between group I (clinically healthy controls), group II (hyperthyroidism), and group III (hypothyroidism)

Biochemical parameters	Group I (n = 45)	Group II (n = 45)	Group III (n = 45)	ANOVA F value with significance, p*
Serum total T3 (ng/mL)	1.21 ± 0.2	1.69 ± 0.7	0.97 ± 0.37	27.110, <0.001
Serum total T4 (µg/dL)	8.151 ± 8	14.07 ± 3.4	5.53 ± 2.9	108.589, < 0.001
Serum TSH (µIU/mL)	2.46 ± 1.0	0.45 ± 2.3	31.51 ± 36.3	28.609, < 0.001
Serum albumin (g/dL)	4.54 ± 0.8	3.9 ± 0.76	3.7 ± 1.0	10.895, < 0.001
Serum total calcium (mg/dL)	10.34 ± 0.4	9.12 ± 1.79	8.69 ± 2.0	10.183, < 0.001
Ionic calcium	1.30 ± 0.14	1.18 ± 0.19	1.14 ± 0.21	8.858, < 0.001

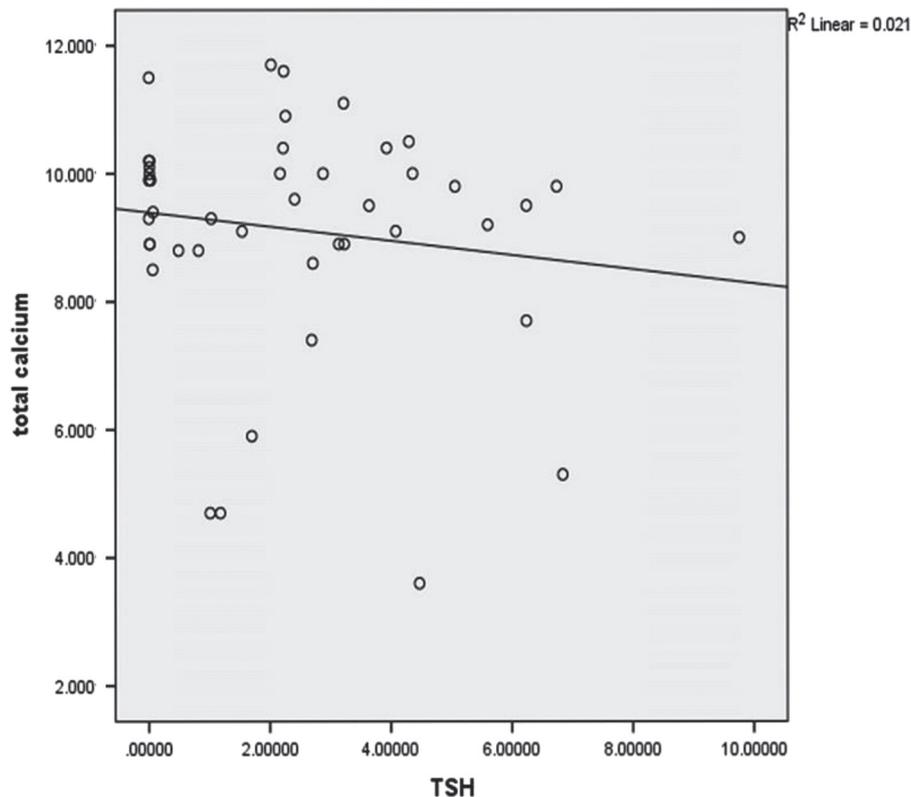
Results are expressed in mean ± SD.

*p < 0.001 is highly significant.

Table 2: Post hoc test comparing group I vs. group II, group I vs group III, and group II vs group III

	Total T3 (ng/mL), p	Total T4 (µg/dL), p	TSH (µIU/mL), p	Albumin (g/dL), p	Total calcium (mg/dL), p	Ionic calcium, p
Group I vs. group II	< 0.001**	< 0.001**	1.000	0.004*	< 0.005*	0.008*
Group I vs. group III	0.054*	< 0.001**	< 0.001**	< 0.001**	< 0.001**	< 0.001**
Group II vs. group III	< 0.001**	< 0.001**	< 0.001**	0.670	0.790	1.000

*p < 0.05 is significant; **p < 0.001 is highly significant.

**Figure 1:** Correlation of total calcium with TSH in hyperthyroidism.

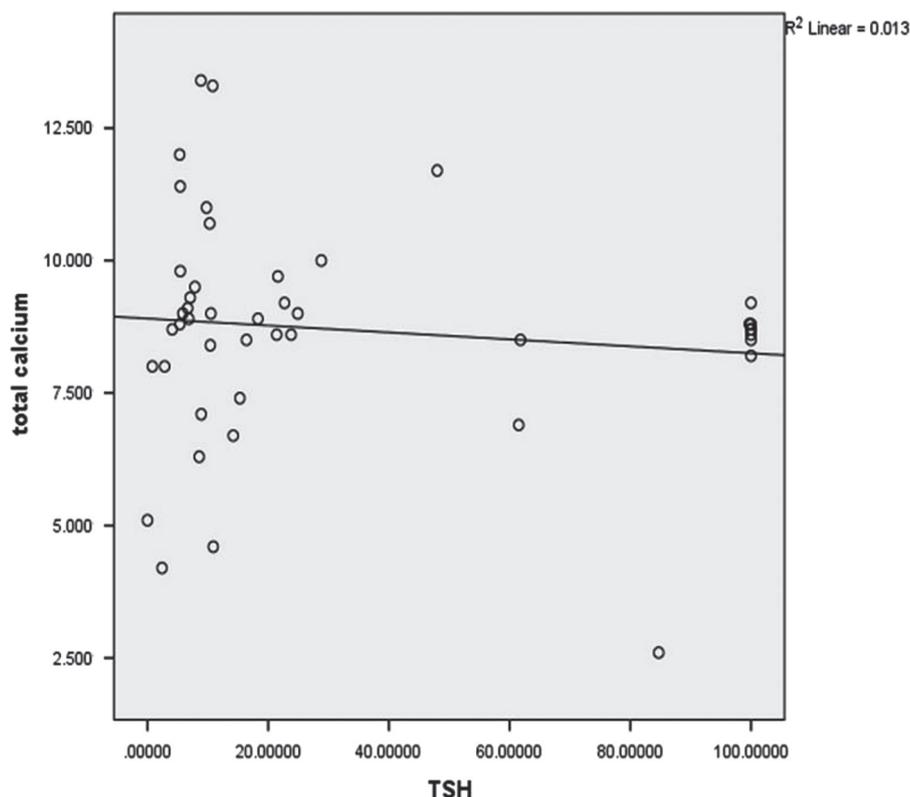


Figure 2: Correlation of total calcium with TSH in hypothyroidism.

into the bone. Our findings showed that when the hypothyroidism subjects and control subjects were compared the result was highly significant only for T3, T4, and TSH, but the change in both the total calcium and ionic calcium was not significant. This was in contrast to the findings of Hassan et al.,^[20] where there was a significant decrease in mean serum calcium levels in their test group when compared with the control group. A significant decrease in the ionized calcium and normal total calcium levels in hypothyroid cases were seen in a study done by Al-Hakeim.^[21] Although measuring serum ionized calcium should give a better indication than the total calcium levels, our study showed that there does not appear to be a significant difference between the measurement of total calcium and ionic calcium in hypo- and hyperthyroidism.

Conclusion

This study concludes that there is an association between the serum calcium levels and thyroid function, which may be relevant in marked cases of hypo- or hyperthyroidism. Hence, it is better to estimate the levels of serum calcium in all thyroid disorders. However, this will have to be correlated with the duration and severity of thyroid disorders. Further studies are required, where direct estimation of ionic calcium by ion

selective electrode is done to derive a meaningful conclusion. Our study population of 45 in each group is comparatively small, and the study can be extended to a larger population. Dietary habits of the persons should also be taken into consideration.

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