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An Study Of Calcium And Phosphorus Levels Among Hypothyroid Patients Aged Above 40 Years.

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ABSTRACT

Mineral metabolism is frequently disturbed in thyroid dysfunctions. Among thyroiddysfunctions, hypothyroidism is one of the most common form resulting from thedeficiency of thyroid hormones. Studies done on serum calcium and phosphorus in hypothyroid patients earlier have conflicting results. Hence the present study has been undertaken to study the levels of serum calcium and phosphorus among hypothyroid patients above 40 years and analyse theircorrelation with thyroid stimulating hormone (TSH). The observational study was conducted in the Department of Biochemistry in Kanyakumari Government Medical College hospital for a period of 6 months. The study was undertaken involving 50 hypothyroid cases and 50 healthy volunteers as controls after proper ethical clearance and informed consent of all the study subjects. Serum calcium, phosphorus were measured along with tri-iodothyronine (FT3), tetra-iodothyronine (FT4) and TSH among all study subjects. The mean value of serum total calcium levels was lower among hypothyroid cases and phosphorus value was increased as compared to controls.($P < 0.001$) Statistically significant negative correlation was observed between serum calcium and TSH among hypothyroid cases. Statisticallysignificant positive correlation was observed between serum phosphorus and TSH among hypothyroid cases. Among hypothyroid patients the values of serum calcium and phosphorus is significantly altered. Thyroid disorders have an important role in bone and mineral metabolism. Thus, monitoring of these minerals among hypothyroid patients in regular follow up may effectively improve the clinical manifestations in them. Hence, monitoring of mineral status of the hypothyroid patients on follow-up will be of benefit to the patients.

Keywords: Hypothyroidism, Calcium, Phosphorus.

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INTRODUCTION

Thyroid is one of the largest endocrine glands in the body. It is situated in anterior neck like a small bow tied across and in the front of trachea. Thyroid gland secretes two hormones, thyroxine (T4) & triidothyronine (T3) which plays a critical role in cell differentiation during development and also maintain the thermogenic & metabolic homeostasis in the adult [1]. It also produces the hormone calcitonin which plays a role in calcium homeostasis. Hence thyroid hormones perform a wide range of metabolic functions like regulation of lipid, carbohydrates, protein, electrolytes & mineral metabolism.

One of the most common forms of thyroid disorder is hypothyroidism. It is caused by any structural or functional derangement interfering with the production of adequate levels of thyroid hormone. So it may be congenital or acquired, primary or secondary, chronic or transient. Iodine deficiency is the most common cause of hypothyroidism worldwide, whereas in iodine sufficiency areas autoimmune disease (Hashimoto's thyroiditis) and iatrogenic causes (treatment of hyperthyroidism) found to more common. The mean annual incidence of spontaneous hypothyroidism during the 20-year follow up of the Whickham cohort was 3.5 per 1000 and 0.6 per 1000 in women and men respectively [2].

Optimal health maintenance requires adequate and balanced amount of macronutrients and micronutrients.Macro-minerals have a definite role in various biological functions by influencing enzymatic activity, protein functionand cell membrane permeability. Hormones influence mineral metabolism at several levels of action, including transport and excretion of minerals. Mineral metabolism is frequently disturbed in thyroid dysfunctions. Among thyroid dysfunctions, hypothyroidism isone of the most common forms resulting from the deficiencyof thyroid hormones. Studies done on serum calcium and phosphorus in hypothyroid patients earlier have conflicting results.

Calcium, an essential dietary element and humans contain a vast store of calcium (i.e., >1Kg) in their bones. It is an intracellular signaling molecule, which plays a variety of extracellular functions. Calcium plays a key role in many physiological processes which includes contraction of cardiac, skeletal & smooth muscles, blood clotting, transmission of nerve impulses. Thyroxine & Calcitonin play a role in calcium homeostasis. Hypothyroidism results in depressed turn over due to impaired mobilization of calcium into the bone which leads to hypocalcemia.

Thyroid hormones are essential for normal growth and maturation of skeletal system. Calcium and phosphorus homeostasis is frequently altered in thyroid dysfunction. Hence thyroid disorders are important causes of secondary osteoporosis. Serum calcium levels can be fairly used as anindex of bone resorption [3]. The depressed turnover due to impaired mobilization of calcium into the bone in hypothyroidism leads to decrease in blood calcium level. In hypothyroidism the increased production of calcitonin can promote tubular reabsorption of phosphate and tubular excretion of calcium [4]. The renal phosphate reabsorption is elevated by FT3 and hence elevates the serum phosphorus levels in rats. Animal studies propose thyroid hormones as long-term regulators for phosphate metabolism [5]. Normal calcium and phosphorus have been shown in few studies [6, 7] while other studies have shown decreased levels in hypothyroidism [8, 9]. Even though the changes in calcium and phosphorus may be slight in thyroid disorders, these disturbances will be important for the patient in long run [10]. Hence the present study was undertaken to study the levelsof serum calcium, and phosphorus among hypothyroid patients age above 40 year in particular and to analyze their correlation with TSH.

METHODOLOGY

This observational study was conducted in the Department of Biochemistry in Government Kanyakumari Medical College hospital for a period of 6 months. The study was conducted after approval from ethical committee and informed consent was taken from all patients. Study participants of age group above 40 years were selected from patients who had hypothyroidism. Among 100 participants, 50 were selected as cases and 50 as controls based on their thyroid profile report. The reference range of thyroid profile according to Tietz textbook [11] was followed and patients were categorized as controls and hypothyroid cases based on the report. The reference ranges are Free T3: 2.1 - 4.4 (pg/ml), Free T4: 0.8 - 2.7 (ng/dl) and TSH: 0.4 - 4.2 (mcIU/ml). Patients below age of 40 years suffering from infectious diseases, renal diseases, hepatic diseases, pituitary diseases, bone diseases, diabetesmellitus, alcoholism and patients on mineral supplementation were excluded from the study.

Routine IQC was run and after confirmation the samples were analyzed for biochemical parameters. Serum was analyzed for FT3, FT4 and TSH by eCLIA method in Cobas e411 auto-analyzer followed by calcium (Arsenazo IIImethod), phosphorus (phosphomolybdate UV method) in MindrayBS420 auto- analyzer. Data was entered in Microsoft Excel and analyzed using SPSS software. Descriptive statistics such as mean and standard deviation were computed for the data respectively. Pearson's correlation was done to correlate therelationship between FT3, FT4, TSH and calcium and phosphorus.

RESULTS

There were a total number of 42 females and 8 males in controls and 33 females and 17 males in hypothyroid cases. The mean age of controls was 48.8 ± 12.45 (years) and the mean age of cases was 47 ± 10.06 (years). The mean TSHvalues were 2.15 ± 0.81 µIU/L among controls and 61.49 ± 34.82 µIU/L among hypothyroid cases. There was a statistically significant increase in TSH among cases ascompared to the controls. The mean FT3 values were 2.84 ± 0.44 pg/ml among controls and 2.84 ± 0.44 pg/ml among hypothyroid cases. FT3 values were significantly decreased in cases as compared to the controls (2.52 ± 0.91 vs 2.84 ± 0.44 pg/ml). The mean FT4 values were 1.28 ±0.18 ng/ml among controls and 0.85 ± 0.36 ng/ml among hypothyroid cases. Similarly, FT4 values were also decreased among cases as compared to the controls (0.85 ± 0.36 vs 1.28 ± 0.18 ng ml).

The study observed a significant decrease level of calcium among cases 8.01 ±0.17 (mg/dl) as compared to the controls 10.16 ± 1.47 (mg/dl) and the serum phosphorus values were increased among cases as compared to the controls (4.81 ± 0.88 vs 3.83 ± 0.40 mg/dl). The mean calcium values were 10.16 ± 1.47 mg/dl among controls and 8.01 ± 0.17 mg/dl among hypothyroid cases. The mean phosphorusvalues were 3.83 ± 0.40 mg/dl among controls and 4.81 ± 0.88 mg/dl among hypothyroid cases. The mean calcium were significantly lower in hypothyroidism cases compared to healthy controls. ($P < 0.001$). Similarly, significant increase in serum phosphorus concentration was found among hypothyroidism patients ($P < 0.001$) when compared to controls.

Table 1: Comparison Between Groups

PARAMETERS	CASES	CONTROLS	P VALUE
AGE	48.8± 12.45	47± 10.06	0.913
SEX(MALE/FEMALE)	17:33	08:42	NA
FT3	2.52± 0.91	2.84± 0.44	<0.01
FT4	0.85± 0.36	1.28± 0.18	<0.001
TSH	61.49± 34.82	2.15± 0.81	<0.001
CALCIUM	8.01± 0.17	10.16± 1.47	<0.001

The correlation coefficient between TSH and calcium wasr = [-0.566] and correlation coefficient between TSH and phosphorus was r = [0.376]. The serumTSH values of hypothyroid patients were studied in relationto serum calcium and phosphorus levels. On statistically analyzing the values, a significant negative correlation was observed between serum TSH with serum total calcium. Also, a statistically significant positive correlation was observed between serumphosphorus levels and TSH. Table 2 shows correlation between TSH and other parameters.

Table 2: Pearson Correlation

PARAMETERS	R VALUE	P VALUE
TSH VS CALCIUM	-0.566	0.001
TSH VS PHOSPHORUS	0.376	0.01

DISCUSSION

Normal growth and maturation of skeletal system needs the thyroid hormones. In thyroid dysfunction, calcium and phosphorus homeostasis is frequently altered. Hence secondary osteoporosis is commonly seen in thyroid disorders. Serum calcium levels can be fairly used as an index of bone resorption. The depressed turnover due to impaired mobilization of calcium into the bone in hypothyroidism leads to

decrease in blood calcium level. Theincreased production of calcitonin in hypothyroidism can promote tubular reabsorption of phosphate and tubular excretion of calcium. The renal phosphate reabsorption is elevated by FT3 and hence elevates the serum phosphorus levels in rats. Animal studies propose thyroid hormones as long-term regulators for phosphate metabolism. Normal calcium and phosphorus levels have been shown in few studies while other studies have shown decreased levels in hypothyroidism. Even though the changes in calcium and phosphorus may be slight in thyroid disorders, these disturbances will be important for the patient in long run.

Our study has shown significant low levels of serum calcium in cases than controls. The serum phosphorus levels were markedly increased among hypothyroid patients in the present study compared to the controls. There was a significant positive correlation between serum phosphorus and TSH and negative correlation between serum calcium, magnesium and TSH.

Normal growth and maturation of the skeleton needs thyroid hormones. In hypothyroidism there is a decreased turnover due to impaired mobilization of calcium into the bones, which leads to the decrease in blood calcium. In hypothyroidism there is also an increased production of calcitonin which promotes the tubular reabsorption of phosphate and favours the tubular excretion of calcium which leads to hypocalcaemia and hyperphosphatemia. Thyroxin regulates blood calcium level by releasing calciumfrom cells, but in hypothyroidism, less thyroxin enters the cells and hence less calcium is released leading to hypocalciemia [12].

Roopa M et al [12] & Jaikiran K et al [13] studied the changes inelectrolyte profile in patients with hypothyroidism and reported that calcium level is significantly reduced andmagnesium and phosphorus level is increased in patients with hypothyroidism. It was also found that there was a significant negative correlation between serum calcium andTSH, positive correlation between serum TSH and magnesium and phosphorus.

Suneel B et al [14] studied mineral status in patients of thyroid disorders and found decreased calcium andincreased phosphorus in hypothyroidism mainly due to influence of parathyroid hormone (PTH) and calcitonin.Abbas MM et al [15] study also indicated elevated phosphate and decreasedcalcium levels in hypothyroid patients which are in accordance with our study.

Asamaik AS et al. have observed that phosphorus levelsare significantly increased in subclinical hypothyroid cases (SCH) and overt hypothyroid cases (OH) which is in accordance with our study finding of increased phosphate among hypothyroid cases [16]. In another study by AlTonsi, found altered phosphate concentrations in hypothyroid patients. The increased serum phosphate levels in hypothyroid cases is in accordance with our study [17]. SchwarsC et al. study of 9012 patients found a significant positive correlation between TSH and phosphate levels. Phosphate levels are higher in cases with elevated TSH than in controlswhich is also matching with our present study [18].

Thyroid hormones determine the mineral pool in the blood by influencing the mobilization of minerals like calciumand phosphorus, in the blood by influencing their clearancethrough urinary excretion by its effect on GFR or renal plasma flow. Low levels of calcium in hypothyroid cases reflect poor metabolism of calcium. The treatment modalities can also be framed while treating the hypothyroid patients keeping in view of altered mineral metabolism.

CONCLUSION

Our study demonstrated that hypothyroid patients show lowserum total calcium, and increased serum phosphorus levels compared to the healthy controls. Hence monitoring of mineral status of the hypothyroid patients onfollow-up will be of benefit to the patients. Supplements canbe initiated based on these values to avoid the effects resulting from changes in the mineral levels mainly related to bone metabolism. In addition, other markers related to mineral metabolism like vitaminD, PTH and calcitonin can also be studied for better understanding.

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