# **Original** Article



# Calcium Imbalance and Hypothyroidism: Exploring the Relationship

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## Abstract

**Background:** The thyroid gland synthesizes mainly two hormones, triiodothyronine (T3) and thyroxin (T4) which are important to maintain various functions especially metabolic, mineral and thermogenic homeostasis in body. The disorders of thyroid function especially hypothyroidism is important it can cause of disturbance in calcium metabolism by their direct action on bone turnover. **Objective:** This study was designed to assess the role of hypothyroidism in serum calcium levels.

*Materials and Methods:* This case-control study was done in the Laboratory Service Department, Khwaja Yunus Ali Medical College and Hospital, Enayetpur, Sirajganj from February 2023 to June 2023. A total of 45 subjects of hypothyroidism of both sexes were selected for the purpose. Data were collected in and analysis was done by IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) software. The categorical variables were represented as percentages and measurable variables as mean  $\pm$  SD. Pearson's correlation test was used to observe the correlation of calcium level with other variables. P value  $\leq 0.05$  was considered to be statistically significant.

**Results:** There is a significant positive correlation of serum T3 & T4 with serum calcium in hypothyroid patients. The r value is +0.73(p value = 0.02). (r value + 0.78 and p value < 0.05) respectively. There is strong negative correlation between TSH and serum calcium levels in hypothyroid patients (r value -0.58 and p value-0.38).

**Conclusion:** This study result shows, serum calcium levels significantly decrease in hypothyroid patients. Therefore, it is important to check the level of calcium in thyroid disorder. If necessary, the supplementation of mineral should be given in order to prevent further bone complication.

Key words: Hypothyroidism, Calcium, Thyroid Stimulating Hormone, Thyroid Hormone.

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# Introduction

Triiodothyronine (T3) and thyroxine (T4) are the two hormones that are produced and secreted by the thyroid gland and are referred to as thyroid hormones. This hormone is necessary for the skeleton's proper growth and development.<sup>1</sup> Thyroid hormones are essential for cell differentiation during development and to maintain mineral, metabolic, and thermogenic homeostasis in adult. Thyroid gland disorders are commonest among endocrine disorders. About 200 million people worldwide are suffering from various thyroid disorders, and more than half of them remain undiagnosed.<sup>2</sup>

Hypothyroidism is a common endocrine condition results from either insufficient thyroid hormone or, less frequently, from the thyroid gland's delayed activity. Hypothyroidism has a mean

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yearly incidence rate of up to 4 per 1000 women, 1 per 1000 men, and 1 in 4000 newborns. With advancing age, overt hypothyroidism becomes more common.<sup>3</sup>

One of the most vital minerals in our bodies, calcium is controlled by a number of different systems. Any changes to this mineral's homeostasis will have dangerous consequences for the body. Thyroid hormones are thought to be involved in the control of calcium and phosphorus in our bodies in addition to the normal regulators such as vitamin D, calcitonin, and parathyroid hormones.<sup>4,5</sup> According to the study, thyroid hormone levels affected the expression of several proteins that regulate calcium homeostasis inside the cell. Thyroid hormone levels boosted the levels of SR Ca2±ATPase and reduced its inhibitor, phospholamban. The opposite changes occurred in

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these two proteins when thyroid hormone levels decreased. In addition, the changes in the affinity of the SR Ca2±transport system corresponded to the changes in the proportion of phospholamban to Ca2±ATPase. These findings imply that thyroid hormone directly influences SR protein levels.<sup>6</sup>

Calcium is a vital mineral that aids in the production of teeth and bones, muscular contraction, blood clotting, normal enzyme function, and normal rhythmic heart contraction. Rickets in young children, osteomalacia in adults, perioral paresthesia, and spontaneous muscle spasms are all symptoms and signs of hypocalcemia. The EEG reveals QT interval prolongation in severe hypocalcemia that suggests the possibility of developing ventricular tachycardia.<sup>7</sup>

In hypothyroidism, which causes a depressed bone turnover, thus lowers the level of calcium in the blood. On the other hand, the low mobilization of calcium in hyperthyroidism raises the level of calcium in the blood.<sup>8</sup> Increased calcitonin production in hypothyroidism can also facilitate calcium excretion from the tubules.<sup>9</sup>

Thyroid diseases are most common in Bangladesh, among other countries. The actual burden of thyroid dysfunction in Bangladesh is largely unknown. Nonetheless, it's estimated that 20% of people in general have thyroid disorders.<sup>10</sup>

Hypothyroidism may lead to hypocalcemia, which may be a cause of many disorders and disabilities. Hence, the treatment modalities should also be framed in mineral status while treating a hypothyroid patient.<sup>11,12</sup>

In Bangladesh there is no published data concerning serum calcium in patients with hypothyroidism. Therefore, the present study was conducted to find out the status of calcium in hypothyroid patients.

### **Materials and Methods**

In this cross-sectional study, 45 consecutive subjects with primary hypothyroidism attending Khwaja Yunus Ali Medical College Hospital, OPD a tertiary level health care center located at northern part of Bangladesh, during the period from February to June 2023 fulfilling the inclusion and exclusion criteria were investigated. Subjects between 20-45 years age group were considered. Known case of hypothyroid patients on analysis with serum T3, Free thyroxin (FT4) and Thyroid Stimulating Hormone (TSH) were included in this study. Patients suffering with other comorbidities such as renal diseases, hepatic diseases, diabetes mellitus, alcoholism, other serious medical conditions and patients on mineral supplementation or any drugs that will affect mineral metabolism were excluded. Estimation of Serum T3, FT4 and TSH were estimated by enhanced chemiluminescence technique using a fully automatic analyzer Beckman Coulter immunoassay access 2(USA). Serum Calcium was estimated by fully automatic analyzer

Beckman Coulter DXC AU 700 (USA). Normal range value for T3 was 0.80-2.00 mg/ml, for FT4 the normal range is  $4.50-12.00 \mu$ g/dl and  $0.47-5.01 \mu$ IU/ml for TSH. Hypothyroidism was defined as an elevated TSH (>5 mIU/L) together with a decrease serum thyroid hormone level. The normal range for total calcium, about 8.6-10.2 mg/dl (2.15-2.54 mmol/l). Hypocalcemia was defined as serum calcium level less than 8.4 mg/dl.<sup>13</sup>

#### **Statistical Analysis**

Statistical analysis was done by using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) software. The categorical variables were represented as percentages and measurable variables as mean  $\pm$  SD. Pearson's correlation test was used to observe correlation of calciumlevel with other variables. P value  $\leq 0.05$  was considered to be statistically significant.

### Results

A total 45 patients with primary hypothyroidism were included. The mean age of subjects of hypothyroidism was  $31.60\pm10.65$  years. Majority of the participants were home-maker, residing in rural areas, as shown in Table I. About 64.44% participant was female. (Figure 1)

Table I: Demographic variables

Variables		N (%)
Age, Years	mean ±SD	31.60±10.65
Residence		
Urban		17(37.77)
Rural		28(62.22)
Occupation		
Homemaker		21(46.66)
Service		15(33.33)
Student		9(20)
TSH (µIU/ml)		$6.28 \pm 1.3$
F T4 (µg/dl)		$2.8\pm0.89$
T3 (ng/ml)		0.5 ±0.32
Serum calcium (mg/dl)		$6.2\pm0.24$

#### Figure 1: Gender distribution



 Table II: Correlation of Serum Calcium with T3, FT4 and TSH among Cases

Parameters	Correlation coefficient (r value)	P Value
Serum T3 and Serum Calcium	r value = +0.73	0.02
Serum FT4 and Serum Calcium	r value = +0.78	0.05
Serum TSH Vs Serum Calcium	r value = - 0.58	0.03

As shown in Table II there is significant positive correlation of serum T3 with serum calcium in hypothyroid patient. The r value is +0.73(p value = 0.02). There is also strong positive correlation of serum FT4 with serum calcium in hypothyroid patient (r value + 0.78and p value < 0.05). There is strong negative correlation between TSH and serum calcium levels in hypothyroid patients (r value -0.58 and p value0.03).

#### Discussion

Thyroid hormones, which are secreted by the thyroid gland, have an impact on practically all metabolisms, including glucose, lipid, and protein metabolism also maintain fluids and electrolytes balance. Thyroid hormones have recently received more interest due to their effects on mineral metabolism.<sup>14</sup>

As the most common endocrine disease, hypothyroidism can cause a variety of clinical problems such as electrolyte and mineral imbalances, congestive heart failure, and coma. Thyroid dysfunctions frequently disrupted calcium, magnesium, and phosphorous homeostasis, have a direct effect on calcium and magnesium resorption by influencing glomerular filtration rate and blood flow.<sup>15</sup> The aim of this study was to investigate the effects of hypothyroidism on serum calcium. The current investigation demonstrated a considerable decrease in serum calcium levels in the study population. Which has similarity with some other studies.<sup>16-18</sup> There is significant positive relation of calcium with T3 and T4. Significant negative relation was found in calcium with TSH in this study.

Shivallela et al also demonstrated a significant decrease in serum calcium of SCH group than control. This is mainly due to the low levels of Parathyroid hormone and low levels of calcitonin in hypothyroidism.<sup>19</sup>

A study conducted by Mani V  $^{20}$  showed decreased concentrations of total calcium and ionic calcium in hypothyroid patients when compared to the group of controls with normal thyroid function with a highly significant p value of <0.001. Similar results were also observed by the studies conducted by Abdel-Gayoum AA.<sup>21</sup>

AlaEldin S. In their study found a significant correlation between S. Ca++ and serum TSH, T3 and T4 in hypothyroid patients. <sup>22</sup> This was further confirmed by the study done by Christoph Schwarza, et al.<sup>23</sup> who reported that there was a significant correlation between S. Ca++ and serum TSH, T3 and T4 in hypothyroid patients. Animal study done by Kumar and Prasad also concludes that renal calcium excretion was increased in rats with high TSH levels.<sup>24</sup>

Based on our findings, it was found that mineral metabolism is closely related to thyroid hormones. Thyroid hormones control the mineral pool in the blood by regulating calcium mobilization and clearance via urinary excretion due to its effect on GFR/ renal plasma flow.

# Conclusion

According to our findings, hypothyroidism causes a decrease in serum calcium levels. In hypothyroid people, there was a strong negative correlation between serum TSH levels and serum calcium levels. Serum calcium levels in hypothyroid patients should be checked on a regular basis, as early detection and correction can prevent further complications from mineral metabolism dysfunction.

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### References

- Shlomo Melmed, Kenneth S. Polonsky, P. Reed Larsen and Henry M. Kronenberg. William's text book of endocrinology.Calcium and phosphorus metabolism in hypothyroidism. 12thedition .2011;10-11.
- Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol.2018;14(5):301-316.

- Simsek G. Andican G, Karkoc Y et al. Ca, Mg & Zn status in experimental hypothyroidism. Biol. Trac.Elem.Res.1997; 60 (3):205-213.
- DM Vasudevan, Sreekumari S and Kannan Vaidyanathan, mineral metabolism and abnormalities. In: DM Vasudevan, Sreekumari S and Kannan Vaidyanathan, Textbook of biochemistry for medical students, 8th edition; Jaypee Brothers Medical Publisher (P) Ltd, 2016;491-497.
- Kavitha MM, Chandrashekharyya SH. Alteration in levels of serum calcium, phosphorous and magnesium in patients of hypothyroidism. International journal of biological and medical research. 2014;5(4):4594-4596.
- Carr AN, Kranias EG. Thyroid hormone regulation of calcium cycling proteins. Thyroid. 2002 Jun;12(6):453-457.
- Goltzman D, Rosen CJ, Mulder JE. Clinical manifestations of hypocalcemia. UpToDate. Rose BD, ed. Wellesley MA: UpToDate. 2010.
- Bassett JH, Williams GR. Role of thyroid hormones in skeletal development and bone maintenance. Endocr Rev 2016; 37:135–187.
- 9. Melmed S, Polonsky KS, Larsen PR, Kronenberg HM. William's text book of endocrinology. Calcium and phosphorus metabolism in hypothyroidism. 12th edition. 2011; 10-11.
- Paul AK, Miah SR, Mamun AA, Islam S. Thyroid disorders in Khulna district: A community-based study. Bangladesh Med Res Counc Bull .2006;32:66-71.
- Modi A, Sahi N. Effect of thyroid hormones on serum calcium and phosphorous. Int J. Clin. Biochem Res. 2018; 5:570-573.
- Vasanthan M, Vinodhini V M, Gayathri B. A Study of Mineral Status in Hypothyroidism. JMSCR.2018; 06: 378-382.
- Goldstein DA. Chapter 143 Serum Calcium. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990.
- Susanna TY, Sagayaraj A. A correlative study of thyroid profile and mineral status in patients with hypothyroidism – a hospital base case control study. Asian journal of Pharmaceutical and Clinical Research. 2016;9(3):292-294.

- McCaffrey C, Quamme GA. Effects of thyroid status on renal calcium and magnesium handling. Can J Comp Med 1984; 48:51–57.
- Rakesh Kumar Jha, Ankita A. Kondhalkar, Shweta A Panchbudhe. Study of Calcium, Magnesium and Phosphorus in Hypothyroidism Patients In Vidarbha Region. Biosc.Biotech.Res.Comm.2021; Special Issue Vol 14(7):99-103.
- D. Sridevi, Amrut A Dambal, Sidrah. A Study of Serum Magnesium, Calcium and Phosphorus in Hypothyroidism. International Journal of Clinical Biochemistry and Research. 2016;3(2):236-239.
- Shrestha S, Bharti A, Rai R, Singh M. Assessment of serum minerals and electrolytes in thyroid patients. International Journal of Advances in Scientific Research. 2015;1(6):259-263.
- Shivallela MB, Poornima RT and Jayaprakash Murthy DS. Serum calcium and phosphorous levels in thyroid dysfunction. Indian journal of fundamental and applied life science. 2012; 2(2):179-183.
- Mani V, Natarajan MS, Mohanakrishnan VV. Comparison of Total and Ionic Calcium in Hypothyroidism. Journal of Clinical & Diagnostic Research. 2019;13(5).
- Abdel-Gayoum AA. Dyslipidemia and serum mineral profiles in patients with thyroid disorders. Saudi Med J. 2014;35(12):1469-1476.
- 22. AlaEldin S. Ashmaik, Haala M. Gabra, Amna O M. Elzein, Nassr Eldin M A.Shrif, Elhashimi E. Hassan. Assessment of Serum Levels of Calcium and Phosphorous in Sudanese Patients with Hypothyroidism. Asian Journal of Biomedical and Pharmaceutical Sciences.2013;03 (25): 21-26.
- Christoph Schwarza, Alexander Benedikt Leichtle, Spiros A, Georg Martin F, HeinsZ, Aristmenis K, Gregor L. Thyroid function and serum electrolytes. Swiss Medical Weekly.2012; 13669-13669.
- Kumar V, Prasad R. Molecular basis of renal handling of calcium in response to thyroid hormone status of rat. Biochem Biophys Acta. 2002; 1586(3):331-143.