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Original article

A Study of Serum Calcium, Magnesium and Phosphorous Level in Hypothyroidism Patients

Mukesh G Gohel[1*], Aashka M Shah[2], Akash M. Shah[3], Jemil S Makadia[4]

[1,4]Assistant Professor, [2]Resident, Department of Biochemistry, B. J. Medical College, Ahmedabad (Gujarat), India

[3]Intern, Smt NHL Municipal Medical College, Ahmedabad

ABSTRACT

Introduction: 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. Previous studies done on serum calcium, magnesium and phosphorous levels in thyroid disorders have conflicting results. The present study has been undertaken to study the serum total calcium, total magnesium and phosphorous levels in patients with hypothyroidism. **Materials and Methods:** A hospital based cross sectional study consists of 100 cases of hypothyroidism and 100 normal healthy controls meeting the selection criteria. Serum calcium total, magnesium total and phosphorous level along with thyroid profile was measured. **Results:** Statistically significant decrease in serum total calcium and total magnesium level as well as increase in serum phosphorous level is found in cases compared to control ($p<0.001$). A statistically significant negative correlation between serum TSH with calcium total and magnesium total levels was noticed ($p<0.001$). Also statistically significant positive correlation between serum TSH and phosphorous levels was observed. **Conclusions:** Serum calcium, magnesium & phosphorous levels are significantly altered in patients having hypothyroidism. Thyroid diseases have wide spread systemic manifestations including their effects on bone and mineral metabolism. Also thyroid hormone affects the glomerular filtration rate, renal blood flow, tubular reabsorption and excretion of minerals which have direct effect on Calcium, Magnesium and phosphorous level. Thus monitoring of these minerals in hypothyroid patient will be of great benefit in improving clinical manifestation and can be treated appropriately.

KEYWORDS: Calcium, Hypothyroidism, Magnesium, Phosphorous

INTRODUCTION

Dysfunction and anatomic abnormalities of the thyroid are among the most common diseases of endocrine glands. Hypothyroidism and hyperthyroidism are two primary pathological conditions that involve thyroid glands [1]. Hypothyroidism is one of the most common forms of thyroid dysfunction resulting from the deficiency of thyroid hormones or from their impaired activity [2].

Hypothyroidism is ten times more common in women than men and its prevalence increases with age [3].Biochemically decrease in T3 and T4 concentration leads to hyper secretion of pituitary TSH and an amplified increase in serum TSH levels. This is a key laboratory finding in diagnosis of hypothyroidism [4].

Thyroid hormones perform a wide array of metabolic functions including regulation of lipids, carbohydrates, protein and electrolytes and mineral metabolism [5]. Mineral metabolism like calcium, magnesium and phosphorous is frequently disturbed in thyroid dysfunctions. Thyroid hormones exert its effects on osteoblasts via nuclear receptors to stimulate osteoclastic bone resorption [6].

Thyroid hormones probably stimulate bone resorption directly, thereby increasing serum calcium and phosphorous concentrations and also suppressing serum parathyroid hormone and 1,25-dihydroxyvitamin D_3 concentrations. The decrease in these bone-resorbing hormones limits further increase in serum calcium concentration but also results in enhanced intestinal calcium absorption. In adult hypothyroidism the opposite effects are seen [7].

Although the changes in analytes, including magnesium and calcium may be slight in thyroid disease, it is possible that these disturbances will be important for a patient in long term. Recently, it has been suggested that some of metabolic disorders, hypertension and cardiovascular disease are linked by common defects in metabolism of divalent cations such as calcium and magnesium. The exact mechanism underlying these relationships is not fully understood, potential mechanism is the basic role of these cations in metabolic pathways [8].

Thyroid diseases have wide spread systemic manifestations including their effects on bone and mineral metabolism. Previous studies done on serum calcium and phosphorous levels in thyroid disorders have conflicting results. Some studies have reported normal levels, while others have reported decreased serum calcium and phosphorous levels in hypothyroidism [6]. Deranged thyroid hormones results in significant elevation in phosphate levels [9]. They are also believed to influence calcium metabolism [10]. Tereshchenko IV has analyzed the causes for magnesium deficit in cases with hypothyroidism [11].

Indian patients are different from western patients from bone mineral homeostasis point of view. On one hand, thyroid disorders are most common prevalent conditions and on the other hand, Indian studies focusing on the blood levels of calcium & phosphorous in thyroid disorders are sparse[6]. The effect of thyroid hormones on minerals has not been well established and the underlying mechanism is not well understood also. So, the present study was undertaken to assess the alterations in the levels of serum calcium total, phosphate and magnesium total in patients with hypothyroidism. We also investigated the correlation between TSH levels and the serum concentration of the above minerals.

MATERIALS AND METHODS

Study design and Subjects

This study was a hospital based cross sectional study conducted at Biochemistry Department, B. J. Medical College and Civil hospital, Ahmedabad (India) between May 2013 to December 2013. A cross sectional study consists of 100 cases of hypothyroidism and 100 normal healthy controls were selected. Subjects were recruited according to simple random sampling method that met the selection criteria.

Selection Criteria

Inclusion Criteria: Age group between 25–75 years. The diagnosis of hypothyroidism was made by the presence of decreased serum total T_3 (<1.08 nmol/l) and total T_4 (<59 nmol/l) levels associated with increased with TSH levels (> 4 µIU/ml).

Exclusion Criteria: Patients with history of hepatic disease, renal disease, bone diseases, alcoholism, diabetes mellitus, pediatric age group, other major medical conditions and those who were on mineral supplementation or any medications that might affect serum calcium, magnesium and phosphorous concentrations were excluded from the study.

Ethical Considerations

The objectives of study were explained to all eligible subjects for this study. Informed consent of all subjects included in the study was obtained for involvement in study groups and for venipuncture. Emphasis was given that participation in this study was voluntary.

Blood Sample Collection

A 3ml of venous blood was drawn from each volunteer using a disposable plain vacuttainer system in fasting condition. Serum was separated within half an hour by centrifugation and stored at 2-8°C temperature till analysis was done.

Analysis of Sample

Serum TSH was measured by DS-EIA-Thyroid TSH kit by sandwich ELISA method and serum total T3 and total T4 were estimated by DS-EIA-Thyroid-T3 Total & T4 Total kit by competitive ELISA method on Tulip Lisaquant TS microplate ELISA reader and Lisawash junior microplate ELISA washer. Serum total calcium level was estimated by Arsenazo III method, serum magnesium total was estimated by Calmagite method and serum inorganic phosphorous was measured by UV Molybdate method on XL 640 fully autoanalyzer using commercially available kits.

Statistical Analysis

Data are expressed as Mean±S.D. Comparison between patients and control for all variables was performed by student t-test and correlation between parameter was studied by Pearson's correlation coefficient using GraphPad statistical software. $p<0.05$ was considered as statistically significant and <0.01 was considered as highly significant.

RESULTS

The TSH level is significantly increased in cases as compared to controls. Total T_3 and total T_4level is significantly decreased in cases as compared to controls. It indicates the patient is having hypothyroidism. The mean serum calcium and magnesium levels were significantly lower in hypothyroidism patients compared to healthy controls ($p<0.001$). Similarly a significant increase in mean serum phosphorous concentration was found in Hypothyroidism patients ($p<0.001$) when compared to controls (Table 1).

The serum TSH values of patients were studied in relation to the values of serum calcium, magnesium and phosphorous level. On analyzing the values, a statistically significant negative correlation between serum TSH with calcium total and magnesium total levels was noticed ($p<0.001$). Also statistically significant positive correlation between serum TSH and phosphorous levels was observed (Table 2)

Table 1: Comparison of Thyroid hormones, Calcium, Magnesium and Phosphorous level in healthy controls and hypothyroid cases

Parameters	Controls (n=100)	Cases (n=100)	P Value
Age (Years)	43.2 ± 6.4	46.7 ± 7.3	-
Sex (M/F)	48/52	36/66	-
TSH (Thyroid stimulating hormone) (µIU/ml)	2.49 ± 0.99	13.87 ± 9.78	< 0.001
Total T_3 (Tri- iodothyronine) (nmol/l)	1.81 ± 0.69	0.69 ± 0.26	< 0.001
Total T_4 (Thyroxine) (nmol/l)	109.1 ± 20.7	57.72 ± 19.84	< 0.001
Calcium Total (mg/dl)	9.28 ± 0.53	8.21 ± 0.66	< 0.001
Magnesium Total (mg/dl)	1.98 ± 0.31	1.36 ± 0.49	< 0.001
Phosphorous (mg/dl)	3.32 ± 0.61	4.71 ± 0.97	< 0.001

***The values are expressed as Mean ± SD, n is number of patients**

Table 2: Correlation with Serum Calcium, Magnesium and Phosphorous level with TSH

Parameters	Correlation coefficient (r value)	p value
TSH Vs Calcium Total	- 0.8368	< 0.001
TSH Vs Magnesium Total	- 0.7383	< 0.001
TSH Vs Phosphorous	0.8755	< 0.001

DISCUSSION

Thyroid hormone is a central regulator of body hemodynamics, thermoregulation and metabolism. Therefore, it has an influence on renal hemodynamics, glomerular filtration and electrolyte handling [12]. Thyroid hormone affects the glomerular filtration rate and blood flow and has a direct effect on Ca and Mg resorption [13].

Our study demonstrated a significant low level of serum calcium in cases then controls. In the present study the serum phosphorous 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 phosphorous levels and significant negative correlation between TSH and serum calcium level. Total 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 turnover 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 hypothyroidism there is hypomagnesaemia because of urinary output and fractional excretion of magnesium through urine.

Suneel B et al. studied mineral status in patients of thyroid disorders (Hypo & Hyper) and found decreased calcium and increase phosphorous level in hypothyroidism, mainly due to influence of PTH and calcitonin. Magnesium level is reduced due to influence on GFR and decreased clearance. In hypothyroidism there is an increased renal blood flow leading to high clearance of magnesium from the kidneys. So, low levels of magnesium will be causing hypomagnesemia [14].

Roopa M et al & Jaskiran K et al studied changes in electrolyte profile in patient with hypothyroid and reported that calcium level is significantly reduced and magnesium and phosphorous level is increased in patient with hypothyroidism. It was also found that there was a significant positive correlation between serum TSH and

magnesium and phosphorous level. At same time there was a significant negative correlation between TSH and calcium level[15, 16]. Thyroxin normally regulates blood calcium level by releasing calcium from cells, by decreasing thyroxin level in blood, less thyroxin enters the cells and less calcium is released leading to hypocalcemia[15].

Abbas MM et al also had shown decrease in serum calcium level and increase in magnesium as well as phosphorous level in women with subclinical hypothyroidism [8]. Alcalde et al. reported that thyroid hormones regulate phosphorous metabolism. In the study, phosphorous level is increased significantly in Subclinical hypothyroid subjects than in control group[17].Schwarz C et al in their study of 9012 patients found that, there was a significant positive correlation between serum TSH and phosphate level. Phosphates levels were higher in cases with elevated TSH then in controls[18].

Al Tonsi et al in their study found altered serum phosphates concentrations in patients with thyroid disorders. Their result also indicated a significantly elevated phosphate levels in the hypothyroid patients, which are also in accordance to our study [9]. Kadhem H had shown reduced total and ionized magnesium in patient with hypothyroidism along with study of lipid profile [19]. Shivaleela M B et al studied serum calcium and phosphorous level in thyroid dysfunction patients and found low calcium and phosphorous in hypothyroid patients [6].In a study done by Frizel et al, both plasma ionized magnesium and total magnesium levels were increased in hypothyroidism [20].

Mane AY et al had shown lower level of total calcium, ionized calcium and magnesium in hypothyroidism. Also opposite changes was observed in hyperthyroidism patients. Thyroid hormones affect bone metabolism by altering normal bone remodeling processes. Lower serum magnesium level in hypothyroid patients is due to impaired magnesium homeostasis [21].

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 phosphorous, in to the blood and also by influencing their clearance through urinary excretion due to its effect on GFR 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.

Our study is limited by the retrospective design and limited number of patients. Additionally, the list of potential confounders for above mineral disturbances is long which need to be studied in details. Also there are many markers associated with above minerals like vitamin D concentration, PTH level, calcitonin level in such patients which can also be studied for better understanding.

CONCLUSION

Our study demonstrated that hypothyroid patients show low serum total calcium, total magnesium and increased serum phosphorous 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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*Corresponding author: Dr Mukesh G Gohel
E-Mail: mks.gohel@gmail.com