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Original Article

Biochemistry Section

Calcium and Magnesium Levels in Subclinical and Overt Hypothyroidism: A Cross-sectional Study

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ABSTRACT

Introduction: Hypothyroidism, one of the most common thyroid gland disorders, can cause electrolyte disturbances in the body. Hypothyroidism can alter mineral metabolism by changing the levels of serum calcium and magnesium. Therefore, it is essential to study any abnormalities in calcium and magnesium metabolism in patients with hypothyroidism.

Aim: The aim of this study was to assess the levels of calcium and magnesium in patients with hypothyroidism and to study the correlation between Thyroid Stimulating Hormone (TSH), fT3, and fT4 with calcium and magnesium in subclinical and Overt Hypothyroidism (OH).

Materials and Methods: This cross-sectional study was held from August 2019 to January 2020 in the Department of Biochemistry, BS Medical College, Bankura. A total of 150 subjects were included in the study, distributed equally among three groups: euthyroidism, subclinical hypothyroidism, and OH. Serum TSH, fT3, fT4, calcium, and magnesium levels were determined in the laboratory, and the data obtained were statistically analysed using ANOVA test and Pearson's correlation test.

Results: Out of a total of 150 subjects, 61 were female, among whom 23 had subclinical hypothyroidism and 21 had OH. There were significant differences in the mean levels of TSH, fT3, fT4, calcium, and magnesium between the SCH, OH, and euthyroid groups. The study showed that the mean serum calcium level was significantly lower in SCH and OH compared to euthyroids, while the level of serum magnesium was significantly increased in SCH and OH compared to euthyroid. There was a statistically significant negative correlation between TSH and serum calcium in both OH and SCH, while a statistically significant positive correlation was observed between TSH and serum magnesium levels in both groups.

Conclusion: The present study revealed that serum magnesium levels were high while serum calcium levels were low in both subclinical hypothyroidism and OH when compared to euthyroid subjects. Additionally, calcium levels negatively correlated with TSH, while magnesium levels positively correlated with TSH levels.

Keywords: Electrolyte imbalance, Euthyroid, Thyroid gland, Thyroid stimulating hormone

INTRODUCTION

The thyroid gland plays a significant role in regulating lipid, carbohydrate, protein, and mineral metabolism [1]. Hypothyroidism (SCH) is defined as an elevated serum TSH level associated with normal serum levels of thyroxine (T4) and triiodothyronine (T3). OH is defined as an elevated TSH and decreased serum T3 and T4 levels. SCH is much more common than OH, so early diagnosis and treatment may prevent the onset of OH. Thyroid hormone is essential for the physiological growth and maturation of the skeletal system. Thyroid dysfunction is frequently associated with disturbances in calcium homeostasis and hypocalcaemia [2,3].

Thyroid hormone causes the release of calcium from cells and regulates the blood levels of calcium. Previous research has found that as the level of thyroid hormone is low in hypothyroidism, the release of calcium from cells is decreased [4,5]. Thyroid disorders are an important cause of secondary osteoporosis. Some studies have shown normal serum calcium and phosphorous levels [6,7], while others have shown decreased levels in hypothyroidism [5,8]. In a previous study, researchers found disturbances in magnesium metabolism in hypothyroidism [8]. Researchers also found an increase in serum magnesium levels in hypothyroidism [9,10].

Although the changes in calcium and magnesium are negligible in thyroid disorders, these disturbances may cause damage in the later stages of life [9]. Few studies have shown that some metabolic disorders, hypertension, and cardiovascular disease are related to metabolic aberrations of divalent cations such as calcium and magnesium [10,11].

A review of the literature shows a paucity of data in the West Bengal region. Hence, the present study was conducted to examine the changes in serum calcium and magnesium levels in subclinical and OH. Additionally, serum calcium and magnesium levels were compared among cases of hypothyroidism and euthyroid cases and the correlation between TSH, fT3, fT4 levels, and serum calcium and magnesium was assessed.

MATERIALS AND METHODS

This institution-based cross-sectional study was conducted in the Department of Biochemistry, Bankura Sammilani Medical College, Bankura, West Bengal, for six months from August 2019 to January 2020. The study was approved by the institutional ethical committee (Memo no: PR-HC/6-119/111(53), dated 09/04/2019). Written consent was obtained from all the participants.

Inclusion criteria: Patients aged between 20 and 60 years who underwent thyroid profile evaluation in the institution were included in the study. Additionally, healthy controls with a normal thyroid profile, i.e., euthyroid, were included in the study.

Exclusion criteria: Patients with a history of hepatic disease, renal disease, bone disease, diabetes mellitus, alcoholism, or those who were on supplementation with calcium and other mineral supplements were excluded from the study.

Sample size: A total of 100 patients, 50 with SCH, 50 with OH, and 50 controls with a normal thyroid profile, i.e., euthyroid, were enrolled in the study using purposive sampling method.

Subclinical hypothyroidism: SCH is defined as increased TSH (ranging between 5.5 mIU/L and 10 mIU/L) and normal T3 and T4 levels.

Overt Hypothyroidism (OH): OH is defined as increased TSH and decreased T3 and T4 levels (TSH >10 mIU/L, fT4 <0.8 ng/dL, and fT3 is less than 1.4 pg/mL) [12].

Data collection: After 12 hours of overnight fasting, a 3 mL venous blood sample was collected in a yellow or red top vacuum-evacuated tube with clot activator. Samples were centrifuged at 3000 rpm for 10 minutes, and the obtained serum samples were analysed for fT3, fT4, TSH, calcium, and magnesium levels using a CLIA-based fully automated analyser (ADVIA Centaur CP). The reference values in the laboratory were as follows: TSH: 0.50-5.50 µIU/mL, fT3: 1.4-4.2 pg/mL, and fT4: 0.8-2.0 ng/dL. Serum magnesium and calcium were estimated using the Calmagite Dye [13] and o-Cresolphthalein Complexone (OCPC) [14] methods, respectively. The normal reference values for calcium and magnesium were 8.7-11.0 mg/dL and 1.3-2.5 mEq/L, respectively [13,14].

STATISTICAL ANALYSIS

The data were statistically analysed using SPSS version 27.0. An ANOVA test was used for comparison, and Pearson's correlation analysis was conducted to determine the relationship between the different parameters among groups.

RESULTS

The mean age in the control and case groups was 33.32±4.75 years and 35.31±7.56 years, respectively. Among the total of 150 subjects, 27 males had Subclinical Hypothyroidism (SCH) and 29 males had Overt Hypothyroidism (OH), while 23 females had SCH and 21 females had OH. There was no significant difference found in gender distribution among the groups [Table/Fig-1].

Sex	Euthyroidism (n=50)	Hypothyroidism (n=100)		Total (n=150)	p-value
		Subclinical (n=50)	Overt (n=50)		
Male	33	27	29	89	>0.05
Female	17	23	21	61	
Age (in year)	33.32±4.75	35.56±7.00	35.06±8.12	34.32±6.16	0.001

[Table/Fig-1]: Distribution and comparison of thyroid disorders according gender and age.

The mean TSH level was significantly higher in the OH group compared to the SCH and euthyroid groups. The mean serum calcium level was significantly lower in both the SCH and OH groups compared to the euthyroid group. Similarly, the levels of serum magnesium were significantly increased in both the SCH and OH groups compared to the euthyroid group [Table/Fig-2].

Parameters	Euthyroid subject	Subjects having subclinical hypothyroidism	Subjects having overt hypothyroidism	ANOVA F/ value	p-value
Serum TSH (µIU/mL)	2.12±1.40	9.88±1.35	23.24±5.89	56.33	≤0.001
Serum fT3 (pg/mL)	1.99±0.44	2.11± 0.19	1.06± 0.64	27.25	0.001
Serum fT4 (ng/dL)	1.34±0.29	1.03±0.22	0.65±0.17	15.05	0.01
Serum calcium (mg/dL)	9.36±0.84	8.31±1.21	8.09±0.99	67.14	≤0.001
Serum magnesium (mg/dL)	2.14±0.32	2.22±0.17	2.54±0.36	21.25	0.01

[Table/Fig-2]: Distribution and comparison of participants according to their serum parameters.
*ANOVA test

The present study showed a statistically significant negative correlation between TSH and serum calcium levels in both the OH and SCH groups. Additionally, a statistically significant positive correlation was observed between TSH and serum magnesium levels in both groups [Table/Fig-3,4].

	Parameter	Correlation coefficient (r)	Significance (p-value)
Subclinical hypothyroidism	TSH Vs Calcium	-0.925**	<0.001
	TSH Vs magnesium	0.493**	<0.001
	fT3 Vs Calcium	0.084	0.564
	fT3 Vs Magnesium	0.037	0.08
	fT4 Vs Calcium	0.199	0.166
	fT4 Vs Magnesium	0.417**	0.003

[Table/Fig-3]: Correlation between variables in study group having subclinical hypothyroidism.
**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed)

	Parameter	Correlation coefficient (r)	Significance (p-value)
Overt Hypothyroidism (OH)	TSH Vs Calcium	-0.835**	<0.001
	TSH Vs Magnesium	0.788**	<0.001
	fT3 Vs Calcium	0.118	0.416
	fT3 Vs Magnesium	-0.073	0.615
	fT4 Vs Calcium	-0.178	0.215
	fT4 Vs Magnesium	0.835**	<0.001

[Table/Fig-4]: Correlation between variables in study group having overt hypothyroidism.
**Correlation is significant at the 0.01 level (2-tailed)
*Correlation is significant at the 0.05 level (2-tailed)

DISCUSSION

Reduced production of thyroid hormone is the central feature of the clinical state termed hypothyroidism. Although a number of clinical manifestations have been associated with this early or mild phase of hypothyroidism, the term "subclinical" is used here to describe this group. Subclinical hypothyroidism is defined as an elevated serum TSH level with a normal serum fT4 concentration. It can progress to OH and may be associated with various manifestations. In some patients, these manifestations can be improved with treatment [15].

In this present study, the mean calcium levels were 8.31±1.21 mg/dL and 8.09±0.99 mg/dL in SCH and OH patients, respectively. The study also showed a statistically significant negative correlation between TSH and serum calcium levels in both OH and SCH groups. Additionally, the serum calcium level was significantly lower in both the SCH and OH groups compared to the euthyroid groups. These findings in the present study may be due to long-term hyperthyroidism resulting in a net negative calcium ion (Ca^{2+}) balance in response to increased skeletal turnover. It is noteworthy that a long-term hyperthyroid state is also associated with calcium malabsorption and increased bone resorption.

A study conducted by Shivallela MB et al., found a significant decrease in serum calcium levels in hypothyroid patients compared to controls, which was similar to the present study [8]. In that study, the mean calcium level in hypothyroidism was 9.14±0.51 mg/dL, whereas in the present study, calcium levels were 8.31±1.21 mg/dL in SCH and 8.09±0.99 mg/dL in OH. An animal study conducted by Kumar V et al., observed an increase in renal calcium was increased in rats with high TSH levels [16]. A study done by Roopa M et al., revealed that thyroxin can normally regulate blood calcium levels by releasing calcium from cells and decreasing T4 levels in the blood [17]. This finding is similar to the present study. The significant negative correlation of TSH with serum calcium levels found in this study was the same as reported in several human and animal studies [18,19].

In the present study, the serum magnesium levels were 2.22±0.17 mg/dL and 2.54±0.36 mg/dL in the SCH and OH groups, respectively. The study also showed a statistically significant positive correlation

between TSH and serum magnesium levels in both groups. Additionally, the present study observed significantly elevated levels of serum magnesium in both the subclinical and OH groups compared to euthyroid individuals, which was similar to a study done by Jaskin K et al., [20]. The mean calcium and magnesium levels were 8.99±0.53 mg/dL and 1.27±0.28 mg/dL, respectively, which were closer to the findings of the present study. In this study, we observed a significant positive correlation between magnesium levels and TSH in both overt and subclinical hypothyroidism. However, literature suggests a decrease in magnesium levels in hypothyroidism compared to controls and also shows a negative correlation with thyroid hormones [21,22].

To the best of our knowledge, no similar study has been conducted in this region. The present study may be helpful in the early detection of morbidity in hypothyroidism.

Limitation(s)

Since this study was a cross-sectional study, no follow-up could be conducted. However, future studies with a larger sample size and follow-up can be pursued.

CONCLUSION(S)

Our study revealed that serum calcium levels were decreased in both patients with subclinical and overt hypothyroidism, compared to euthyroid individuals, with a negative correlation observed between serum TSH levels and serum calcium in both cases. Additionally, we observed that serum magnesium levels were increased in both patients with subclinical and overt hypothyroidism, and a significant correlation between TSH and serum magnesium was found in both cases. Hence, thyroid disorders can be associated with disturbances in calcium and magnesium metabolism. Clinicians should consider screening hypothyroidism patients for these analytes to enable early detection of bone and mineral metabolic disorders.

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