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Role of Thyroid Hormone in Calcium and Phosphorous Homeostasis – A Case Control Study of Hypothyroid patients in M.Y. Hospital Indore

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ABSTRACT

***Introduction*;** Hypothyroidism is the hormonal dysfunction due to deficiency or impaired activity of thyroid hormone. Thyroid hormones play an important role in Calcium and Phosphorous homeostasis by their direct action on bone turnover. Aim of our study was to assess and analyze the levels of serum calcium, phosphorous and magnesium and their relation with T3, T4 and TSH in hypothyroid patients in central India and to compare it with healthy normal controls.

***Material and Methods*;** The study was conducted in the Department of Clinical Biochemistry M.G.M. Medical College and M.Y. Hospital in Indore. 60 diagnosed patients of Hypothyroidism of both gender as a test group and 60 apparently healthy control were selected for the study. Venous blood samples were collected from both the groups and estimated for serum levels of Calcium, Phosphorus, Thyroid stimulating hormone, Thyroxin and Tri-Iodothyronine.

***Results*:** Serum calcium levels were found significantly decreased among cases as compared to controls ($p<0.001$). Serum phosphorous ($p<0.001$) and magnesium ($p<0.001$) levels were significantly increased among cases compared to controls. An inverse relationship was found between serum calcium with serum phosphorous and magnesium.

Conclusion: Our study has concluded that serum phosphorous and magnesium levels were raised whereas serum calcium level was low in hypothyroidism as compared to normal healthy control subjects. A regular follow up, treatment of the primary cause and supplementation of minerals should be done in order to prevent further bone complications in thyroid hormone deficiency which would be of great help in its management.

Keywords: Hypothyroidism, Calcium, Phosphorous, Thyroid stimulating hormone, Thyroxin, Tri-Iodothyronine

INTRODUCTION

Thyroid hormone T3 & T4 are very essential for normal growth and maturation of the skeletal tissue, cell differentiation, thermogenesis and mineral homeostasis. It is also involved in various metabolic functions like regulation of lipid, carbohydrate, protein and mineral metabolism. [1]

Hypothyroidism is the subnormal activity of thyroid gland cause decrease in basal metabolic rate which results in mental and physical sluggishness [2].

In early life deficiency of thyroid hormone leads to both delay in the bone development and stippled appearance of epiphyses and results in dwarfism. In hypothyroidism there is impaired mobilization of calcium into the bone leads to decrease the blood

calcium level causing secondary osteoporosis.[3] Serum Calcium& Phosphorous can be used as a sensitive parameter of bone resorption.

The prevalence of hypothyroidism increases with age. In global perspective occurrence of thyroid diseases are very common cause of morbidity and its incidence rises with age with female preponderance. In India about 42 million people are suffering from thyroid diseases among which, hypothyroidism is the commonest [4]. One of the diagnostic biochemical finding in hypothyroidism is reduced T3 and T4 concentration results in increased secretion of pituitary TSH [5].

Thyroid hormone acts through nuclear receptors and exert its effects on osteoblasts and osteoclasts to stimulate bone resorption [6]. It has a critical role in maintenance of ionic balance in the body by increasing the serum calcium and phosphorous concentrations and also by suppressing serum parathyroid hormone and 1, 25-dihydroxyvitamin D3 concentrations.

Disturbance of calcium homeostasis which manifests as hypocalcemia due to decreased turnover and impaired mobilization of calcium was very frequently observed with hypothyroidism [7,8]. Also increased production of calcitonin promotes the tubular reabsorption of phosphate results in hyper-phosphatemia and also favors the tubular excretion of calcium [9].

Various studies done previously on serum calcium and phosphorus levels in thyroid disorders have shown very conflicting results. Studies by Beqic KS et. al and Sabuncu T et. al., have reported normal levels [9,10], while Gammage MD et al have reported decreased serum calcium and phosphorous levels in hypothyroidism [11].

B. Suneel et al., have reported study that serum calcium levels were significantly decreased ($p<0.001$) in hypothyroid patients [12]. Similar finding in a study by Shivaleela MB et al., that the mean serum calcium & phosphorous levels were significantly lower in Hypothyroidism patients ($p<0.01$) compared to controls [6].

In an another research by Christoph Schwarza et al, it has been reported that the patients with elevated TSH have raised serum phosphate levels and significantly decreased serum calcium levels as compared to patients with normal TSH. Serum calcium & phosphate levels were correlated significantly with TSH [13].

It has been suggested that disturbed metabolism of divalent cations like calcium & magnesium has an impact on metabolic syndrome and cardiovascular disorders in hypothyroid patients. [14,15]

So aim of our study is to assess the serum levels of Calcium, Phosphorous and Magnesium in Hypothyroid patients and to compare it with normal healthy controls in central India.

MATERIAL AND METHODS;

The study was conducted in the Department of Clinical Biochemistry M.G.M. Medical College and M.Y.Hospital Indore after ethical approval. Written informed consent was obtained from 60 clinically diagnosed and confirmed patients of hypothyroidism of age group 20-58 years of both gender as a test group and 60 apparently healthy age and gender matched control were selected for the study. Patients suffering from bone diseases, kidney diseases, liver disorders, alcoholism, pituitary adenomas, diabetes mellitus and patients receiving mineral supplementation or drugs which affects mineral metabolism were excluded from study.

Venous blood sample (4 ml) were collected after all aseptic precaution from both the groups and serum levels of Calcium, Phosphorus, Magnesium, Thyroid stimulating hormone, Thyroxin and Tri-Iodothyronine were estimated. Estimation of serum T3, T4 and Thyroid stimulating hormone (TSH) was done by double sandwich ELISA method. Serum Calcium was estimated by Arsenazo III methods, Serum Magnesium by Xylidyl blue and Phosphorous by Phosphomolybdate by turbidimetric method.

STATISTICALANALYSIS;

All the data were expressed as Mean ± Standard Deviation using software SPSS 15. The Comparison of the all parameters between cases and controls was conducted by student t test. Pearson's correlation coefficient to correlate the parameters among the cases with $p<0.05$ were considered as statistically significant.

RESULTS;

In our analysis we found that out of 60 cases 61% of the females were having hypothyroidism whereas

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39% were males. The mean age of the controls and cases were 34.06±9.42 years and 35.11±8.09 years respectively.

In our study table 1 indicate there is no significant statistical difference between males and females regarding serum calcium, phosphorous and magnesium levels in cases. Table 2 shows significantly raised serum levels of TSH among cases compared to controls *(p<0.001)*. The mean serum TSH among controls were 3.1 ± 1.56 mIU/L and in cases 49.97±30.71 mIU/L respectively. The mean serum T3 among controls were 1.22±0.38 ng/L and in cases 0.37±0.12 ng/L with significant p value < 0.001. Controls have mean serum T4 value 9.01±2.08 mg/L and in cases it was 3.08±1.43 mg/L with statistically significant p value *p<0.001*.

A significant hypocalcemia *(p<0.001)* was observed in cases with mean and standard deviation of 7.54± 0.56 mg/dl calcium and in controls it was 9.13± 0.43 mg/dl.

The mean serum phosphorous in cases were 4.04± 1.36 mg/dl and in controls 3.29± .514 mg/dl respectively with highly significantly raised levels was noticed in cases compared to controls *(p<0.001)*.

A statistically significant increase in magnesium levels in cases 3.17±0.25 mg/dl as compared to controls 1.94± 0.12 mg/dl *(p<0.001)*. (Table 1, Fig. 1)

Serum Calcium, Phosphorous and Magnesium levels were correlated with TSH levels in the cases. On analysis a strong negative correlation was observed between serum TSH and Calcium.

DISCUSSION; -

Thyroid hormone is essential for normal growth and maturation of the skeleton, body hemodynamic, thermoregulation and metabolism. Therefore, it has an influence on renal blood flow, glomerular filtration and has a direct effect on Ca and Mg resorption [16,17]. Laura & McCaffrey C Hypothyroidism is the most prevalent endocrine disease results in disturbed calcium, magnesium and phosphorous homeostasis. In hypothyroidism there is impaired mobilization of calcium from the bone that leads to decrease blood calcium level. Thyroid hormones also affect glomerular filtration rate and renal blood flow and have direct effect on calcium and magnesium resorption [18].

The present study was done to assess the levels of serum calcium, phosphorus and magnesium levels in patients with hypothyroidism in central India shows significantly low level of serum calcium in cases than in controls. As thyroid hormone is responsible for bone growth, development & maturation. Reduced thyroxine level in the bloodstream causes less thyroxine entry into the cells thus results in reduced extracellular calcium release. This ultimately cause reduction of blood calcium levels also there is reduced turnover and disturbed calcium homeostasis in the skeletal tissue.

Results of our study was similar with study conducted by Shivaleela MB et al [6] which concluded that significant decrease of the mean serum calcium was observed in patients with hypothyroidism than in control. This is mainly due to the low levels of Parathyroid hormone and low levels of calcitonin in hypothyroidism. Study by Murgod R et al [8], D. Sridevi et al [19] have also demonstrated similar results. A significant negative correlation was observed in between serum TSH levels and calcium levels.

Serum phosphorous levels were markedly increased in hypothyroid patients as compared to healthy controls (p value<0.001). There was an insignificant positive correlation between TSH and serum phosphorous levels. Our findings were consistent with finding of study by B. Suneel, et al [12] who observed that hypothyroid patients have significantly raised phosphorous levels as compared to control.

Calcitonin plays a major role in regulation of tubular reabsorption of phosphorous. Raised levels of phosphorous is due to compensatory effect of calcitonin and parathormone which favor tubular excretion. Similar results were observed in a study conducted by Schwarz C et al [20] and Abbas MM et al [21] however finding by Gammage et al [11] was opposite to our study that decreased serum phosphorous levels in hypothyroidism.

In our study serum magnesium levels were significantly increased in hypothyroid patients had an insignificant correlation between TSH and magnesium levels. The probable explanation of low serum magnesium by animal studies by McCaffrey et

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al,[17] who mentioned that renal retention of magnesium as the thyroid hormones had effect on the tubules.

CONCLUSION; Our study concludes that in hypothyroid patients of central India, Serum calcium and Serum Phosphorous levels are not affected by gender and duration of the disease. The levels of Serum calcium was reduced as compared to control group with an inverse correlation between the Serum Calcium & serum TSH levels, and the levels of Serum Phosphorous and serum Magnesium was increased compared to control group with a positive correlation between the Serum Phosphorous & serum TSH. Hence yearly monitoring of serum Calcium, Phosphorous and Magnesium levels and their supplementation in follow up study of hypothyroid patients will avoid the damaging effects of disturbed mineral metabolism. Although a larger population study is recommended to establish the precise correlation.

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TABLE 1; DEMOGRAPHIC VARIABLES

Variables	Male N=24	Female n=36	P value
S. Calcium(mg/dl)	8.24 ± 0.317 (7.36 – 9.14)	7.06± 0.628 (6.24 – 8.08)	= 0.138
S. Phosphorous (mg/dl)	4.18± 1.20 (3.03 – 8.69)	4.40± 1.51 (3.11 – 8.16)	= 0.725
S. Magnesium (mg/dl)	2.10±0.19 1.62-3.12	2.03±0.26 1.84-2.99	=0.632

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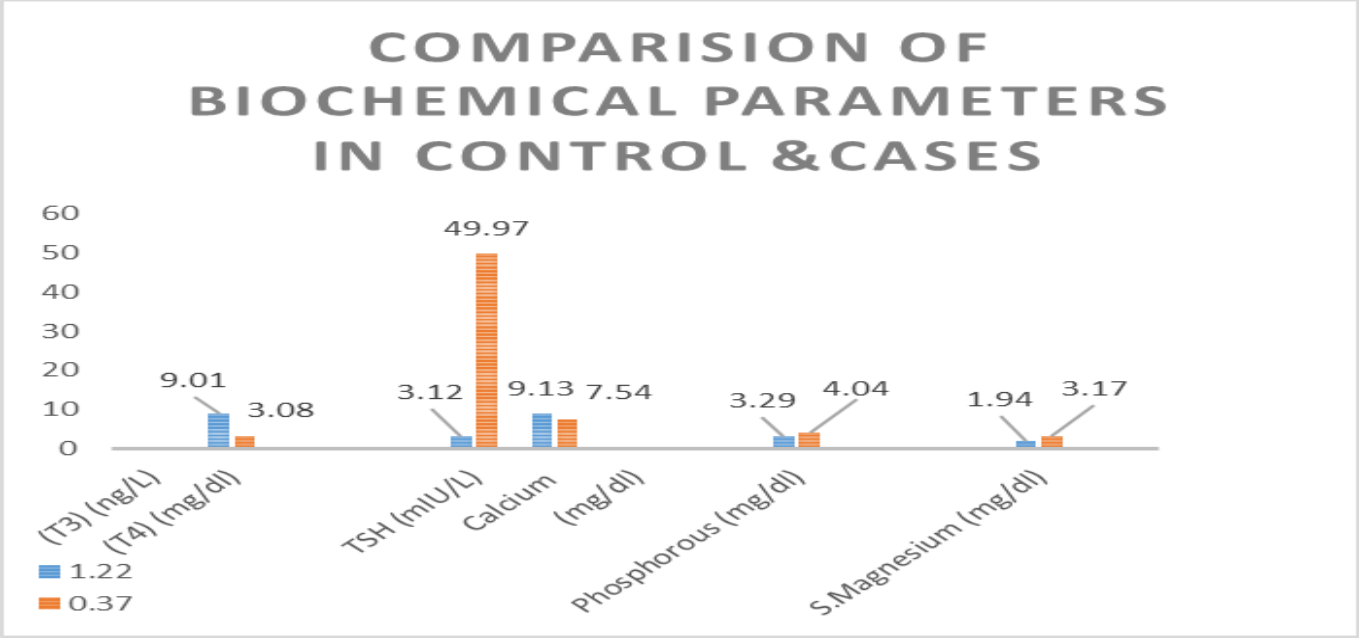
TABLE 2; BIOCHEMICAL PARAMETERS

Parameter	Control n=60	Case n=60	P value
Tri iodothyronine (T3) (ng/L)	1.22±0.38	0.37±0.12	< 0.001
Tetra iodo-thyronine (T4) (mg/dl)	9.01±2.08	3.08±1.43	< 0.001
TSH (mIU/L)	3.12±1.56	49.97±30.71	< 0.001
S. Calcium (mg/dl)	9.13± 0.43 (8.24-10.53)	7.54± 0.56 (6.23 – 8.78)	<0.001
S. Phosphorous (mg/dl)	3.29± .514 (2.69 – 4.56)	4.04± 1.36 (3.22 – 10.03)	<0.001
S. Magnesium (mg/dl)	1.94± 0.12 1.36-2.79	3.17±0.25 2.83-4.71	<0.001



GRAPH -1

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