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Original Research Article

Evaluation of mineral status in hypothyroidism in a tertiary care centre

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ABSTRACT

Background: Hypothyroidism is known to be the commonest form of endocrine disorders and has been linked with disturbances in various minerals metabolism. Calcium, phosphorus and magnesium and trace element zinc are required for many enzymes in various metabolic pathways which are directly or indirectly regulated by thyroid hormones. Aim and objectives of the study was to estimate serum zinc, calcium, magnesium and phosphorus in hypothyroid patients, with the objectives to evaluate any relationship with TSH and to compare them with euthyroid controls.
Methods: The analytical cross-sectional study included 50 hypothyroid subjects with TSH levels >4.5 mcg IU/mL and 50 euthyroid subjects of 20-50 years in RMCH, Bareilly. TSH was estimated by ECLIA, serum calcium and phosphorus were estimated by autoanalyzer and serum zinc & magnesium by the kit method using semi autoanalyzer. All the biochemical parameters were expressed as median with Interquartile Range (IQR). Mann-Whitney test was applied to compare the parameters of cases and control. Spearman's rank correlation coefficient 2-tailed was used to correlate the parameters among the cases.
Results: A significantly decreased level of serum calcium and increased level of serum magnesium and phosphorus were observed in hypothyroid cases. A significant negative correlation between TSH and serum calcium while a significant positive correlation of serum magnesium and phosphorus with TSH was observed.
Conclusions: The indexed study indicates the significant effect of overt or subclinical hypothyroidism over the mineral status of the body which may have inconsistent effect over the various metabolism and enzymes and thereby clinical manifestations.

Keywords: Hypothyroidism, Magnesium, Serum calcium, Thyroid stimulating hormone, Zinc

INTRODUCTION

Optimal heath maintenance requires adequate and balanced amount of macronutrients, micronutrients and essential trace elements. Macro minerals and trace elements have definite roles in various biological processes by influencing enzymatic activity, protein function, and cell membrane permeability. Trace elements are also known to influence hormones at levels of their secretion, activity and binding to target tissue. Conversely, hormones influence mineral metabolism at several levels of action, including transport and excretion of trace metals.[1]

Thyroid gland produces triiodothyronine and tetraiodothyronine which are commonly known as T3 and T4 respectively. T3 is biochemically more active form of thyroid hormone and is produced by deiodination of T4

by the enzyme 1-5'deiodinase in the peripheral tissues. These hormones are in turn regulated by Thyroid Stimulating Hormone (TSH) and Thyrotropin Releasing Hormone (TRH) secreted by pituitary gland and hypothalamus respectively. Thyroid hormones play a major role in cell differentiation, in fetal development and also help to maintain thermogenic, metabolic, and mineral homeostasis in the adult. Hypothyroidism is the subnormal activity of thyroid gland that leads to many metabolic processes to slow down causing many clinical, psychological and biochemical alterations.

Thyroid disorders are the most common endocrine disorder worldwide including India and among them hypothyroidism is the commonest.[2] According to recent studies, the prevalence of hypothyroidism in India varies from 4-11%, more prevalent in women and in elderly age group.[3]

Calcium, phosphate and magnesium, the divalent ions and trace element zinc are required for many enzymes in various metabolic pathways which are directly or indirectly regulated by thyroid hormones. Hypothyroidism has been implicated in disturbances of mineral metabolism influencing bone turnover leading to osteoporosis and has also been related to metabolic syndrome and cardiovascular diseases.[4,5] Magnesium has a role in influencing membrane permeability thereby secretion of thyroid hormones. Zinc, an essential trace element, is known to have its effect on the synthesis, secretion, bioavailability and activity of thyroid hormones.[6] Thyroid hormones also in turn affect its metabolism and clearance. However, the changes in calcium, magnesium, phosphorus and zinc levels are minimal but the disturbances are vital in long run.

The effect of thyroid hormones over mineral status is observed to be quite complex in the various studies. No study has been conducted so far in Rohilkhand region of North India to establish correlation of the minerals with thyroid status. This study was undertaken to evaluate any alteration in mineral status in diagnosed cases of hypothyroidism. The aim of this study was to estimate serum zinc, calcium, magnesium and phosphorus in patients with hypothyroidism and to evaluate any relationship with thyroid status. The objectives were to estimate the serum levels of zinc, calcium, magnesium and phosphorus and TSH in patients with hypothyroidism and to compare it with euthyroid controls; and to evaluate any correlation of serum calcium, magnesium, phosphorus and zinc with TSH in hypothyroid patients.

METHODS

The indexed study was conducted in Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India, a tertiary care centre in Rohilkhand region over a period of one-year May 2018 to April 2019 after taking ethical approval from the Institutional Ethics Committee. The study design was an analytical cross-sectional study. The study included 50 cases with diagnosed hypothyroidism and 50 matched apparently healthy subjects with euthyroid status as control.

Inclusion criteria

- Clinically diagnosed patients of hypothyroidism with TSH levels >4.5 mcg IU/mL in age group of 20-50 years from OPD and IPD of Rohilkhand Medical College and Hospital, Bareilly were selected as cases. Clinically healthy subjects were selected from the same community with normal thyroid profile.

Exclusion criteria

- Patients suffering from renal diseases, hepatic diseases, pituitary adenomas, bone diseases, diabetes mellitus, alcoholism, and other serious medical conditions.
- Patients on antithyroid drugs, mineral supplementation or any drugs that would affect mineral metabolism.
- Antenatal mothers and psychiatry patients.
- Smokers and tobacco chewers.

After taking valid informed consent from all the subjects, 5 ml of blood was withdrawn under aseptic conditions and collected in plain red capped vacutainers. Blood was allowed to clot for 30 minutes, then centrifuged at 3000 rpm for 10 minutes and serum was immediately separated for biochemical analysis.

TSH was estimated by Electrochemiluminescence Immunoassay (ECLIA) using Vitros ECI immunodiagnostic system by 'gohnson n gohnson'. Serum calcium and phosphorus was estimated by Arsenazo and Molybdate method respectively using EM360 Autoanalyzer by Vitros Transasia. Serum magnesium level was estimated by Calmagite method and serum zinc by Nitro-PAPS method (Phospho adenosyl phospho sulphate method) using ERBA CHEM5 semi autoanalyzer.

Statistical analysis

Data was entered in Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) Version 22 statistical software. The data was not normally distributed which was confirmed by applying Shapiro Wilk test. All the biochemical parameters were expressed as median with Interquartile Range (IQR). Mann-Whitney test was applied to compare the parameters of cases and control, $p<0.05$ being considered as statistically significant. Spearman's rank correlation coefficient 2-tailed was used to correlate the parameters among the cases.

RESULTS

The age of cases and controls was recorded as 35 years with IQR (26.75-40.5) and 26.5 years with IQR (21-40)

respectively. TSH was significantly increased in hypothyroid cases as compared to controls. The significant lower level of serum calcium (p-value <0.01) was observed but serum magnesium and phosphorus were found to be significantly high (p-value <0.05) in hypothyroid cases. Although serum zinc level was found to be low in cases but the difference in its level between cases and control was not statistically significant (Table 1).

Table 1: Distribution of serum TSH, calcium, zinc, magnesium, and phosphorus among case and control subjects.

Variables	Case (n=50) [median (IQR)]	Control (n=50) [median(IQR)]	p-value
Serum TSH (µ IU/ml)	18.5(7.3-44.3)	2.2(1.6-2.9)	0.00*
Serum calcium (mg/dl)	8.2(8.0-8.4)	9.1(8.6-9.6)	0.00*
Serum zinc (mg/dl)	67.0(57.0-78.0)	94.0(90.0-101.0)	0.112
Serum magnesium (mg/dl)	2.0(1.8-2.1)	1.8(1.7-1.9)	0.01*
Serum phosphorus (mg/dl)	4.3(1.7-6.2)	3.8(3.5-4.1)	0.00*

* p-value<0.05 was considered to be significant.

Table 2: Correlation of serum calcium, phosphorus, magnesium, and zinc with serum TSH in cases.

	Serum calcium	Serum phosphorus	Serum magnesium	Serum zinc
Serum TSH	-0.48*	0.32*	0.61*	0.03*
p- value	0.00**	0.02**	0.00**	0.82

*Correlation Coefficient**
p-value<0.05 was considered to be significant.

A statistically significant negative correlation was found between serum TSH and serum calcium (p-value <0.05) in hypothyroid cases. Serum magnesium and serum phosphorus were also having significant positive correlation with serum TSH. On the contrary, no correlation between serum zinc and TSH was observed (Table 2).

DISCUSSION

Thyroid hormones regulate body hemodynamics, thermoregulation and various metabolisms. They have an influence on renal hemodynamics, glomerular filtration, electrolyte regulation and the mineral homeostasis.[7]

Studies have shown that thyroid hormones are vital for skeletal growth and maturation and TSH also acts as a direct regulator of bone remodelling.8 Hypothyroidism can lead to a various clinical manifestation including electrolyte and mineral disturbances, osteoporosis and congestive heart failure.[9] In the present study, authors found significant decreased level of serum calcium in cases of hypothyroidism and a significant negative correlation with TSH among the cases which was in accordance with other studies conducted on human subjects and animals.[10-16] Serum phosphorus was found to be increased with a significant positive correlation with serum TSH in hypothyroid cases which was statistically significant. These findings were similar to those by other researchers who also observed a significant increase in serum phosphorus in cases of hypothyroidism though there was insignificant correlation with TSH.[12,17,18]

Thyroid hormones determine mineral pool in the blood by influencing their mobilization into the blood, and also their clearance through effect on Glomerular Filtration Rate (GFR). There is increased renal blood flow leading to increased clearance of calcium as well as decreased extracellular release of calcium in hypothyroidism.[19] According to Buollin and Moore the sensitivity of bone and kidney to Parathormone (PTH) decreases in hypothyroidism which further leads to hypocalcaemia.[20] On the other hand, increased production of calcitonin favours the tubular excretion of calcium and promotes the tubular reabsorption of phosphate leading to hypocalcaemia and hyperphosphatemia in hypothyroidism.[11]

A statistically significant increase in serum magnesium was observed in hypothyroid cases in this study and a significant strong positive correlation with TSH was also observed in the cases. Similar findings were also reported by Mamatha et al, and Bharti et al.[15,21] According to a study conducted by McCaffrey and Quamme, magnesium retention increased by 15-30% from kidneys due to increased reabsorption in renal tubules as the thyroid hormones have direct effect on renal tubules as well.[9] However, Suneel et al, and Sussanna et al, showed decrease in serum magnesium in hypothyroid patients with negative correlation with TSH which was in contrast to these findings.[19,22]

As far as the serum zinc level in hypothyroid cases of this study was concerned, it was found to be decreased but the difference was not statistically significant as well as no correlation was established with serum TSH in the cases. Similar results were also observed in various other studies.[19,23-25] The possible explanations for low zinc level are impaired gastrointestinal absorption of zinc, sequestration of zinc by liver and other tissues leading to change in its distribution.[26] On the other hand, zinc also influence the thyroid hormone synthesis by modulating thyroid transcription factors which contain zinc at its cysteine residues as well as its metabolism by increasing thyroxine binding proteins.[23,27,28] Therefore, relationship

between zinc and thyroid function is complex and needs more specific studies.

Limitation of the study: All the parameters of thyroid function test were not included in the study which would have given better correlation between mineral status and thyroid hormones. In addition to this, vitamin D3 could also be included in the study to avoid some confounding factor.

CONCLUSION

The indexed study can be concluded with serum calcium being decreased in hypothyroid cases while serum magnesium and phosphorus to be at higher level. However, the variations in mineral status among overt hypothyroid cases were inconsistent in other studies due to variations in dietary intake, renal and intestinal absorption status, some underlying subclinical pathologies, and complex metabolism of these minerals affected by various other hormones and cellular mechanisms. Nevertheless, the present study demonstrated and emphasized on the importance of evaluation of mineral status in all hypothyroid cases so as to prevent alteration of various metabolism, bone complications and other clinical manifestations in these patients.

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