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Original Research Article

To Evaluate the Levels of Serum Calcium, Magnesium and Phosphorus in Hypothyroid Patients

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Abstract:

Background: Hypothyroidism is one of the most prevalent forms of thyroid dysfunction in which the disease causes generalized slowing of metabolic processes. Thyroid dysfunction frequently disturbs mineral metabolism. The aim of the present study was to evaluate the levels of serum calcium, magnesium and phosphorus in patients with hypothyroidism.

Materials and Methods: We conducted the present study on 100 lab-diagnosed cases of hypothyroidism based on the thyroid profile. 50 healthy controls were included in the study. We estimated serum calcium, magnesium and phosphorus in both cases and controls.

Results: This study found that in people with hypothyroidism, the mean levels of calcium and magnesium in blood were significantly (p value<0.001) lower than in controls, while the levels of phosphorous were significantly (p value<0.001) higher. We found a significant negative correlation between both serum calcium and magnesium and serum TSH levels, and a significant positive correlation between serum phosphorous and serum TSH levels.

Conclusion: The current study concluded that hypothyroidism alters the metabolism of minerals. Estimation of these minerals in hypothyroid patients will be of great benefit in the prevention and treatment of subsequent clinical manifestations.

Keywords: Serum TSH, Calcium, Magnesium and Phosphorus.

Introduction

In India, hypothyroidism is notably more prevalent among females than males. Various epidemiological studies have indicated that the condition affects approximately 10-11% of the Indian population [1]. A biochemical decline in T3 and T4 concentrations causes the pituitary to secrete more TSH than usual, which amplifies the rise in serum TSH levels [2]. Thyroid hormones (T3, T4 and TSH) are very important for cell growth, thermogenesis, metabolism and the breakdown of minerals like calcium, magnesium and phosphorous. [3].

These minerals are divalent metal ions, which are necessary for metalloenzymes and many important metabolic pathways regulated by thyroid hormones. Thyroid dysfunction causes disturbances in the metabolism of these minerals [4]. TSH regulates thyroid function by binding to receptors on the surface of thyroid follicular cells, which leads to an increase in cAMP production. These receptors are G-protein coupled receptors (GPCR). TSH attaching to these receptors turns on the G protein, which then turns on adenylyl cyclase, an enzyme that converts ATP to cAMP. The production of cAMP serves as a second messenger, amplifying the signal initiated by TSH binding [5]. When it comes to serum calcium and thyroid hormones, thyroid hormones change the activity of osteoblasts and osteoclasts, which are the cells that build and breakdown bones respectively[6].

Hypothyroidism induces a low bone turnover due to reduced osteoclastic as well as osteoblastic activity. These changes in bone metabolism result in increased bone mineralization leading to low calcium levels in hypothyroidism [7]. Hypothyroidism can change the levels of calcium

and phosphorus in the blood. The relationship between the two is more complicated, but normally low to slightly lower calcium levels and higher phosphorous levels are linked to hypothyroidism [8]. Tightly regulated renal excretion controls the extracellular concentration of phosphorous in relation thyroid hormone and serum phosphorous.

The renal Na/Pi co-transporters (Npt2a, Npt2c, and Npt1) primarily mediate renal proximal tubular Pi reabsorption. In the Npt2a gene there are also some regulatory elements such as E-boxes, GATA and CREB (c-AMP-response-element –binding-protein)-binding consensus sequences, and CREB. In this way Npt2a gene is very important for maintaining Pi homeostatis in the kidney because it is a target gene for thyroid hormones [9].

When it comes to serum magnesium and thyroid hormones, magnesium is an important nutrient that is needed for many biochemical reactions, such as those that make energy and proteins and nucleic acids [10].

Thyroid hormones have an influence on renal hemodynamics, glomerular filtration and electrolyte handling. Thyroid hormones affect GFR and blood flow and have a direct effect on magnesium resorption. Hypothyroidism is associated with decreased serum magnesium levels probably due to altered renal clearance of magnesium [11]. Magnesium raises the activity of 3,5-nucleotide phosphodiesterase enzymes, which help turn off protein kinase A.

This leads to less thyroid hormone production [12]. Also, magnesium is an important enzyme cofactor for mitochondrial oxidative phosphorylation and ATP synthesis .Not having enough magnesium can stop the sodium iodide co-transporter from working, which needs energy from the mitochondria. This can cause thyroid hormone production to drop and TSH levels to rise [13].

We conducted the current study to assess the levels of serum calcium, magnesium and phosphorus in patients with Hypothyroidism and to analyze their correlation with serum TSH.

Materials and Methods

The Department of Biochemistry at Government Medical College and Rajindra Hospital in Patiala conducted the present analytical study. The study group consisted of 100 lab-diagnosed patients with hypothyroidism. We diagnosed the patients based on serum thyroid profile lab reports (TSH >4.2µIU/ml). 50 healthy, age and gender-matched individuals constituted the control group. The Institutional Ethical Committee granted clearance to initiate the study. We obtained informed written consent in the regional language from all subjects (cases and controls).

Inclusion criteria

1. Lab-diagnosed cases of hypothyroidism on the basis of lab investigation reports with serum TSH levels >4.2µIU/ml.
2. Subjects in age group 20-65 years.

Exclusion criteria

1. Patients with age group <20 years and >65 years.
2. Patients with history of diabetes mellitus, renal disease, bone disease, alcoholism or critically ill patients.
3. Pregnant women
4. The study excluded patients who were taking any mineral supplements, anti-thyroid medications or any other medications that affect the levels of calcium, magnesium and phosphorus.

Sample Collection: We collected 5-6 ml of venous blood under aseptic conditions from the antecubital vein. We collected the blood in red – top vacutainers. After collection, we allowed the blood to clot and centrifuged it at 2200-2500 rpm for 5 -10 minutes to separate the serum. We stored the serum in aliquots under aseptic conditions at 2-8ºC for 5 days and at – 20 ºC for up to one month and conducted the analysis after bringing the samples to room temperature.

Methods

1. Serum TSH was done by Solid phase sandwich ELISA method.
2. Serum Calcium was done by Arsenazo III method.
3. Serum Magnesium was done by Xylidyl Blue method.
4. Serum Phosphorus was done by UV Molybdate method.

Serum Calcium, Magnesium and Phosphorus were estimated on fully - automated analyser (XL-1000) by using system pack kits.

Statistical Analysis

We conducted the data analysis using the statistical package for the social sciences [SPSS] Version 23.0.Results were expressed as Mean±SD. The statistical significance was calculated by using the student's T-test; $p>0.05$ is considered not significant, $p<0.01$ is significant and $p<0.001$ is highly significant.

Results

The study group consisted of 35 males and 35 females, while the control group consisted of 31 females and 19 males. The average age of the hypothyroid patients was 38 years in the study group and 40 years in the control group. The maximum number of cases (38%) belonged to the

age group 31-40 years in the study group and 31-50 years (36%) in the control group.

Table 1: Comparison of Serum TSH, Calcium, Magnesium and Phosphorus in study group and control group

Parameters	Study group(N=100) (Mean±SD)	Control group(N=50) (Mean±SD)	p value	Significance
TSH (µIU/ml) (N.V=0.4-4.2 µIU/ml)	**15.08±13.38**	1.12±0.82	<0.001	HS
Serum Calcium (N.V=8.6-10.2 mg%)	**7.55±0.82**	9.22±0.45	<0.001	HS
Serum Magnesium (N.V=1.6-2.6 mg%)	**1.40±0.40**	2.06±0.32	<0.001	HS
Serum Phosphorus (N.V=2.4-4.5 mg%)	**6.21±2.09**	3.68±0.88	<0.001	HS

Table 1 demonstrates a significant increase in serum TSH and phosphorous levels in the study group compared to the control group, and a significant decrease in the serum calcium and magnesium levels in the study group.

Table 2: Correlation of Serum TSH with Serum Calcium, Magnesium and Phosphorus in study group

S.No	Parameters	r value	p value	Significance
1	S. TSH vs S. Calcium	-0.488	<0.001	HS
2	S. TSH vs S. Magnesium	-0.454	<0.001	HS
3	S. TSH vs S. Phosphorus	+0.731	<0.001	HS

Table 2 shows that serum TSH has a significant negative correlation with serum calcium (r=-0.488 and p<0.001) and serum magnesium(r= -0.454 and p<0.001) and positive correlation with serum phosphorus (r= +0.731 and p<0.001).

Discussion

Thyroid hormones are central regulators of the body's hemodynamics, thermoregulation and metabolism [14]. They are essential for normal growth and maturation of the skeleton [15]. Hypothyroidism is one of the most common endocrine disorders [16]. Hypothyroidism is more prevalent in females as compared to males due to hormone imbalances (estrogen, progesterone), hormone fluctuations (menstrual cycle) and autoimmune susceptibility [17]. Our study revealed a predominance of females in cases of hypothyroidism. Hypothyroidism frequently disturbs the homeostasis of calcium, magnesium and phosphorous. The deficiencies of these minerals can lead to impairment of thyroid functions [18].

Thyroid hormones play a major role in calcium homeostasis through their direct action on bone turnover. Hypothyroidism extends the duration of the osteoclastic resorption by two times, while prolonging the time for osteoblastic bone formation and secondary mineralization by four times. These changes result in low bone turnover and overall gain in bone mineralization leading to decreased serum calcium levels [19]. The study group's mean ± SD serum Calcium level was 7.75 ± 0.82 mg%, while the Control group's was 9.22 ± 0.45 mg%. This shows that the study group had significantly lower calcium level than the control group (p value <0.001). Another study by Bushra et al. (2022) found that the average serum calcium level was 8.06 ± 0.99 mg% in the study group and 9.10 ± 0.67 mg% in the control group. This finding fits with theirs and is consistent with ours [20]. This study found a strong negative relationship between serum calcium and TSH (r= -0.488 and p value <0.001), which is the same study done by Srinivas M et al. (2021) (r= -0.8368 and p value <0.001) [21]. Through TREs (Thyroid hormone Response Elements) thyroid hormones change how the Npt2a gene is translated and how much phosphate is taken up by the kidneys. In hypothyroidism, there is hyperphosphatemia due to tubular reabsorption of phosphate [22].

There was a very big difference between the study group and the control group in terms of serum phosphorous levels. In study group it was 6.21 ± 2.09 mg%, while in control group, it was and 3.68 ± 0.88 mg%. Abbas et al. (2013) found that the mean ± SD of serum phosphorus levels was 4.01 ± 0.14 mg% in Study group and 3.80 ± 0.14 mg% in control group [23]. This finding from this study fits with that finding. A highly significant positive correlation was found between serum phosphorus and TSH (r= 0.731 and p value<0.001). This finding is consistent with the study done by Athokpham D et al. (2020) (r= 0.927 and p value<0.001) [24].

Thyroid hormones change the rate of glomerular filtration and blood flow. They also affect magnesium absorption, which makes magnesium homeostatis worse. In hypothyroidism, there is hypomagnesemia because of the fractional excretion of magnesium through urine [25].

In this study, the mean ± SD of serum magnesium levels was 1.40 ± 2.09 mg% in the study group and 3.68 ± 0.88 mg% in the control group. This shows that the study group had significantly lower magnesium levels than the control group (p value <0.001). This is similar to the study done by Susanna TY et al. (2016), which found that the mean ± SD of serum magnesium levels was 1.88 ± 0.15 mg% in the study group and 3.10 ± 0.50 mg% in the control group [26].

A highly significant negative correlation was found between Serum Magnesium and TSH (r= -0.454 and p value<0.001) This outcome is consistent with findings from study done by Gohel MG et al.(2014) (r= -0.7383 and p value<0.001) [27].

Conclusion

In the current study we observed significantly lower serum calcium and magnesium levels in hypothyroidism cases compared to healthy controls, and higher serum phosphorus levels in these patients. These changes can play an important role in assessing the complications of hypothyroidism. The impaired metabolism of these minerals may have a contributing role in the progression of thyroid disease and the later development of complications. Therefore, it is crucial to regularly evaluate the serum calcium, magnesium, and phosphorous levels of patients with hypothyroidism to detect and diagnose mineral metabolism dysfunction at an early stage.

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