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VITAMIN-D STATUS IN RELATION TO CALCIUM AND PHOSPHOROUS IN HYPOTHYRODISM.

Biochemistry

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ABSTRACT

Objective: The present study was planned to assess the association of thyroid function with serum level of Vitamin D, Calcium and phosphorus.
Methods: 100 hypothyroid patients visiting the outpatient Department were enrolled for the study based on predefined inclusion and exclusion criteria. 50 age-matched healthy individuals constituted the control group. The data obtained was subjected to statistical analysis using SPSS 20.0 Version.
Results: The results of the study suggested that hypothyroidism favors hypovitaminosis D. Hypoactivity of thyroid gland also reduces the calcium level and increases phosphorus level due to decreased metabolism. A significant correlation was observed for TSH and T_4 with vitamin D and Calcium; whereas Serum T_3 did not show a significant correlation with Vitamin D, Calcium or phosphorus.
Conclusion: The study emphasizes that regular screening for Vitamin D, calcium & phosphorus should be done in patients of thyroid dysfunction. Maintaining proper Vitamin D and mineral levels in hypothyroid patients will be helpful in diminishing the risk of developing various structural & physiological complications.

KEYWORDS

Vitamin D; Serum calcium; Serum phosphorus; Hypothyroidism; Thyroid stimulating hormone.

INTRODUCTION:

Thyroid hormones perform a wide array of metabolic functions including regulation of carbohydrate, lipid, protein, electrolyte and mineral metabolism [1]. Plasma levels of thyroid hormones i.e. triiodothyronine (T_3) & thyroxine (T_4) are regulated by a feedback mechanism, in which hypothalamic thyrotropin-releasing hormone (TRH) stimulates the synthesis and release of thyrotropin (TSH) by the anterior pituitary, thus stimulating the secretion of T_4 and T_3 by the thyroid gland [2].

Thyroid dysfunction constitutes the most common endocrine abnormality in the world second only to diabetes mellitus [3]. Females are eight times more affected than males. It has been estimated that there are about 42 million people in India suffering from thyroid diseases [4]. Hypothyroidism is one of the most common forms of thyroid dysfunction resulting from the deficiency of thyroid hormones or from their impaired activity due to biochemically decrease in T_3 and T_4 concentration leading to hyper secretion of pituitary TSH [5].

Various studies have been done to assess the association between the hypothyroidism & vitamin D levels. It has been observed that there is an association between high prevalence of thyroid autoimmunity and vitamin D deficiency in the Indian population. There are few symptoms of vitamin D deficiency that overlap with that of the hypothyroidism [6]. Globally over billions of people are vitamin D insufficient [serum 25(OH)D_3 of 10-24ng/ml] or deficient [serum 25(OH)D_3 less than 10ng/ml], which associates with risk of chronic illnesses including autoimmune, cardiovascular and infectious diseases [7,8]. Vitamin D is not just a vitamin, but also a hormone which effects the optimal functions of the cardiac, skeletal, reproductive and endocrine system. It is also an important immune-modulator. Both vitamin D and thyroid hormones also act through steroid receptors and may affect each other's action as they have similar response elements on gene [9]. The inter relationship between vitamin D deficiency and hypothyroidism exists, thus stating a putative role of vitamin D as a potential modifiable risk factor for hypothyroidism [10-12].

The present study was conducted to assess the level of serum vitamin D, calcium and phosphorus level in patient suffering from hypothyroidism; and to investigate the correlation between Vitamin D, calcium & phosphorous with serum T_3, T_4 and TSH levels.

MATERIALS AND METHOD:

The study was conducted in the Department of Biochemistry in association with Department of General Medicine and Endocrinology after taking approval from **Institutional Ethics Committee** MGMCH/IEC/JPR/2016/309 dated 06/04/2017. A total of 100 hypothyroid patients were taken with 50 controls. They were recommended not to have heavy exercise at least 24hours before examination.

The study subjects included for the study should be clinically diagnosed and biochemically confirmed cases of hypothyroid disorder, with age up to 60 years, of either gender. Patients who were willing to give consent for participation and comply with the protocol requirements were included in study.

Pediatric age group, patients with renal and hepatic disorders, patients with bone disease, pregnant females, patients suffering from diabetes, hypertension, cerebrovascular disease, alcoholism or any other systemic illness that may affect the Vitamin D status, calcium & phosphorus status were excluded from study. Patients on Vitamin D or calcium supplementation or any other medications which can affect thyroid function such as Diuretics, Calcium, Oral contraceptives, Oestrogen, Glucocorticoids, Iron tablets were also excluded from study.

Informed consent was taken from patients before enrolling them for the study. Blood samples after overnight fasting were collected by standard aseptic techniques and subjected to investigations like Serum T_3, T_4, TSH by CLIA using Vitros ECI, Serum vitamin D, Serum Calcium, Serum Phosphorous, Free T_3 and Free T_4. The results obtained were subjected to statistical analysis using SPSS 20.0 Version at level of significance p-value<0.05.

RESULTS:

Blood samples of patients were collected by standard aseptic technique and analyzed for thyroid profile including T_3, T_4, Thyroid stimulating hormone (TSH), free T_3, free T_4, 25(OH) Vitamin D, calcium and phosphorus. The results obtained were presented as mean±SD and compared among the hypothyroid patients and healthy control group. The mean age of control group and study subjects was 40.08±15.17yrs and 43.81±11.00yrs respectively. The study comprised of more females (82%) as compared to males (18%) suffering from hypothyroid. The mean vitamin D level of control

group was significantly higher than hypothyroid group. The serum T_3, T_4 and TSH levels were recorded. The mean serum TSH level was significantly higher; whereas serum T_3 and T_4 levels were significantly lesser than that for the control group. The mean level of both free T_3 and free T_4 were lower in the hypothyroid group than control. However, the difference was found to be statistically significant in case of serum free T_3. Serum calcium levels were significantly lower; whereas serum phosphorus was found to be significantly higher in the hypothyroid patients (p-value<0.05), (Table no. 1).

Table 1: Mean levels of Vitamin-D, T_3, T_4, TSH, FT_3, FT_4, Serum calcium, phosphorus of subjects in control and hypothyroidism patients

PARAMETERS	Control group (n=50)	Test group (n=100)	t value	P-value
Vitamin-D (ng/ml)	24.70 ± 12.58	18.57 ± 8.08	3.611	0.000**
T_3 (ng/ml)	1.37 ± 0.27	1.00 ± 0.39	6.021	0.000**
T_4 (µg/ml)	8.12 ± 1.63	5.64 ± 1.89	7.919	0.000**
TSH (µIU/ml)y	2.26 ± 1.06	12.86 ± 12.13	-6.157	0.000**
FT_3 (pg/ml)	3.08 ± 0.74	2.62 ± 0.85	3.258	0.001**
FT_4 (mg/dl)	1.13 ± 0.41	1.04 ± 0.37	0.995	NS
Calcium (mg%)	9.58 ± 1.00	8.80 ± 0.53	6.251	0.000**
Phosphorus (mg%)	3.68 ± 0.73	4.01 ± 0.74	-2.900	0.004*

***p<0.05, **: p<0.01**

The correlation of serum TSH level with serum vitamin D, calcium and phosphorus levels of hypothyroid patients was evaluated by applying Pearson s correlation, and a significantly negative correlation was observed between TSH with Vit D and calcium (Table no. 2). Serum TSH levels were insignificantly correlated with serum phosphorus.

Table 2: Correlation between TSH, Vitamin D and Mineral Profile

Intergroup comparison	Correlation coefficient (r)	P value
TSH v/s vitamin D	-0.320	0.001**
TSH v/s Calcium	-0.296	0.0027*
TSH v/s Phosphorus	-0.1658	NS

***p<0.05, **: p<0.01**

Further correlation of Vitamin D, calcium and Phosphorus levels was evaluated with serum T3 and T4 levels. The statistical analysis did not show any significant correlation with serum T3 (Table no. 3). However, a significant positive correlation was observed for serum T4 with Vitamin D and calcium levels (Table no. 4).

Table 3: Correlation between T3, Vitamin D and Mineral Profile

Intergroup comparison	Correlation coefficient (r)	P value*
T_3 v/s vitamin D	0.037	NS
T_3 v/s Calcium	0.149	NS
T_3 v/s Phosphorus	-0.151	NS

***p-value>0.05 is insignificant**

Table 4: Correlation coefficient between T4, Vitamin D and Mineral Profile

Intergroup comparison	Correlation coefficient (r)	P value
T_4 v/s vitamin D	0.333	0.000**
T_4 v/s Calcium	0.243	0.014*
T_4 v/s Phosphorus	-0.020	NS

***p<0.05, **: p<0.01**

DISCUSSION:

The present study was planned to evaluate the status of Vitamin D level in patients of hypothyroidism in relation to calcium and phosphorus. Present study showed more females affected with hypothyroidism. Our results were similar with study by Fred F et al [13], who found that hypothyroidism was 10 times more common in females than in males, while their frequency increases with age.

The present study revealed significantly lower serum vitamin D level in the hypothyroid group. Similar results were observed in Tahir et al [14] and Bizzaro et al [15] who confirmed an association of vitamin D status with thyroid diseases. They reported a strong correlation of vitamin D deficiency with higher incidence of autoimmune thyroidits. This might be because of the fact that the precursor of vitamin D i.e. provitamin D_3 is synthesized from 7- Dehydrocholesterol. This reaction mainly takes place in the keratinocytes present in the epidermis of skin [16]. Thyroid hormones are believed to effect skin and their hypo-activity has been linked with thinning of epidermis and hyperkeratosis [17]. This impairs the process of Vitamin D production, thus suggesting a direct association between hypothyroidism and Vitamin D deficiency.

Thyroid hormones impose their impact on various metabolic pathways including those involving mineral metabolism. They are reported to exert their effects on osteoblasts with the help of nuclear receptors that leads to osteoclastic bone resorption [18]. Various studies have suggested a significant role of thyroid hormones in resorption of bone minerals [19]. According to Sunnel B et al [20], Jaskiran et al [21] and Roopa et al [22], the derangement of serum calcium and phosphorus level during thyroid disorder is primarily due to the disturbed activity of parathyroid hormone and calcitonin.

Calcium levels are affected by thyroid hormones, PTH and Vitamin D levels; and further phosphorus metabolism is accordingly affected. Study by Begic KS et al, [23] reported a direct influence of thyroid dysfunction on calcium metabolism. Similar results were noticed in our study that found statistical correlation between thyroid hormone levels and calcium metabolism.

Various studies have demonstrated contradictory results in context of serum phosphorus levels in relation to thyroid dysfunction. Our study revealed an insignificant correlation between thyroid dysfunction and serum phosphorus levels. Similar results were seen in study by Al Tonsi AA et al [24] showing that an impaired thyroid function has been found to cause elevation of serum phosphorus level.

Findings of the present study suggested that decreased thyroid hormones activity has a significant influence on vitamin D level and mineral balance. The similarity in functioning of vitamin D and thyroid hormones through VDRs (vitamin D receptors) suggests that deficiency of vitamin D may result in hypoactivity of thyroid hormones.

Thus, the patients diagnosed for hypothyroidism should be regularly screened for the levels of serum calcium and serum phosphorus as well as vitamin D levels. Early identification of patients developing deficiency or insufficiency of these factors may be helpful for the clinician in advising proper supplementation and lifestyle changes.

Since Patients diagnosed for hypothyroidism are advised thyroxin supplementation, further research or the influence of thyroxin dosage and duration of treatment on Vitamin D, calcium and phosphorous is suggested. Effect of lifestyle and dietery habits should also be verified in further studies.

CONCLUSION:

The present study suggests that thyroid function significantly influences the status of Vitamin D and mineral profile. Hypothyroidism has wide spread systemic manifestations including its effect on BMR, bone and mineral metabolism. In hypothyroidism, there is a depressed turnover due to impaired mobilization of calcium into the bone than leads to decreased blood calcium level and increased production of thyroid calcitonin. This promotes tubular resorption of phosphate and also favours the tubular excretion of calcium. Thus, our study emphasizes that regular screening for Vitamin D, calcium and phosphorus should be done in patients of thyroid dysfunction. Maintaining proper Vitamin D and mineral levels in hypothyroid patients will be helpful in diminishing the risk of developing various structural and physiological complications.

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