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Original Research Article

Study of Serum Calcium, Magnesium and Phosphorous Levels in Hypothyroidism

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Abstract

Introduction: Hypothyroidism is receiving greater attention as an important cause of disturbance in mineral metabolism by its direct action on bone turnover, and also as one of the causes for secondary osteoporosis. Calcium (Ca2+), phosphorus (PO4 2−), and magnesium (Mg2+) are necessary for metalloenzymes and various crucial metabolic pathways directly or indirectly regulated by thyroid hormones. ***Methodology:*** Patients attending the General Medicine department who were diagnosed clinically as hypothyroid for the first time (n=120) and referred to the central laboratory for thyroid function tests were enrolled for the study. 60 normal healthy individuals were chosen as controls. Results: In hypothyroid patients, the mean values of calcium and magnesium were found to be higher compared to that of the controls'. Whereas mean value of phosphorous was found to be lower compared to that of the controls'. ***Conclusion:*** Serum calcium, magnesium & phosphorous levels are widely altered in patients having hypothyroidism. So we suggest that constant monitoring of these minerals in hypothyroid patients will be of great benefit in improving clinical manifestation. Complications can be avoided by planning holistic disease management strategies for these patients.

Keywords: Calcium, Magnesium, Phosphorous, Hypothyroidism.

INTRODUCTION

Hypothyroidism manifestations occur due to impaired activity of thyroid hormones at the tissue level. Currently, it is a common condition, with a prevalence of 1.9 percent in women, and prevalence increases with age. Hypothyroidism can be congenital or acquired, primary or secondary and chronic or transient. Primary hypothyroidism is due to disease or any treatment which destroys the thyroid gland or interferes with the hormone biosynthesis [1].

The clinical presentations of hypothyroidism depend on the patient's age, the presence of other diseases, and the rate at which it develops. Thyroid hormones are universal determinants of organ functions. Hence there may be a multiplicity of symptoms. Especially in the elderly, clinical presentations may be atypical and goes undiagnosed. First line tests for hypothyroidism are analyses of the concentrations of free thyroxine (T4) and TSH in serum [2].

In primary hypothyroidism, serum content of T4 is low and TSH is high. In central hypothyroidism, serum content of T4 is low and TSH is low or normal. Subclinical hypothyroidism is characterized by normal serum level of T4, increased level of TSH, and absence of clinical symptoms [3].

Thyroid diseases have widespread systemic manifestations. Frequently bone and mineral metabolism are disturbed in thyroid dysfunctions. Thyroid hormone affects the renal blood flow, glomerular filtration rate, tubular reabsorption and excretion of minerals and has a direct effect on calcium, magnesium and phosphorous levels. Thus monitoring of these minerals in a hypothyroid patient is of great benefit in improving clinical condition and appropriate treatment [4].

Studies done on serum calcium, phosphorous and magnesium levels in thyroid disorders have conflicting results. Normal thyroid function is important for the regulation of cellular activity. It influences the basal metabolic rate and general body metabolism. Hence, thyroid dysfunction often is associated with dyslipidemia and disturbances in mineral metabolism. It is known that hypothyroidism causes hypercholesterolemia, elevated low-density lipoprotein

(LDL), and hypertriglyceridemia [5]. High circulating thyroid stimulating hormone (TSH) levels were reported to be associated with abnormally elevated serum lipids. It also triggers increased oxidation of the LDL particle [6].

The occurrence of deranged lipid profile, metabolic, hormonal, endothelial dysfunction, coagulation disturbances, and hemodynamic changes increased the cardiovascular risk in thyroid dysfunctional patients. Hence, they are considered to be at high risk of cardiovascular diseases [7]. Some studies revealed normalized lipid profiles in hypothyroid patients after treatment [8-10]. Not many studies have been conducted in this part of our society focusing on these parameters. Hence this study was planned to investigate the changes in serum levels of calcium, phosphate, and magnesium associated with thyroid disorders.

MATERIALS AND METHODS

This study was conducted over a period of six months in association with the Department of General Medicine, at Sri Siddhartha Medical College and Hospital, Tumkuru. Both sexes were included and all of them were in the age group of 20-60 years. Patients attending the General Medicine department who were diagnosed clinically as hypothyroid for the first time(n=120) and referred to the central laboratory for thyroid function tests were enrolled for the study. 60 normal healthy individuals working at Sri Siddhartha Medical College were enrolled as controls. Patients with a history of hepatic disease, renal disease, alcoholism, or other major medical conditions or those who were on mineral supplementation, or any medications that might affect serum calcium, magnesium, phosphorous and electrolytes levels were excluded from the study. Informed consent was taken from all subjects.

SAMPLE COLLECTION: After overnight fasting 5 ml of blood sample was collected and allowed to clot for serum separation. The serum was used for the estimation of the following parameters. TSH, FT3, FT4, serum calcium levels, serum phosphate levels and serum magnesium levels.

FT3 Method

Enzyme Linked Immunosorbant Assay (ELISA) method. Normal value: 1.4 - 4.2 pg/ml.

FT4 Method

ELISA method. Normal value: 0.8-2 ng/dl.

TSH Method

Classical sandwich ELISA technique. Normal values: 0.3 – 6.2 mIU/ml.

Estimation of Serum Calcium

OCPC-method (o-cresolphthalein complexone method) measured at 570nm.

Calculations: Calcium in mg/dl = Absorbance of test /absorbance of standard X 10

Reference value: calcium- 8.7-11 mg/dl.

Estimation of serum phosphorus

Phosphate reacts with molybdate in strong acidic medium to form a complex. The absorbance of this complex in the near ultra violet is directly proportional to the phosphate concentration. Reference values in adults = 2.5- 5 mg/dl.

Estimation of serum magnesium

By GEDTA-Method. The colored complex is measured at 520nm. Reference value: 1.9—2.5 mg/dl. Results were obtained using Transasia - Erba EM 200 fully automated analyzer and their reagent kits.

STATISTICAL ANALYSIS

Data was analysed using statistical software SPSS 12.0 version. Values were expressed as mean ± SEM. Comparison of continuous variables were done using Student's 't' test. Correlation between two parameters was done using Pearson's correlation and in case of skewed variables, either log transformed or Spearman's rank correlation test was used. A p value of <0.05 was considered statistically significant.

RESULTS

In hypothyroid patients the mean values of fT3 is found to be 3.12 pg/ml, which is significantly lower when compared to controls mean value of 2.01 pg/ml and the mean values of fT4 is found to be 1.98ng/ml, which is significantly lower when compared to controls mean value of 1.61ng/dl.

Table-1: Comparative study of hypothyroid patients with controls

Sl.no	Parameter	Patients		controls		t'value	P'value
		Mean	S.D	mean	S.D		
1.	FT3	3.12	1.00	2.01	0.76	6.8454	<0.0001
2	FT4	1.98	0.50	1.61	0.54	3.8944	0.0002
3	TSH	26.20	13.61	2.55	1.25	13.4037	<0.0001
4	Calcium	13.34	2.38	10.02	1.40	9.3135	<0.0001
5	Phosphorus	2.03	1.03	4.91	0.99	15.6152	<0.0001
6	Magnesium	4.29	1.46	2.82	0.98	6.4755	<0.0001

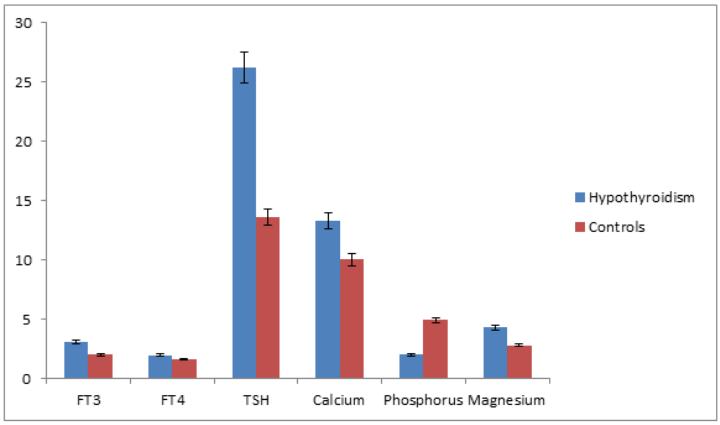

Fig-1: Biochemical values in both Cases and Controls

FT3 P value and statistical significance: The two-tailed P value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant. Confidence interval: The mean of Hypothyroidism subjects minus Controls equals 1.1100 and 95% confidence interval of this difference: From 0.7889 to 1.4311. Intermediate values used in calculations: t = 6.8454, df = 118 and standard error of difference = 0.162.

FT4 P value and statistical significance: The two-tailed P value equals 0.0002. By conventional criteria, this difference is considered to be extremely statistically significant. Confidence interval: The mean of Hypothyroidism subjects minus Controls equals 0.3700 95% confidence interval of this difference: From 0.1819 to 0.5581. Intermediate values used in calculations: t = 3.8944, df = 118 and standard error of difference = 0.095.

TSH P value and statistical significance: The two-tailed P value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant. Confidence interval: The mean of Hypothyroidism subjects minus Controls equals 23.6500. 95% confidence interval of this difference: From 20.1559 to 27.1441. Intermediate values used in calculations: t = 13.4037, df = 118 and standard error of difference = 1.764. The mean values of TSH are found to be 26.20 miu/l, which is significantly higher when compared to controls' mean value of 2.55 miu/l.

Calcium P value and statistical significance: The two-tailed P value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant. Confidence interval: The mean of Hypothyroidism subjects minus Controls equals 3.3200. 95% confidence interval of this difference: From 2.6141 to 4.0259 Intermediate values used in calculations: t = 9.3135, df = 118 and standard error of difference = 0.356. The mean values of calcium are found to be 13.34 mg/dl, which is significantly higher when compared to controls' mean value of 10.02 mg/dl.

Phosphorous P value and statistical significance: The two-tailed P value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant. Confidence interval: The mean of Hypothyroidism subjects minus Controls equals -2.8800. 95% confidence interval of this difference: From -3.2452 to -2.5148. Intermediate values used in calculations: t = 15.6152, df = 118 and standard error of difference = 0.184. The mean values of phosphorus are found to be 2.03 mg/dl, which is significantly lower when compared to controls' mean value of 4.91 mg/dl.

Magnesium P value and statistical significance: The two-tailed P value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant. Confidence interval: The mean of Hypothyroidism subjects minus Controls equals 1.4700. 95% confidence interval of this difference: From 1.0205 to 1.9195. Intermediate values used in calculations: t = 6.4755, df = 118 and standard error of difference = 0.227. The mean values of magnesium are found to be 4.29 mg/dl, which is significantly higher when compared to controls' mean value of 2.82 mg/dl.

DISCUSSION

Thyroid hormones and its effect on various organs and metabolic systems, of late, have been the focus of intensive research. Normal thyroid function is essential for the regulation of cellular activity. It influences the basal metabolic rate and body metabolism. Thyroid dysfunction is often associated with disturbed mineral metabolism due to its influence on renal hemodynamics and glomerular filtration.

In our study, we observed that females, especially between the age group of 31-41years are more vulnerable to hypothyroidism.

Calcium, phosphorus and magnesium are necessary for metallo enzymes and various crucial metabolic pathways which are directly or indirectly regulated by thyroid hormones. Elevated serum calcium

levels promote CVD and atherogenesis by vascular calcification and increase in coagulability. Hypothyroidism has been associated with disturbed kidney function in human and animals. Some authors like Saini V et al have demonstrated severe kidney function impairment in overt hypothyroid patients [11].

Conflicting results were revealed in previous studies which investigated serum calcium and phosphorous in thyroid disorders. Some authors reported normal levels and some others have reported decreased serum calcium and phosphorous in hypothyroidism with increased or decreased levels in the hyperthyroidism like Mosekilde L *et al.* [12] and Al-Tonsi *et al*.[13] This controversy in the results shows the complexity of hormonal and cellular mechanisms that are involved in regulation of calcium and phosphate metabolism at the intestinal and renal tubular levels, which are disturbed in thyroid dysfunction.

It has also been reported by Majima T *et al*. [14] that thyroid hormones stimulate bone resorption and increase the serum calcium and phosphorous levels and suppresses parathyroid hormone secretion. 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.

Magnesium, an important cation, ameliorates atherosclerosis and hypertension, promotes coronary vasodilatation. In hypothyroidism, a defect in magnesium transport occurs. Also, there is an increased renal blood flow which leads to high clearance of magnesium from the kidneys. In our study, the magnesium levels in hypothyroid patients were significantly increased with positive correlation with T3 and T4 and negatively correlated with TSH which is not in accordance with the study conducted by Al Hakeim *et al*. [15] who found a significant decrease in Mg levels in hypothyroid patients compared with of the control group.

Martin *et al*. [16] mention that alterations in serum calcium, phosphate, and magnesium levels are considered as cardiovascular risk factors.

CONCLUSIONS

Thyroid diseases have profound effects on bone and mineral metabolism. They have a direct effect on Calcium, Magnesium and phosphorous level by altering the glomerular filtration rate, renal blood flow, tubular reabsorption and excretion of these minerals. Hence Serum calcium, magnesium & phosphorous levels are widely altered in patients having hypothyroidism. So we suggest that constant monitoring of these minerals in hypothyroid patients will be of great benefit in improving clinical manifestation. Complications can be avoided by planning holistic disease management strategies for these patients.

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