

A CORRELATIVE STUDY OF THYROID PROFILE AND MINERAL STATUS IN PATIENTS WITH HYPOTHYROIDISM - A HOSPITAL BASED CASE CONTROL STUDY

SUSANNA TY¹, SAGAYARAJ A², SHASHIDHAR KN¹, GOMATHI M³, MAHESH V⁴

¹Department of Biochemistry, Sri Devaraj Urs Medical College and Research Centre, Kolar - 563 101, Karnataka, India. ²Department of Otorhinolaryngology, Sri Devaraj Urs Medical College and Research Centre, Tamaka, Kolar - 563 101, Karnataka, India.

³Sri Devaraj Urs Medical College and Research Centre, Tamaka, Kolar - 563 101, Karnataka, India. ⁴Department of Community Medicine, Sri Devaraj Urs Medical College and Research Centre Tamaka, Kolar, Karnataka, India. Email: drsusannaty@gmail.com

Received: 19 February 2016, Revised and Accepted: 27 February 2016

ABSTRACT

Objective: To evaluate the alteration in mineral status by estimating serum calcium, phosphorus, and magnesium in hypothyroid patients compared to healthy volunteers and its correlation with thyroid profile (triiodothyronine [T3], thyroxine [T4], and thyroid stimulating hormone [TSH]).

Methods: Blood samples were collected from 30 hypothyroid patients and 30 healthy volunteers and analyzed for serum levels of calcium, magnesium, and phosphorus and for thyroid profile.

Results: There were 22 females and 8 males in the hypothyroid patients group and 24 females and 6 males in the control group. The mean age in the two groups was 39±13. The study observed a significantly decreased levels of serum magnesium, significantly increased serum phosphorus and serum creatinine levels among hypothyroid patients as compared to the control group ($p < 0.001$), respectively, serum calcium levels did not show a significant change in hypothyroid patients compared to the control group. Among hypothyroid subjects, there was a significant positive correlation of T3 and T4 with serum magnesium and a negative correlation of T4 with serum phosphorus and serum creatinine. TSH showed a positive correlation with serum phosphorus and serum creatinine and a negative correlation with serum magnesium. However, T3, T4, and TSH did not show any correlation with serum calcium levels.

Conclusion: The direction of effect of overt hypothyroidism on the blood levels of calcium, magnesium, and phosphorus is inconsistent affecting the various metabolisms and clinical manifestations; in these patients, hence all patients with overt hypothyroidism need to be evaluated for mineral status to provide individualized holistic disease management strategies to these patients.

Keywords: Hypothyroidism, Calcium, Magnesium, Phosphorus.

INTRODUCTION

The thyroid gland secretes two important hormones thyroxine and triiodothyronine, which are commonly known as T4 and T3, respectively. T3 is biologically more active form of thyroid hormone and is produced by local deiodination of T4 by the enzyme T4-5' deiodinase in the peripheral tissues including kidneys and uremia significantly reduces the synthesis of an active form of thyroid hormone [1]. These thyroid hormones have important biological effects such as regulation of body hemodynamic, thermoregulation, and various metabolisms. It influences almost all metabolisms in the body including carbohydrate, proteins, lipids, and maintenance of water and electrolyte homeostasis, which are well-established [2,3]. Recently, the disorders of thyroid function particularly hypothyroidism is receiving greater attention as an important cause of disturbance in mineral metabolism by their direct action on bone turnover [4], and also as one of the causes for secondary osteoporosis. Calcium (Ca^{2+}), phosphorus (PO_4^{2-}), and magnesium (Mg^{2+}) are all divalent metal ions, which are necessary for metalloenzymes and various crucial metabolic pathways directly or indirectly regulated by thyroid hormones. Few animal studies have proposed that thyroid hormones act as long-term regulators for phosphate metabolism, and the free T3 elevates renal phosphate reabsorption and elevates serum phosphate levels in rats [5]. Studies on hypothyroid subjects have shown contradictory findings where the levels of serum calcium and phosphorus were low in patients with overt hypothyroidism [4] and magnesium levels were reduced, some studies show a normal serum calcium and phosphorus levels [6] while others have observed a low serum calcium and magnesium levels and an increase in serum phosphorus levels in patients with hypothyroidism [4,7].

Hence, this study was undertaken to evaluate alteration in mineral status by estimating serum calcium, phosphorus, and magnesium in patients diagnosed of hypothyroidism and its correlation with thyroid profile T3, T4, and thyroid-stimulating hormone (TSH) levels in these patients and to observe the importance to check the levels of these minerals in overt hypothyroid disorders.

METHODS

This study was conducted at Sri RL Jalapa Hospital and Research Centre following approval by the Institutional Ethics Committee from July 2014 to June 2015. The study includes patients aged between 30 and 60 years. 30 patients diagnosed with hypothyroidism were included in the study group, and 30 clinically healthy volunteers with normal T3(ng/mL), T4(mcg/mL), and TSH(mIU/mL) levels will be included in the control group.

Inclusion criteria

Patients clinically diagnosed of hypothyroidism with TSH levels $>4.2 \text{ mc IU/mL}$.

Exclusion criteria

Patients with history of hepatic disease, renal disease, alcoholism or critically ill patients or those on mineral supplementation, antithyroid drugs or any other medications known to affect the calcium, phosphorus, and magnesium metabolism will be excluded from the study.

After taking an informed consent, under complete aseptic precautions, 5 ml of fasting venous blood was drawn in red capped plain vacutainer tubes. Serum separated by centrifugation was analyzed for serum

T3, T4, and TSH were estimated using Vitros ECI Immunodiagnosics autoanalyzer; serum calcium (mg/dL), phosphorus (mg/dL), and magnesium (mg/dL) were estimated using Ortho Vitros 250 dry chemistry autoanalyzer working under the principle of reflectance photometry.

Routine IQAS was run and after confirmation the samples were analyzed for the biochemical parameters, care was taken to avoid hemolysis, pre-analytical, analytical, and post-analytical errors throughout the procedure.

Statistical methods

Data were entered into Microsoft Excel and analyzed using SPSS version 20.

Descriptive statistics such as mean and standard deviation (SD) were computed for quantitative and qualitative data, respectively. Pearson's correlation was done to correlate the relationship between thyroid profile and minerals. Independent t-test was used as test of significance between cases and controls for quantitative data.

RESULTS

The results of this study are presented in Tables 1 and 2. There were a total number of 22 females and 8 males in the hypothyroid patients group and 24 females and 6 males in the control group. The mean age of the hypothyroid patients and controls was between 39±13.

This study observed a significantly decreased levels of serum magnesium (1.88±0.15) among hypothyroid patients as compared to control group (2.25±0.23) ($p<0.001$) and a significantly increased levels of serum phosphorus (5.56±2.03) and serum creatinine (0.95±0.31) among hypothyroid patients as compared to the control group (3.1±0.5) (0.71±0.1) ($p<0.001$), respectively.

However, the serum calcium levels (8.98±0.61) did not show a statistically significant change in hypothyroid patients as compared to the control group (8.98±0.49) (Table 1).

We found a significant positive correlation of T3 and T4 with serum magnesium and a significant negative correlation of T4 with serum phosphorus and significant negative correlation of T3 and T4 serum creatinine. TSH showed significant positive correlation with serum phosphorus and serum creatinine and a significant negative correlation with serum magnesium (Table 2).

However, T3, T4, and TSH did not show any statistically significant correlation with respect to serum calcium levels among hypothyroid subjects (Table 2).

DISCUSSION

Hypothyroidism is one of the most common endocrine diseases resulting from deficiency of thyroid hormones, with a wide clinical manifestations ranging from metabolic disorders to cardiovascular disease, electrolyte, and mineral disturbances.

In our study, the magnesium levels in hypothyroid patients were significantly decreased with positive correlation with T3 and T4 and negatively correlated with TSH which are in accordance with the study conducted by Gohel *et al.*, and Nisa *et al.* The decreased magnesium levels in these hypothyroid patients may be due to increase urinary output and fractional excretion of magnesium through the urine [8,9]. As a result of thyroid hormones affecting the glomerular filtration rate, renal blood flow, tubular sodium transport, and reduced tubular reabsorption of magnesium [6], the increased levels of serum creatinine in these patients observed in our study strongly suggest a defect at the level of renal glomerulus. These findings are in contrast to the observations made by Frizel *et al.*, and were both the plasma

Table 1: Comparison of serum levels of T3, T4, TSH, calcium, phosphorus, magnesium, and creatinine in hypothyroid cases with normal controls

Serum levels	Mean±SD		p value
	Group		
	Cases	Controls	
T3	0.80±0.37	1.15±0.17	<0.001*
T4	2.97±1.76	8.03±1.24	<0.001*
TSH	79.79±21.69	1.90±0.70	<0.001*
Calcium	8.98±0.61	8.98±0.49	0.993
Magnesium	1.88±0.15	2.25±0.23	<0.001*
Phosphorus	5.56±2.03	3.10±0.50	<0.001*
Creatinine	0.95±0.31	0.71±0.10	<0.001*

* $p<0.001$; highly significant (significance of difference between hypothyroid cases and normal controls). SD: Standard deviation, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone

Table 2: Correlation of thyroid profile (T3, T4, and TSH) with serum calcium, phosphorus, magnesium, and serum creatinine in patients with hypothyroidism

Serum levels	Calcium	Magnesium	Phosphorus	Creatinine
T3				
Pearson correlation	-0.246	0.355**	-0.245	-0.494**
r value				
Sig. (two-tailed)	0.058	0.005	0.059	0.000
N	30	30	30	30
T4				
Pearson correlation	-0.100	0.552**	-0.474**	-0.475**
r value				
Sig. (two-tailed)	0.446	0.000	0.000	0.000
N	30	30	30	30
TSH				
Pearson correlation	0.102	-0.657**	0.479**	0.457**
r value				
Sig. (two-tailed)	0.438	0.000	0.000	0.000
N	30	30	30	30

**Correlation is significant at the 0.01 level (two-tailed), T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone

ionized magnesium and total magnesium levels were increased in hypothyroidism [10].

In vitro studies have shown that the decreased magnesium levels will influence the action of the thyrotrophic hormone on the thyroid gland through the formation of cyclic amp involved in the activation of adenylyl cyclases and stimulates cyclic 3, 5 nucleotide phosphodiesterase [9] disrupting the various metabolisms in the body. However, a few studies conducted in patients with subclinical and overt hypothyroidism, and hyperthyroidism shows decreased serum calcium and increased phosphorus and magnesium levels in patients with Hypothyroidism [11].

Our study also observed a significant increase in the serum phosphorus levels that may be due to increased production of thyroid calcitonin which promotes the tubular reabsorption of phosphate and tubular excretion of calcium, resulting in hyperphosphatemia and hypocalcemia, respectively [12]. T4 showed negative correlation; TSH showed significant positive correlation with serum phosphorus levels; T3, which is the active form of the thyroid hormone required for the stimulation of phosphorus reabsorption from renal tubules mediated through Na/iP cotransporter, did not show a significant correlation with serum phosphorus indicating that the renal mechanism mediated through T3 was not the only processes by which serum phosphorus levels were elevated but which can be as a result of bone demineralization. Schwarz

et al., in their study on 9012 patients showed a positive correlation between serum TSH and phosphate levels (1). However, there was no significant alteration in the serum levels of calcium in hypothyroid patients when compared with healthy controls in our study; however, studies have reported conflicting results with reduced serum calcium and phosphate levels among patients with overt hypothyroidism [13].

CONCLUSION

Metal ions and hormones are necessary for the intricate regulation of metabolic pathways. It is clear that the reduction in the blood levels of T3 and T4 and an increase in TSH in overt hypothyroidism is a consistent finding, yet their direction of effect on the blood levels of calcium, magnesium, and phosphorus is inconsistent which can be due to the variations in the dietary intake and absorption of these minerals in these patients, presence of subclinical glomerular or tubular defects, and due to the complex hormonal and cellular mechanisms involved in the regulation of calcium phosphorus metabolism at the bone, renal, and intestinal level. It is, therefore, necessary that all patients with overt hypothyroidism be evaluated for the blood levels of calcium, magnesium, and phosphorus, which will affect the various metabolisms and clinical manifestations in these patients, in view of providing individualized holistic disease management strategies to these patients.

REFERENCES

- Mariani LH, Berns JS. The renal manifestations of thyroid disease. *J Am Soc Nephrol* 2012;23(1):22-6.
- Schwarz C, Alexander BL, Spiros A, Georg MF, Heinz Z, Aristomenis KE, *et al.* Thyroid function and serum electrolytes: Does an association really exist? *Eur J Med Sci* 2012;142:w13669.
- Farnsworth AE, Dobyns BM. Hypercalcaemia and thyrotoxicosis. *Med J Aust* 1974;2(21):782-4.
- Shivaleela MB, Poornima RT, Murthy DS. Serum calcium and phosphorus levels in thyroid dysfunction. *Indian J Fundam Appl Life Sci* 2012;2(2):179-83.
- Alcalde AI, Sarasa M, Raldúa D, Aramayona J, Morales R, Biber J, *et al.* Role of thyroid hormone in regulation of renal phosphate transport in young and aged rats. *Endocrinology* 1999;140(4):1544-51.
- Sabuncu T, Aksoy N, Arıkan E, Ugur B, Tasan E, Hatemi H. Early changes in parameters of bone and mineral metabolism during therapy for hyper - and hypothyroidism. *Endocr Res* 2001;27(1-2):203-13.
- Kavitha MM, Chandrashekharyya SH, Kashinakunti SV, Sunitha H, Neela BM, Ratna S. Alteration in levels of serum calcium, phosphorus and magnesium in patients of hypothyroidism. *Int J Biol Med Res* 2014;5(4):4594-6.
- Gohel MG, Shah AM, Shah AM, Makadia JS. A study of serum calcium, magnesium and phosphorus level in hypothyroidism patients. *Int J Med Health Sci* 2014;3(4):308-12.
- Nisa F, Mumtaz A, Ullah MI, Atif M, Sami W. Determination of serum zinc and magnesium levels in patients with hypothyroidism. *Trace Elem Electrolytes* 2013;15:1-5.
- Frizel D, Malleson A, Marks V. Plasma levels of ionised calcium and magnesium in thyroid disease. *Lancet* 1967;1(7524):1360-1.
- Bharti A, Shrestha S, Rai A, Singh MK. Assessment of serum minerals and electrolytes in thyroid patients. *Int J Adv Sci Res* 2015;1(6):259-63.
- Suneel B, Nagendra DR, Aparna RR, Balakrishna D, Naidu JN. Mineral status in thyroid disorders (hypo and hyper). *Int J Appl Biol Pharm Technol* 2011;2(4):423-9.
- Abdel-Gayoum AA. Dyslipidemia and serum mineral profiles in patients with thyroid disorders. *Saudi Med J* 2014;35(12):1469-76.