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ORIGINAL RESEARCH

Study of Serum Calcium, Magnesium and Phosphorous Levels in Hypothyroidism

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ABSTRACT

Background: Thyroid disorders are the most common endocrine abnormality in the world secondary to diabetes mellitus. Thyroid hormones are essential for growth, neuronal development, reproduction and regulation of energy metabolism. It influences the metabolism of all substrates including minerals. Many studies have shown that mineral metabolism is frequently disturbed in thyroid disorders.

Materials and Methods: The study was conducted on sixty newly confirmed hypothyroid cases based on the thyroid profile and sixty euthyroid cases were recruited as controls. Blood samples were collected from all the patients for the estimation of serum T3, T4, FT3, FT4, TSH, calcium, phosphorus and magnesium by auto analyzer method. Modified spectrophotometric micro-method was used to measure Serum copper using Bathocuprine Disulphonate Disodium Salt (BCDS) and Guanidine hydrochloride salt. The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data.

Results: It was found that the levels of serum sodium, potassium and calcium were significantly decreased in cases than the controls. Serum magnesium and phosphorus were significantly elevated in cases than controls.

Conclusion: Serum calcium, magnesium and 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: Thyroid stimulating hormone, Thyroxin, Tri-Iodothyronine, Minerals and Subclinical hypothyroidism, Hypothyroidism, Mineral metabolism, Thyroid hormones, Electrolytes, Hypothyroidism, Minerals, T3, T4, TSH, Calcium, Hypothyroidism, Magnesium, Phosphorous.

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INTRODUCTION

The thyroid gland is involved in a variety of metabolic functions, including lipid, carbohydrate, protein, and mineral metabolism.[1,2] Thyroid hormones are necessary for the physiological growth and maturation of the skeletal system. Thyroid disease is widespread, and its incidence and prevalence are thought to rise with age. Hypothyroidism is one of the most common endocrine illnesses today, caused by a lack of thyroid hormones. The condition causes metabolic processes all across the body to slow down. The disease affects between 12% and 15% of the world's population. Women have a higher rate of infection than men.[3,4]

Thyroid hormones are essential for the development and growth of the skeletal system. According to this research, TSH is a direct regulator of bone remodeling, highlighting the significance of the hypothalamo pituitary thyroid axis' integrity.[5] Thyroid disorder has a negative impact on mineral and bone homeostasis.[6] Thyroid hormones control several metabolic pathways, and divalent metal ions like calcium, phosphorus, and magnesium are required for metalloenzymes.[7]

According to the literature, hypocalcemia is a common finding in hypothyroid patients. Thyroid hormones regulate calcium levels in the bloodstream by releasing calcium from cells. Since thyroxine levels are lower in hypothyroidism, calcium outflow from cells is reduced.[8] In hypothyroidism, increased calcitonin output can help with calcium tubular clearance and phosphate tubular absorption.[9] In hypothyroidism, disturbances in magnesium metabolism have also been discovered in a few studies.[10] According to the literature, serum magnesium levels are higher in hypothyroid disorders.[11] Despite the fact that increases in calcium and magnesium account for minor levels in thyroid disorders, these disruptions were critical in the long run for the patients.[12]

Secondary osteoporosis is caused by a variety of factors, including thyroid disorders. Hypothyroidism causes reduced calcium levels due to poor calcium mobilization into the bone. Furthermore, calcitonin synthesis rises, facilitating phosphate reabsorption and calcium excretion from the tubules of the kidney. Mineral metabolism problems, such as calcium and magnesium deficiency, have been linked to major metabolic disorders including hypertension and cardiovascular disease. Mineral levels in hypothyroidism have been studied extensively, with mixed results. Mineral status in subclinical hypothyroidism has received very little research. As a result, the current study was conducted to establish the mineral status of hypothyroid patients in terms of calcium and phosphorus. Since the impact of hypothyroidism on these minerals is complicated, this research was conducted to determine their changes.

MATERIALS & METHODS

A case control study was done for the duration of one year on the confirmed patients of hypothyroid visiting Department of Biochemistry, at tertiary care teaching Hospital. Age, sex matched euthyroid healthy individuals visiting hospital for routine health checkups were taken as controls. Sixty clinically healthy volunteers with euthyroid status and sixty newly diagnosed and untreated cases of hypothyroidism patient among the age group of 25-60 years were taken for the study. Estimation of sample size was done by using sample size calculator Piface 1.72 and Power of the study was calculated more than 80%. The study was approved by the ethical committee of the institution. Informed consent was taken from all the participants.

Inclusion criteria:

Biochemically, diagnosis of hypothyroidism was established based on decreased serum T3 (<0.5 ng/mL) and T4 (<4.6 µg/dL) levels associated with increased with TSH levels (>5.4 µIU/mL) and were included as cases in the study.

Exclusion criteria:

Pregnant women, patient with history of hepatic disease, renal disease, alcoholism or critically ill patients or the patients who were on mineral supplementation, anti-thyroid drugs or any other medications that influence the calcium, magnesium, phosphorus and copper metabolism were excluded.

A 5 mL of venous blood samples was collected from median cubital vein by venipuncture avoiding hemolysis into an evacuated vacuum tube under aseptic precaution. Samples were centrifuged after 30 minutes at 3000 rpm for ten minutes. The sample was aliquoted and kept at -20°C as per standard protocol until analysis was done. All the analysis was carried on serum samples.

Statistical Analysis

Statistical analysis was done by SPSS 18.0, and R environment version.3.2.2 was used for the data analysis. Student paired t-test was used to compare the results of cases and controls. P-value of <0.05 was considered as significant. All the parameters were compared with T3, T4, TSH, FT3, FT4 levels and correlation between parameters was done by Pearson's correlation coefficient.

RESULTS

A total of 60 cases and 60 controls were studied. Among the cases 18 (30%) were male and 42 (70%) were female. In the control group 22 (37%) were male and 32 (53%) were female. There were more females than males among cases. There was also more number of females than males in control group.

Table 1: Age distribution of cases and control.

Age in years	Cases		Control	
	No.	%	No.	%
<30	17	29	9	15
31-40	31	51	25	42
41-50	9	15	19	31
>50	3	5	7	12
Total Mean ± SD	22.37 ±5.1670		25.39 ±5.2976	

[Table 1] shows the highest number (51%) of cases belonged to the age group 31-40 years. The mean age of case was 22.37 ±5.1670 with S.E of mean was 0.5167.

Also there were significant more number of euthyroids in 31-40 years of age in control groups. The mean age of control was 25.39 ±5.29766 with S.E of mean was 0.5297.

Table 2: Comparison of serum TSH, T3 and T4 in two groups studied.

Lab variables	Hypothyroid cases (n=60)	Healthy controls(n=60)	t value	p value
	Mean ± SEM	Mean ± SEM		
TSH (µIU/ml)	36.2348±2.36847	0.6798±0.01028	7.67	< 0.001*
T3 (ng/dl)	28.2348±1.13450	61.1020±0.12041	10.237	<0.001*
T4 (µg/dl)	1.2314±0.00124	2.5467±0.01237	15.317	<0. 001*

[Table 2] shows when serum levels of TSH, T3 and T4 of cases and controls were compared a significant variation was seen. Serum TSH levels in Hypothyroid cases were found to be significantly increased when compared to healthy controls (p<0.001). Serum levels of T3 andT4 in hypothyroid cases were found to be significantly decreased when compared to healthy controls (p<0.001).

Table 3: Comparison of serum Sodium (Na), Potassium (K) and Calcium (Ca) levels in cases and controls.

Lab variables	Hypothyroid cases(n=60)	Healthy controls(n=60)	t value	p value
	Mean±SEM	Mean±SEM		
Sodium(meq/L)	75.224±0.1034	80.0120±0.01023	19.3642	<0.001*
Potassium(meq/L)	1.5941±0.0048	1.7349±0.0049	14.138	<0.001*
Calcium(mg/dl)	4.3485±0.0041	4.9647±0.0012	15.297	< 0.001*

[Table 3] shows when serum levels of sodium, potassium and calcium of cases and controls were compared a significant variation was seen. The levels of calcium and sodium were significantly decreased in cases when compared to controls (p<0.001). Serum potassium levels were found to be less than that of controls and difference was statistically significant (p<0.001).

Table 4: Comparison of serum Magnesium and Phosphorus levels in cases and controls.

Lab variables	Hypothyroid cases(n=60)	Healthy controls(n=60)	t value	p value
	Mean ± SEM	Mean ± SEM		
Phosphorus(mg/dl)	1.8467±0.0013	1.6487±0.0215	4.36	<0.001*
Magnesium(mg/dl)	1.0438±0.0048	1.0137±0.0043	9.69	<0.001*

[Table 4] shows when serum levels of phosphorus and magnesium of cases and controls were compared a significant variation was seen. Among the minerals, phosphorus and magnesium levels in serum were elevated in patients with hypothyroidism when compared to controls and the difference was statistically significant (p<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 and 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. and 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 and 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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