ORIGINAL RESEARCH PAPER
Volume-9 | Issue-1 | January-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION OF VITAMIN-D LEVEL IN RELATION TO CALCIUM AND PHOSPHOROUS IN HYPOTHYROID PATIENTS

Biochemistry

Ravikant Soni Assistant Professor, Biochemistry, Mahatma Gandhi Medical College & Hospital, Jaipur

Bushra Fiza* Professor, Biochemistry, Mahatma Gandhi Medical College & Hospital, Jaipur *Corresponding Author

Maheep Sinha Professor & Head, Biochemistry, Mahatma Gandhi Medical College & Hospital, Jaipur

Jai Prakash Yogi Demonstrator, Biochemistry, Mahatma Gandhi Medical College & Hospital, Jaipur

ABSTRACT

Thyroid hormones and vitamin D both act through steroid receptors and are expected to affect each other's action. The study was planned to evaluate the association of Vitamin D with thyroid hormones as well as thyroid stimulating hormone. Vitamin D directly influences metabolism of calcium and phosphorus. The study therefore, further studied serum calcium and phosphorus levels in hypothyroid patients. Fifty patients diagnosed for hypothyroidism and fifty age and sex matched subjects were enrolled for the study. Blood samples were collected and analyzed for serum T3, T4, TSH, Vitamin D, Calcium and Phosphorus. On statistical evaluation, serum Vitamin D and calcium were observed to be significantly lower in hypothyroid group and exhibited a negative correlation with respect to TSH levels. The study infers that regular screening of above parameters in hypothyroid subjects can be helpful in managing and averting the associated complications of Vitamin D and calcium deficiency.

KEYWORDS

Hypothyroidism, Vitamin D deficiency, autoimmune thyroiditis, immune modulator, calcium homeostasis

INTRODUCTION

Thyroid gland produces two important hormones triiodothyronine (T3) & thyroxine (T4) which are central regulator of body hemodynamics and thermoregulation. They perform a wide array of metabolic functions including regulation of carbohydrate, lipid, protein, electrolyte and mineral metabolism [1].

Vitamin D and its metabolites play a major role in calcium homeostasis, it also regulate the bone metabolism [2]. Vitamin D deficiency is a worldwide problem. Globally over billions of people are vitamin D insufficient [serum 25(OH) D3 of 10-24ng/ml] or deficient [serum 25(OH)D3 less than 10ng/ml] [3],[4],which associates with risk of chronic illnesses including autoimmune, cardiovascular and infectious diseases [5].

Both vitamin D and thyroid hormones act through steroid receptors. They may affect each other's action as they have similar response elements ongene. A lower level of vitamin D is likely to aggravate the systemic abnormalities associated with hypothyroidism [5,6]. Studies assessing the association between the hypothyroidism & vitamin D levels have produced conflicting results. High prevalence of thyroid autoimmunity and vitamin D deficiency in the Indian population provides us a unique opportunity to assess the association between these two variables. Some of the symptoms of vitamin D deficiency overlap with that of the hypothyroidism [7].

The present study was planned to assess the status of Vitamin D and its association with calcium and phosphorus in hypothyroid patients.

MATERIAL & METHOD

This case control study was conducted on fifty newly diagnosed patients of hypothyroidism. Fifty age and sex matched healthy individuals constituted the control group. All participants were between the ages of 19 to 60 years. Pediatric patients and patients with renal, hepatic or bone disorders were excluded. The study was conducted after seeking approval from the institutional ethics committee and informed consent was obtained from all participants Fasting blood samples were collected from all subjects enrolled in the study by standard aseptic technique and evaluated for thyroid hormones (T3, T4 and TSH) and Vitamin D by Chemiluminescence. S calcium and phosphorus were estimated by dry chemistry. All biochemical investigations were performed on VITROS 5600. Results obtained were presented as mean ± SD and subjected to statistical evaluation. P value ≤ 0.05 was considered as statistically significant.

RESULTS

All analytes were compared between the Hypothyroid and control group by applying student's t-test. Concentration of serum Vitamin D and calcium were significantly low in the hypothyroid group whereas serum phosphorus levels were significantly higher. (Table 1). Pearson's correlation was further applied between thyroid hormones and serum level of vitamin D, calcium and phosphorus in hypothyroid subjects. Vitamin D was observed to have a strong negative association with S TSH levels (r= -0.378) (Fig.1). Similarly a negative association was also observed between TSH and S calcium levels (r = -0.282) (Fig.2). However, no significant association was observed between Vitamin D and T3 and T4 hormones or between serum phosphorus and TSH levels (Table 2).

Table 1: Comparison of analytes between Hypothyroid patients and control group

Analytes	Control group (n=50)	Hypothyroid group (n=50)	t-value	P-value
Age	38.88 + 12.36	43.44 + 10.98	-1.950	NS
Total T3	1.36 + 0.24	0.97 + 0.43	-5.600	<0.0001
Total T4	8.08 + 1.56	5.32 + 1.83	-8.244	<0.0001
TSH	2.30 + 1.13	12.16 + 10.09	6.867	<0.0001
Vitamin D	32.38 + 12.36	17.81 + 7.13	-17.971	<0.0001
S. Calcium	9.64 + 0.95	8.82 + 0.60	-5.160	<0.0001
S. phosphorus	3.61 + 0.76	4.25 + 0.70	4.380	<0.0001

Table 2: Correlation coefficient between various analytes

Test name	Correlation coefficient(r)	P value
TSH v/s vitamin D	-0.378	0.006
T3 v/s vitamin D	-0.176	NS
T4 v/s vitamin D	-0.214	NS
TSH v/s Calcium	-0.282	0.04
TSH v/s Phosphorus	0.150	NS

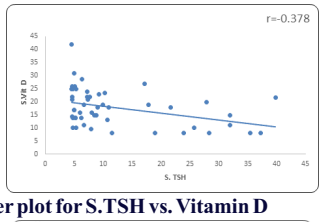

Figure1: Scatter plot for S.TSH vs. Vitamin D

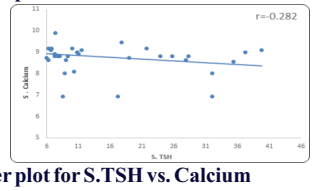

Figure2: Scatter plot for S.TSH vs. Calcium

DISCUSSION

Thyroid hormones are essential for normal growth and maturation of skeletal system. They also affect the metabolism of various minerals. Thyroid dysfunction is frequently associated with disturbances of calcium and phosphorous homeostasis. Thyroid disorders are important cause of secondary osteoporosis. Serum calcium and phosphorous levels can be fairly used as index of bone resorption. Thyroid hormones exert its effects on osteoblasts via nuclear receptors to stimulate osteoclastic bone resorption [8].

Vitamin D initiates its action through binding to vitamin D receptor (VDR) which in turn activates the VDR-Responsive gene [9]. Major function of Vitamin D is said to be regulation of bone metabolism specially calcium homeostasis. Beside this, Vitamin D affects the functioning of several body cells which possess VDRs. Vitamin D binds with its receptor located in thyroid tissue and may play a role in maintaining a normal thyroid function.

Vitamin D has major effects on nearly all cells of the immune system including antigen presenting cells, such as dendritic cells, macrophages, and T and B cells which express vitamin D receptors. As an immune modulator, vitamin D reduces activation of the acquired immune system. Hence, vitamin D deficiency is suggested to increase the risk of autoimmune diseases such as type 1 diabetes, rheumatoid arthritis, multiple sclerosis, Crohn's disease and autoimmune thyroid disease [10-12].

In the present study, mean serum vitamin D and calcium level was significantly lower in the hypothyroid subjects as compared to control group. On the other hand, serum phosphorus levels were significantly higher.

Similar findings have been reported in previous studies also. In a pilot study by Bhardwaj SA et al., 2014 [13] serum 25(OH)vitamin D levels were reported to be significantly lower in the hypothyroid patients as compared to healthy controls.Study by Tahir et al., 2016 [14] reported that deficiency of serum vitamin D is significantly associated with degree and severity of hypothyroidism. Byron Richards et al., 2008 [15] have suggested that low thyroid activity lead to lack of vitamin D.

Recent studies have highlighted the role of Vitamin D as a potential immune modulator which explains its influence on pathogenesis of autoimmune disease [16]. Another study by Esmat F et al., 2013 [17] demonstrated a significant association of vitamin D deficiency with autoimmune disorder. On the contrary, Effraimidis et al., 2012 [18] concluded that vitamin D is not associated with early stage of autoimmune hypothyroidism. In a similar study by Gohel et al., 2014 [19], mineral levels were studied in hypothyroid patients. This study reported results similar to those of present study.

In hypothyroidism increased production of thyroid calcitonin can promote the tubular re-absorption of phosphate and simultaneously favors the tubular excretion of calcium. Further thyroid hormones regulate the activity of sodium potassium pump in most of the tissues [20]. Deficiency of thyroid hormone in early life leads to both delay in the development of bone and stippled appearance of epiphyseal centers of ossification result in dwarfism. In hypothyroidism, there is a depressed turnover due to impaired mobilization of calcium into the bone than leads to decrease the blood calcium level [21]. According to Sunnel B et al., 2014 [22] the derangement of serum calcium and phosphorus level during thyroid disorder is primarily due to the disturbed activity of parathyroid hormone and calcitonin. Jaskiran et al., 2014 [23] and previous study by Roopa et al., 2012 [24] have also reported similar findings.

Calcium homeostasis is a complicated process which is influenced by several factors.These include PTH and Vitamin D besides thyroid hormone. Calcium levels are therefore affected by these factor and further phosphorus metabolism is accordingly affected. Earlier researches have demonstrated contradictory results in context of serum calcium and phosphorus levels in relation to thyroid dysfunction. Impaired thyroid function has been found to cause elevation of serum phosphorus level [25] and also influence calcium metabolism [26].

The correlation of serum TSH level with serum vitamin D, calcium and phosphorus levels of hypothyroid patients was also evaluated by applying Pearson`s correlation. (Table 2). A significant negative correlation was observed between serum TSH and serum vitamin D levels. Similar finding have been reported by Esmat et al., 2013 [17]. Bizzaro and Shoenfeld, 2015 [27] confirmed association of vitamin D status with thyroid diseases. They reported a strong correlation of vitamin D deficiency with higher incidence of autoimmunethyroiditis. Further, Shin et al., 2014 [28] suggested that vitamin D3 levels are an independent factor that affects the positivity of TPO antibody.

Serum calcium was also reported to have an significant correlation with serum TSH levels. Ashmaik et al., 2013 [29] reported a negative correlation between serum calcium and TSH (r = 0.282).Gohel et al., 2014 [19] have reported a very strong correlation (r = -0.8368) between serum calcium and TSH levels in hypothyroid subjects.Serum Phosphorus, however, did not exhibit any significant correlation with serum TSH.

CONCLUSION

The study concludes that there is a strong association between hypothyroidism and vitamin D deficiency as well as hypocalcaemia. It is therefore suggested that there should be regular screening for Vitamin D, calcium & phosphorus in patients of thyroid dysfunction. Maintaining proper Vitamin D and mineral levels in hypothyroid patients will be helpful Iin diminishing the risk of developing various structural & physiological complications

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