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Original Research Article.

Assessment of Thyroid Disorders Among Patients with Vitamin D Deficiency: An Institutional Based Study

Manoj Kumar Sahani[1*], Arun Kumar Anuragi[2]

[1]Associate Professor, [2]Professor, Department of General Medicine,
Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur, Uttar Pradesh, India.

ABSTRACT

Introduction: The vitamin – D deficiency has been observed to be a universal health issue and its role being played in various kinds of diseases have become the recent interest to many researchers globally. The purpose of this study was to examine the relationship between hypothyroidism and vitamin D deficiency and to clarify the relation between serum calcium levels with hypothyroid state.

Materials and Methods: This study included almost 66 participants who were reported to the outpatient ward of Department of General Medicine, Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur, Uttar Pradesh, India. The mean and the standard deviation (SD) for all the variables were calculated. Analysis of variance F test (ANOVA) was applied to compare the results of all the examined cases in both the studied groups. The differences between mean values for each tested variable have been tested by student's 't' test. Results considered significant or non-significant when P> or < 0.05, respectively.

Results: The mean values ± SD of all the studied parameters such as the age and sex distribution in all studied groups. There was no statistical difference (P > 0.05) between groups regarding age and sex. Statistical analysis and results of serum 25(OH) vit D and serum calcium levels in the studied groups. On comparing the two groups, serum TSH level was significantly higher in hypothyroid patients than that of controls (P= 0.000). When the serum TSH levels in hypothyroid patients were compared regarding to the sex, we noticed a non-significant difference between males and female patients (P =0.603).

Conclusion: The results obtained clearly demonstrated that patients developed hypovitaminosis D with hypocalcaemia based on the degree and severity of the hypothyroidic state. Hence the supplementation with Vitamin D should be made mandatory for all hypothyroid patients.

Keywords: Vitamin D, Hypothyroidism, Serum Calcium.

***Correspondence to:**

Dr. Manoj Kumar Sahani,
Associate Professor,
Department of General Medicine,
Rama Medical College Hospital & Research Centre,
Pilkhuwa, Hapur, Uttar Pradesh, India.

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INTRODUCTION

Vitamin D is a proposed biomolecule which is majorly metabolized into the skin through a reaction mainly processed by the UV light from sun, then it is hydroxylated twice to produce its active form which is 1,25 $(OH)_2$ D3 form. This hydroxylation could majorly occur in the liver and kidney respectively.[1,2] Vitamin D3 could actively maintain its biological effects by binding to its nuclear receptor (VDR).[3] The expression of VDR is commonly widespread through the organs of the human body and its associated tissues. Its expression in skin tissue, adipocytes, pancreatic β-cells, non-parenchymal cells of the liver and immune cells which primarily indicates that VD has distinguished physiological roles other than bone and mineral homeostasis.[4] Most importantly, a lower level of VD was actively reported to be associated with Graves' disease and Hashimoto's thyroiditis which are the most abundant autoimmune thyroid diseases. Also, thyroid tumorigenesis was reported to be enhanced by the impaired VD signaling.[1]

Thyroid diseases, on the other hand, are evaluated to be one of the most commonly reported endocrine abnormalities around the worldwide.[5,6] Hypothyroidism and hyperthyroidism are relatively associated with many serious clinical variations in the kidney function, that's why thyroid hormones are necessary in the kidney assessment.[7] On the flip side, the metabolism of thyroid hormones relies greatly on the liver, as it functions as the major organ which is responsible for the conversion of thyroxin (T4) to tri-iodothyronine (T3) by the enzyme Type-1 deiodinase.[7] Liver is also functions as the major organ that can synthesize the thyroid binding proteins (TBP) hence it actively regulates the thyroid hormones in conjugation and excretion. Although there are

various earlier studies that have investigated the thyroid diseases and VD deficiency which still have few limitations. The purpose of this study was to examine the relationship between hypothyroidism and vitamin D deficiency and to clarify the relation between serum calcium levels with hypothyroid state.

MATERIALS AND METHODS

This study included almost 66 participants who were reported to the outpatient ward of Department of General Medicine, Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur, Uttar Pradesh, India. After obtaining approval from the institutional ethical committee, the study has been carried out. All the study participants were basically divided into two groups namely Group I "control group" and Group II "Hypothyroid patients":

Group – I included 33 apparently healthy individuals [14 Male (42%) and 19 Female (58%)], their mean ages ± S.D are 46.3 ± 6.31 years. They were not reported to have any chronic medical diseases with reportedly normal clinical examinations, no history of thyroid diseases or any chronic illness may interfere with our results. They were not actively undertaking vitamin D supplements.

Group II included 33 patients [13 Male (39%) and 20 Female (61%)], their mean ages ± S.D 46.69 ± 5.24 year. They were clinically diagnosed as hypothyroid patients if TSH level was higher than 5.0 mU/L with lower levels of T3 and T4 than normal value.

Results were statistically analysed by SPSS 11.5 for Windows. The mean and the standard deviation (SD) for all the variables were calculated. Analysis of variance F test (ANOVA) was applied to compare the results of all the examined cases in both the studied groups. The differences between mean values for each tested variable have been tested by students 't' test. Results considered significant or non-significant when P> or < 0.05, respectively.

Table 1: Demographical and clinical characteristics

Variables	Group – I	Group – II	p - value
Sex	14-males (42%)	13-males (39%)	p>0.05
	19-females (58%)	20-females (61%)	
Age (years)	46.3 ± 6.31	46.69 ± 5.24	p>0.05
Serum 25(OH) Vit D (ng/mL)	44.59 ± 14.93	14.81 ± 2.13	p=0.0
Serum calcium (mg/dL)	10.41 ± 1.59	7.95 ± 1.82	p=0.0
Serum TSH (mU/L)	3.71 ± 0.96	6.97±0.99	p=0.0
Serum T3 (pg/mL)	2.97 ± 1.04	1.11±1.06	p=0.0
Serum T4 (ng/dL)	1.61 ± 0.33	0.72 ± 0.48	p=0.0

Table 2: Vit D, Calcium and TSH levels in hypothyroid patients according to sex.

Variables	Male – 13	Female – 20	p-value
25 (OH) vit D (ng/mL)	15.61 ± 2.29	14.29 ±1.91	p=0.221
Calcium levels (mg/dL)	7.31 ±2.19	7.91 ±1.61	p=0.992
TSH (mU/L)	6.841.04	7.09± 0.99	p=0.603

RESULTS

The mean values ± SD of all the studied parameters such as the age and sex distribution in all studied groups are shown in table-1. There was no statistical difference (P > 0.05) between groups regarding age and sex. Statistical analysis and results of serum 25(OH) vit D and serum calcium levels in the studied groups are given in table (1).

By using t-test to compare between the two groups, serum 25(OH) vit D level was significantly lower in hypothyroid patients than in controls (P =0.000) as tabulated in table 1. On comparing serum 25 (OH) vit D levels according to the sex distribution, they were insignificantly decreased in females than those of male in controls and hypothyroid patients (P >0.05) respectively as shown in table (2). Serum calcium levels recorded a significant difference between the studied groups (P = 0.000) as inferred in table (1). In hypothyroid patients, serum calcium levels were insignificantly decreased in females than male patients (P =0.992) table (2).

On comparing the two groups, serum TSH level was significantly higher in hypothyroid patients than that of controls (P= 0.000).

When the serum TSH levels in hypothyroid patients were compared regarding to the sex, we noticed a non-significant difference between males and female patients (P =0.603), table (2). Serum T3 and T4 were significantly higher in controls than those of hypothyroidism (P = 0.000) respectively. Regarding the control group, significant positive correlations were recorded between serum 25 (OH) vit D and each of serum calcium levels (P < 0.05), T3 (P < 0.05). On the other hand, there were significant negative correlations between serum 25 (OH) vit D and TSH (P < 0.05), with non-significant correlation with T4 (P > 0.05). Serum calcium levels had a negative significant correlation with serum TSH (P =0.029). Otherwise, it was non-significantly correlated with T3 and T4. There were significant positive correlations between serum 25 (OH) vit D and each of serum calcium levels (P =0.008), T3 (P =0.001) with significant negative correlation with TSH (P =0.000) in hypothyroid patients. Concerning the serum calcium levels, it was noticed to have a negative significant correlation with serum TSH (P =0.010) with a significant positive correlation with T3 and T (P= 0.008).

DISCUSSION

Vitamin D is majorly known for its primary active role in bone and mineral homeostasis, and it has been demonstrated recently that its deficiency is relatively associated with various diseases such as cardiovascular disease, cancer, infection and adiposity as well as osteoporosis.[8]

Fortunately, it has been shown later that vitamin D has a potent immunomodulatory effect which plays an important role in the pathophysiology of autoimmune diseases.[9] Serum concentration of 25(OH)D is the best indicator of vitamin D status. It directly reflects the vitamin D that has produced cutaneously and those obtained from food and other supplements[10] and has a fairly lengthy circulating half-life of about 15 days.[11] Unlike 25(OH)D, the circulating 1,25(OH)2D is basically not a good indicator of vitamin D status actively because it has relatively short half-life which is estimated about 15 hours and serum concentrations are closely monitored by parathyroid hormone, calcium and phosphate.[11]

Levels of 1, 25(OH)2D do not typically reduce until vitamin D deficiency is severe.[12,13] Hence, in the present study we assessed the serum 25(OH)D rather than 1,25(OH)2D to ensure that we are getting more precise results. Few studies have been performed in order to correlate any significant association between the levels of vitamin - D and hypothyroidism and to measure whether vitamin D deficiency that involves in the pathogenesis of hypothyroidism or rather a consequence of the disease. We therefore undertook this study to evaluate the levels of vitamin D and calcium among patients with hypothyroidism compared to healthy controls who did not complain from hypothyroidism or any thyroid diseases. Our results showed reduced serum 25 (OH) vit D levels in females than those of male controls and patients otherwise this decrease was non-significant, but we can refer this non-significant decrease to the small sample size that had been included in our study. In corroboration to our results, earlier studies have precisely observed that serum 25(OH)D levels did not differ significantly between males and females.[14,15]

Additionally, Hashemipour et al[16] researched about the prevalence of Vit D in Tehran and found non-significant variations between males and females without any relative association between Vit D and sunlight exposure. In contrast to our results, Sedrani,[17] Al-Jurayyan et al,[18] Fida,[19] Naeem et al,[20] proposed that the serum levels of vit D are significantly reduced in females when compared with males. Although many authors have reported higher serum levels of 25(OH)D in normal men than in normal women,[21,22] data has not been available for patients with hypothyroidism.[23]

However, a study from Japan including 200 euthyrotic patients with Graves' disease found vitamin D deficiency in 40% of women and around 20% of men ($p < 0.005$).[24] The discrepancies that were observed in these studies could be explained through the differences in the patient's selection, dietary vitamin-D intake, exposure to sunlight and associated seasonal variations. Moreover, the present study demonstrated that vitamin D and calcium serum levels were significantly lower in hypothyroid patients when compared to the controls. We recorded a significant positive association between Vit D and calcium levels in both groups.

Vit D and calcium serum levels had negative correlation when compared to TSH levels. These results suggested that there may be a significant association between vitamin D deficiency and hypothyroidism. Our results were in harmony with the previous studies that showed the prevalence of vitamin D insufficiency in Hashimoto's cases (92%) was significantly higher than that observed in healthy controls (63%, $p < 0.0001$).[25]

Recent studies have demonstrated a role of vitamin D in Grave's Disease (GD). First, Vitamin D related gene polymorphisms such as VDR gene and vitamin D binding protein gene are associated with GD. Second, Vitamin D deficiency modulates Graves' hyperthyroid is induced by thyrotropin receptor immunization in BALB/c mice. Third, Vitamin D analogue that inhibits inflammatory responses in human thyroid cells and T cells.[26] On the other hand, study had been conducted in Netherlands showed that Vitamin D deficiency is not associated with early stages of thyroid autoimmunity.[27]

CONCLUSION

Our results showed that patients reported with hypothyroidism mostly affected from hypovitaminosis D with hypocalcaemia. Moreover, the positive significant correlation was observed between each of serum vit D and calcium with thyroid hormones and that negative significant correlation with TSH levels, suggested that deficiency of serum vit D and calcium levels were significantly associated with degree and severity of the hypothyroidism would enhance the advisability of vit D supplementation. Screening for Vitamin D deficiency and serum calcium levels mandatory for all hypothyroid patients.

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