

Original Article

Influence of Hypothyroidism on Serum Calcium Levels in Postmenopausal Women

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Background : Hypothyroidism, is a common endocrine disorder manifesting with altered mineral metabolism. Hence, we designed this research to compare the levels of total and ionised calcium in postmenopausal women with and without thyroid dysfunction.

Materials and Methods : This is a case control study with 75 hypothyroid postmenopausal women and 25 euthyroids. Triiodothyronine (T3), Thyroxine (T4) level, Thyroid Stimulating Hormone (TSH) and serum total and ionised calcium were analysed. Statistical analysis was done using SPSS software.

Results : Postmenopausal women with hypothyroidism showed a significant reduction in total and ionised calcium levels with increase in duration of disorder. Correlation analysis with calcium (Total and Ionised) showed a significant negative correlation for Thyroid stimulating hormone and positive correlation for Triiodothyronine and Thyroxine.

Conclusion : Reduction in total and ionised calcium level was observed in postmenopausal women with hypothyroidism. It is due to reduced intestinal absorption and increased renal loss which is worsened by dysfunctional thyroid.

[J Indian Med Assoc 2025; 123(1): 60-2]

Key words : Hypothyroidism, Ionised calcium, Osteoporosis, Postmenopausal Women.

Thyroid hormone is a central regulator of body's, hemodynamic system, thermoregulation as well as metabolism which includes regulation of lipid, carbohydrate, protein, electrolytes and minerals¹. India accounts for 42 million individuals with thyroid disease². Hypothyroidism is a common thyroid disorder among postmenopausal women over the age of 50 years. This could be attributed to the physiological negative feedback by Thyroxine during menopause^{3,4}. Calcium ion is the fifth element and most prevalent cation found in body with vital roles. Some of these include skeletal mineralisation, neuromuscular conduction, blood coagulation, maintenance of normal tone and excitability of skeletal and cardiac muscles⁵. Hypothyroidism is receiving greater attention as it causes a wide range of clinical manifestations ranging from metabolic to cardiovascular disorders⁶, deteriorating renal function⁷ and derangement in bone mineral

Editor's Comment :

- Calcium reduction was observed in postmenopausal women with hypothyroidism. Moreover, menopausal oestrogen deficiency induces calcium loss influencing extra skeletal calcium homeostasis. So, evaluation of mineral status in hypothyroidism may support early prediction and prevention of osteoporosis and neuromuscular complications in postmenopausal women.

metabolism. It has an altered mineral metabolism by its direct or indirect action on bone turnover⁸ and exacerbates the risk of secondary osteoporosis. Oestrogens take a role in bone re-modelling by retarding interleukin (IL)-6 productions that reduces bone resorption and influences osteoclast apoptosis. Menopause, therefore results in longevity of osteoclasts; induction of calcium loss by reduction in intestinal calcium absorption and renal calcium conservation⁹. The ionised calcium, owing to its biological active property, has been chosen as a best indicator of calcium status. In our study, serum total and ionised calcium and its correlation with thyroid profile (Triiodothyronine [T3], Thyroxine [T4] and Thyroid Stimulating Hormone [TSH]) in postmenopausal hypothyroid women were assessed.

MATERIALS AND METHODS

It is a prospective, case control study carried out for a period of 2 months. It included 100 postmenopausal women and they were divided into 4 groups.

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Received on : 08/08/2023

Accepted on : 26/08/2023

Group I – 25 Euthyroid postmenopausal women (controls).

Group II – 25 Hypothyroid postmenopausal women (duration less than 2 years).

Group III – 25 postmenopausal women (duration of 2-5 years).

Group IV – 25 postmenopausal women (duration of more than 5 years).

Inclusion Criteria :

Postmenopausal women with TSH levels >5.50 (mIU/ml).

Exclusion Criteria :

Postmenopausal women with hepatic, renal disease or any other critical illness, on mineral supplementation, anti-thyroid drugs or any other medications known to affect the calcium metabolism or postmenopausal women who undergone total or subtotal thyroidectomy were excluded from the study.

Subjects were selected based on inclusion and exclusion criteria. After obtaining informed consent, under aseptic precautions, 5ml of fasting venous blood sample is collected from each patient and analysed for thyroid profile, calcium and albumin. Thyroid profile was done by ELISA; Total Calcium by photometric Arsenazo-III dye binding method and albumin by BCG dye method. Ionised calcium was calculated by the formula:

Ionised Calcium =

$$0.25 \times [0.9 + (0.55 \times \text{total calcium}) - (0.3 \times \text{albumin})]^{10}$$

The data was analysed by SPSS software. Descriptive statistics were expressed as mean and Standard Deviation. Analysis of Variance (ANOVA) was performed to determine the significant differences between the means of independent groups. Pearson's correlation coefficient was used to establish the correlation between Total thyroid profile and calcium. P value <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

Among 100 postmenopausal women, 25 were grouped as controls with no underlying thyroid disorder. Remaining 75 were grouped based on their duration of the disorder. The mean age of the control group was 49.5 years. The mean age of II, III & IV groups were 49.1, 51.8 and 53.6 years respectively. We observed a significant decrease in mean of total (F test = 8.14) and ionised calcium (F test = 8.78) in hypothyroidism with a highly significant p value of <0.001 when compared with

controls (Table 1). Decrease in serum Calcium (Total and Ionised) was noted with increase in duration of thyroid dysfunction. Hypothyroidism for more than 5 years, had a significant decrease in calcium concentration. Pearson's correlation analysis showed a significant negative correlation between TSH and total and ionised calcium with 'r values' of 0.52 and 0.48 respectively; non-significant positive correlation between thyroid hormones and calcium (Table 2).

DISCUSSION

We observed a reduced concentration of calcium (total and ionised) in hypothyroidism when compared to subjects with normal thyroid function. Our findings were in accordance to Neelakshi Kalita, *et al*¹¹ and Susanna, *et al* study¹². Decreasing levels of serum calcium level after thyroidectomy as endorsed in MS Islam study also proved the fact of mineral derangement in thyroid disorder¹³. T3, T4 and TSH levels had a significant difference between the study groups. The reduction in serum calcium is in proportion with the duration of hypothyroidism establishing a negative effect on the mineral and associated with degree and severity of the disorder. Further, a negative significance between TSH and calcium and a non-significant positive correlation with the thyroid hormones and calcium are in accordance with Mackawy AM, *et al* study¹⁴.

Serum calcium level and its rate of turnover were lowered reflecting the risk for progression to osteoporosis during endocrine abnormalities. Hypothyroidism confers to approximately 2% to 3% of bone loss over the following 5 to 10 years of postmenopausal period¹⁵.

Bone loss due to extraction of calcitonin from the gland facilitates tubular retention of phosphate and tubular discharge of calcium from kidneys¹⁶.

Table 1 — Distribution of Serum Total, Ionized Calcium and Thyroid Profile among Various Groups

Parameter	Group 1 (n=25)	Group 2 (n=25)	Group 3 (n=25)	Group 4 (n=25)	F value (n=25)
FT3 (p/ml)	3.08±0.83	2.85±0.67	2.28±1.02	2.66±0.87	3.9*
FT4 (ng/dl)	1.7±0.66	1.35±0.31	1.52±0.24	1.29±0.37	4.68*
TSH (mIU/ml)	1.19±0.36	41.13±13.38	35.1±7.57	59.38±16.05	23.71**
Total Calcium (mg/dl)	9.96±0.87	8.3±0.69	8.07±0.78	7.51±0.66	8.14**
Ionised Calcium (mg/dl)	5.02±0.55	4.91±0.55	4.85±1.19	4.06±0.45	8.78**

*p<0.05-Significant; **p<0.001-Highly significant

Table 2 — Correlation of Calcium (Total and Ionised) with Thyroid Profile in Hypothyroid Postmenopausal Women

Correlation coefficient (r-value)	T3	T4	TSH
Total calcium	0.45	0.67	-0.52*
Ionised calcium	0.29	0.32	-0.48*

*p<0.05-Significant

The mechanisms of calcium reduction in hypothyroid postmenopausal women is attributed to (a) dysfunctional thyroid associated with an increased excretion of calcium and phosphorous¹⁷, (b) Further, oestrogen deficiency after menopause induces loss of calcium by indirect effects on extra skeletal calcium homeostasis as well as decreased intestinal calcium absorption¹⁸.

Altered mineral metabolism emphasizes for the evaluation and supplementation of minerals in hypothyroid postmenopausal women. In addition to osteoporosis, it has been recommended that early diagnosis of hypocalcaemia and its replacement would prevent life-threatening complications like laryngospasm, tetany, seizures and cardiac abnormalities¹⁹.

Limitations :

- The complaints pertaining to osteoporosis and neuromuscular disorders including aesthesia, weakness or tetany accompanied with hypocalcaemia were not incorporated into this study.
- Dietary history was not considered.

CONCLUSION

Serum ionised and total calcium levels were significantly altered in hypothyroidism. The effect of hypothyroidism on the blood levels of total and ionised calcium affects various metabolisms and results in clinical manifestations in these patients. Hence it signifies the need for routine screening and treatment among postmenopausal hypothyroid women. Supplementation of minerals should be carried out early in these patients to prevent severe bone and neuromuscular complications.

Conflict of Interest : None

Funding Sources : None

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