

Trace elements in Hypothyroidism - A case control study

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Abstract

Background and Objectives: Hypothyroidism is one of the most common forms of thyroid dysfunction resulting from the deficiency of thyroid hormones. Mineral metabolism is frequently disturbed in thyroid dysfunctions. The effect of thyroid hormones on electrolytes and minerals has not been well established and the underlying mechanisms are not well understood. Only few data on the association between thyroid function and disorders of mineral metabolism exists. Thus our aim was to assess the levels of serum minerals in the patients with thyroid disorders and to correlate them with Thyroid Stimulating Hormone (TSH) values. **Materials and methods:** It is a case control study. The study was conducted on 90 cases of clinically diagnosed hypothyroidism and 90 age and sex matched healthy controls. Fasting venous blood sample was collected. Serum calcium, magnesium and phosphorous level along with thyroid profile (T3, T4, TSH) were measured. **Results:** Serum calcium and magnesium levels were significantly reduced in cases than controls. Serum phosphorus levels were increased and was statistically significant ($p < 0.005$). There was statistically significant negative correlation between serum TSH and calcium and magnesium where as significant positive correlation was found in between TSH and serum phosphorus levels in cases than controls ($p < 0.005$). **Conclusion:** Serum calcium, magnesium & phosphorous levels are significantly altered in subjects having hypothyroidism. Thus monitoring of these minerals in hypothyroidism will be of great benefit in improving clinical manifestation and also helps in appropriate treatment.

Key Word: Calcium, Hypothyroidism, Magnesium, Phosphorous

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INTRODUCTION

The thyroid gland secretes two important hormones thyroxine(T4) and triiodothyronine(T3), which are commonly known as T4 and T3, respectively. T3 is biologically more active form of thyroid hormone and is produced by local deiodination of T4 by the enzyme T4-5' deiodinase in the peripheral tissues including kidneys.¹ These thyroid hormones have important biological effects

such as regulation of body hemodynamics, thermoregulation, and various metabolisms. It influences almost all metabolisms in the body including carbohydrate, proteins, lipids and maintenance of water and electrolyte homeostasis, which are well-established^{2,3}. Hypothyroidism is one of the most common endocrine diseases resulting from deficiency of thyroid hormones, with a wide clinical manifestations ranging from metabolic disorders to cardiovascular disease, electrolyte, and mineral disturbances. Recently, the disorders of thyroid function particularly hypothyroidism is receiving greater attention as an important cause of disturbance in mineral metabolism by their direct action on bone turnover⁴ and also as one of the causes for secondary osteoporosis. They also increase oxygen consumption and heat production, expressed by an increased basal metabolic rate.⁵ In order that the synthesis and proper functioning of thyroid hormones (THs) occur, many micronutrients are necessary such as iodine, calcium, phosphorus, magnesium and zinc⁶. Calcium (Ca²⁺),

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phosphorus (PO_4^{2-}) and magnesium (Mg^{2+}) are all divalent metal ions, which are necessary for metalloenzymes and various crucial metabolic pathways directly or indirectly regulated by thyroid hormones. Few animal studies have proposed that thyroid hormones act as long-term regulators for phosphate metabolism, and the free T3 elevates renal phosphate reabsorption and elevates serum phosphate levels in rats⁷. Studies on hypothyroid subjects have shown contradictory findings where the levels of serum calcium and phosphorus were low in patients with overt hypothyroidism and magnesium levels were reduced. Some studies show a normal serum calcium and phosphorus levels⁸ while others have observed a low serum calcium and magnesium levels and an increase in serum phosphorus levels in patients with hypothyroidism^{7,9}. Hypothyroidism, a clinical condition resulting from thyroid hormone deficiency, is responsible for various body changes that may induce non communicable chronic diseases (NCD) such as obesity, dyslipidemias and even some neoplasias⁶. However, it should be emphasized that inappropriate diets are one of the risk factors for the emergence and aggravation of hypothyroidism. The influence of nutrients on thyroid functioning is still scientifically unclear, indicating the need for new researches to broaden the knowledge on this field so that preventive or treatment support measures can be taken and effectively help in an adequate thyroid functioning. Hence, this study was undertaken to evaluate alteration in mineral status by estimating serum calcium, phosphorus, and magnesium levels in patients diagnosed with hypothyroidism and its correlation with thyroid profile. T3, T4, and thyroid-stimulating hormone (TSH) levels in these patients and to observe the importance to check the levels of these minerals in overt hypothyroid disorders.

MATERIALS AND METHODS

This is a case control study. The study was conducted on 90 cases of clinically diagnosed hypothyroidism in the age group 20-50 years attending Out Patient Department (OPD) of Ear, Nose and Throat (ENT) and OPD of General surgery. Ninety (90) age and sex matched healthy subjects were taken as controls. Cases of hypothyroidism were selected based on the selection criteria mentioned in Table 1. The study was conducted over a period of two years. Ethical clearance was obtained from the institute's ethical clearance committee. Informed consent was taken from the cases and controls after explaining the procedure.

Inclusion Criteria

- Age group 20-50 years
- Hypothyroidism diagnosed by increased levels of TSH ($> 4 \mu\text{IU/ml}$) and

- Decreased serum T3 ($<1.48 \text{ ng/ml}$) and T4 ($<11.00 \mu\text{g/dl}$) levels

Exclusion criteria

- Pediatric age group
- Patients with renal disorders and hepatic disorders, Alcoholism
- Bone diseases
- Patients on medications such as diuretics, calcium, iron tablets, (anemics) antithyroid drugs and those who are on minerals supplementation which effect serum calcium, magnesium and phosphorus levels
- Diabetes Mellitus, Hypertension
- Pregnant and lactating women

Biochemical analysis: Venous blood sample of 3 ml was collected under aseptic precautions in a plain vial. It was allowed to clot and serum was separated by centrifugation.

- Serum T3 (Triiodothyronine), T4 (Thyroxine) and TSH (Thyroid Stimulating Hormone) levels were measured in serum by chemiluminescence immunoassay (CLIA) method using SnibeMaglumi 1000.
- Serum calcium levels were measured by Arsenazo 3 method using semiautoanalyser
- Serum Magnesium levels were measured by Xylidyl Blue method^{10,11} (Kit by Raichem Diagnostics) using semiautoanalyser.
- Serum phosphorus levels were measured by ammonium molybdate method using semiautoanalyser.

Statistical methodology: Data was expressed in terms of mean \pm SD. Unpaired 't'-test was used to study the changes in serum T3, T4, TSH and serum calcium, magnesium, phosphorus levels among cases. Pearson correlation was performed to establish the relationship between study variables. p value <0.05 was considered statistically significant.

RESULTS

This was a case control study conducted on 90 cases of clinically diagnosed hypothyroidism attending the OPD of ENT and General surgery. Both cases and controls were in the age group of 20-50 years. The mean age of cases and controls is shown in Table 2. There was no statistically significant difference in age between cases and controls. The mean serum T3, T4, TSH and mean values of serum calcium, magnesium and phosphorus are mentioned in Table 3. There was statistically significant difference in values between cases and controls. TSH levels were significantly increased in cases than controls. Serum calcium and magnesium levels were significantly

reduced in cases than controls ($p < 0.05$). Serum phosphorus levels were increased in cases than controls and was statistically significant ($p < 0.005$). There was statistically significant negative correlation between serum TSH and calcium and magnesium where as significant positive correlation was found in between TSH and serum phosphorus in cases than controls ($p < 0.005$) [TABLE 4]

DISCUSSION

This is a case control study conducted on ninety cases of clinically diagnosed hypothyroidism and 90 matched healthy controls. In our study we observed a significant low level of serum calcium in cases than controls. In the present study the serum phosphorus levels were markedly increased in cases of hypothyroidism as compared to healthy controls (p value < 0.001). There was a significant positive correlation between TSH and serum phosphorus levels and significant negative correlation between TSH and serum calcium level. The serum magnesium levels in serum were found to be significantly lowered in hypothyroid patients when compared to controls and there was a significant negative correlation between TSH and magnesium level. Thyroid hormone is essential for normal growth and maturation of the skeleton. In hypothyroidism there is a depressed boneturnover due to impaired mobilization of calcium into the bone that leads to decrease blood calcium level. In hypothyroidism, there is also an increased production of thyroid calcitonin which promotes the tubular reabsorption of phosphate and favors the tubular excretion of calcium which lead to hypocalcemia and hyperphosphatemia. In our study, the magnesium levels in hypothyroid patients were significantly decreased with positive correlation with T3 and T4 and negatively correlated with TSH which are in accordance with the study conducted by Gohel *et al.*, and Nisa *et al.* The decreased magnesium levels in these hypothyroid patients may be due to increase urinary output and fractional excretion of magnesium through the urine^{12,13}. As a result of thyroid hormones affecting the glomerular filtration rate, renal blood flow, tubular sodium transport, and reduced tubular reabsorption of magnesium⁸, the increased levels of serum creatinine in these patients observed in our study strongly suggest a defect at the level of renal glomerulus. In vitro studies have shown that the decreased magnesium levels will influences the action of the thyrotrophic hormone on the thyroid gland through the formation of cyclic amp involved in the activation of adenylyl cyclases and stimulates cyclic 3, 5 nucleotide phosphodiesterase¹³ disrupting the various metabolisms in the body. However, a few studies conducted in patients with subclinical and overt hypothyroidism, and

hyperthyroidism shows decreased serum calcium and increased phosphorus and magnesium levels in patients with Hypothyroidism¹⁴. Our study also observed a significant increase in the serum phosphorus levels that may be due to increased production of thyroid calcitonin which promotes the tubular reabsorption of phosphate and tubular excretion of calcium, resulting in hyperphosphatemia and hypocalcemia, respectively¹⁵. T4 showed negative correlation; TSH showed significant positive correlation with serum phosphorus levels; T3, which is the active form of the thyroid hormone required for the stimulation of phosphorus reabsorption from renal tubules mediated through Sodium/Phosphate cotransporter, did not show a significant correlation with serum phosphorus indicating that the renal mechanism mediated through T3 was not the only processes by which serum phosphorus levels were elevated but which can be as a result of bone demineralization Based on the findings of the study it is inferred that mineral metabolism is intimately associated with thyroid hormone. Thyroid hormone determines the mineral pool in the blood by influencing mobilization of minerals like calcium and phosphorus, in to the blood and also by influencing their clearance through urinary excretion due to its effect on glomerular filtration rate or renal plasma flow. Low levels of calcium in hypothyroid cases reflect poor metabolism of calcium. Low levels of magnesium reflect influence of thyroid hormone on GFR and thereby clearance of these minerals by filtration. The treatment modalities can also be framed while treating hypo & hyperthyroidism patients keeping in view of the altered mineral metabolism.

CONCLUSION

Our study demonstrated that hypothyroid patients show low serum total calcium, total magnesium and increased serum phosphorus levels as compared to healthy control. Hence monitoring of serum levels of these minerals during the follow up of hypothyroid patients will be of great benefit. Also, such disturbances need to be monitored at least once or twice per year and treated appropriately to avoid the ill effects resulting from the changes in their serum levels. We would likely to elaborate our study to a larger cross sectional population, keeping in mind the importance of minerals in the metabolism of thyroid hormones.

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