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Biochemistry

PREVALENCE OF THYROID AUTOIMMUNITY AND VITAMIN D INSUFFICIENCY IN PATIENTS WITH THYROID DISORDERS

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ABSTRACT

Background: Endocrine disorders are on the rise world over. Diseases of thyroid gland are among the most prevalent endocrine disorders in the world, second only to diabetes mellitus. In India, autoimmune thyroid disorders have been estimated to be the most frequent endocrine disorders. Thyroid diseases are more prevalent in the sub Himalayan region even in post iodination phase.

Aim: To assess the prevalence of thyroid autoimmunity and vitamin D insufficiency in patients with thyroid disorders at a tertiary care centre of Himachal Pradesh.

Methodology: Study population comprised of patients above 18 years of age, who were advised thyroid function tests by the clinicians on an outpatient basis.. Patients who were critically ill were excluded from the study.Thyroid function tests (T_3, T_4, TSH) along with anti thyroperoxidase antibody (ATA)was done by chemiluminescence and vitamin D levels were done by ELISA,(Enzyme linked immunosorbent assay) after serum separation of 120 subjects. ATA level >50uIU/ml was taken as positive and Vitamin D <30ng/ml were taken as insufficient.

Results: Mean age of study population was 42.48 (± 12.32) years. Forty hypothyroid and forty hyperthyroid and 40 controls were recruited. ATA positivity was reported in 52.5% (63/120) of the samples. 92% (58/63) were found to be Vitamin D deficient among ATA positives. There was a statistically significant positive association between thyroid autoimmunity and D deficiency (OR=14.8, p value=0.00).

Conclusion: Intervention studies may be carried out to assess the role of insufficiency of Vitamin D in development of auto immune thyroid disorders.

KEYWORDS : Vitamin B12 deficiency, Thyroid disorder, anti thyroperoxidase antibody

INTRODUCTION

Endocrine disorders are on the rise world over. Thyroid diseases are more prevalent in the sub Himalayan region even in post iodination phase. In India, autoimmune thyroid disorders have been estimated to be the most frequent endocrine disorders. Autoimmune hypothyroidism has been reported to be more common than iodine deficiency in areas which are iodine sufficient. Hashimoto's thyroiditis is the most common form of autoimmune thyroiditis.[1]

Hashimoto's thyroiditis (HT) affects women more than men. It may be associated with hypothyroidism, euthyroidism or occasionally hyperthyroidism. However, most cases present with hypothyroidism. The presence of antithyroid antibodies has been reported in patients with this disorder. Antibody against thyroid peroxidase has also been detected in thyroid tissue.

Vitamin D helps to balance the immune system which is when out of balance, attacks the thyroid gland. These findings suggest a potential role of vitamin D in development of Hashimoto's thyroiditis and/or its progression to hypothyroidism. In a study it has been shown that serum 1,25(OH)2D has been observed to be significantly lower in patients with autoimmune as compared with non autoimmune hyperthyroidism.[2] Hence the estimation of vitamin D in thyroid abnormality can help to classify the type of disorder. It has been demonstrated that serum vitamin D levels of Hashimoto's thyroiditis patients were significantly lower than the control, and the severity of vitamin D deficiency correlated with duration of Hashimoto's thyroiditis, thyroid volume, and antibody levels.[3]

Present study was undertaken to estimate levels of vitamin D in thyroid disorders and comparing it with euthyroids.

METHODOLOGY

A hospital based case control study was conducted at Dr. Rajendra Prasad Medical College, Tanda. A total of 120 subjects were enrolled (40 hypothyroid, 40 hyperthyroid and 40 controls (euthyroid) from patients attending hospital laboratory (diagnosed afresh and not taking vitamin supplements. Cases were diagnosed according to laboratory cut-off i.e. TSH more than 5.4µIU/ml as hypothyroid, TSH less than 0.5µIU/ml as hyperthyroidism.Thyroid profile along with ATA was estimated on immulite 1000 and vitamin D was estimated by ELISA.

Statistical analysis was done using EpiinfoV7 software. Variables were expressed as mean. Student t test was used to assess statistical significance between variables. A value of p<0.05 was considered statistically significant. Association was established using odds ratio.

RESULTS

Among the hypothyroid cases, there were 87.5% females and 12.5% males. Similarly among hyperthyroid cases, there were 85% females and 15% males, implying that females are more prone for thyroid disorders.

Anti thyroperoxidase antibody (ATA) status was measured in all 120 cases. It was more than 50 IU/ml in 75% cases of hypothyroidism and in 67.5% cases of hyperthyroidism. While in controls, ATA was more than 50 IU/ml in 15% cases only, implying that auto immunity has significant relation with thyroid function disorder.

Vitamin D deficiency was taken as a value less than 30 ng/ml. It was measured in all the cases and deficiency was found to be maximum in hypothyroidism cases where it was 62.5%. In cases of hyperthyroidism the deficiency was 47.5% whereas in controls it was only 40%. In 40 cases of hyperthyroidism, with TSH value less than 0.53 µIU/ml, Vitamin D deficiency was reported in 19s cases. In 27 cases of ATA positive hyperthyroidism, 14 cases were having Vitamin D deficiency. Mean level of vitamin D among hyperthyroid was 31.9 (±13.2).

As per our study, in hyperthyroid patients, there were 1.36 times more chances of vitamin D deficiency than in controls. Association was positive and the reports were statistically not significant (p-0.65)

Table No 1

	Vitamin D Deficiency		Total	OR (95%CI), p value
	Present	Absent		
Hyperthyroid	19 (47.5%)	21 (52.5%)	40 (100%)	1.36 (0.56-3.29), 0.65
Controls	16 40%)	24	40 (100%)	
Total	39	41	80	

In 40 cases of hypothyroidism (TSH value more than 5.4 µIU/ml) Vitamin D deficiency was reported in 25 cases. In 30 cases of ATA positive hypothyroidism , 20 cases were having vitamin D deficiency. Mean level of vitamin D among hypothyroid was 27.07 (±11.2)

As per our study, in hypothyroid patients, there were 2.5 times more chances of vitamin D deficiency than in controls. Association was positive and the reports were statistically significant (p-0.04)

Table No 2

	Vitamin D Deficiency		Total	OR (95%CI), p value
	Present	Absent		
Hyperthyroid	25(62.5%)	15(37.5%)	40 (100%)	2.5 (1.01-6.14), 0.04
Controls	16(40%)	24(60%)	40 (100%)	
Total	41	39	80	

DISCUSSION:

Vitamin D is a secosteroid hormone which is activated by enzymes and acts via receptors. In the liver, vitamin D is hydroxylated to 25-hydroxyvitamin D3 [25(OH)D3], which is the major circulating and stored form of the hormone and also the form that is measured to determine vitamin D status.Both vitamin D and thyroid hormone bind to similar receptors called steroid hormone receptors. A different gene in the Vitamin D receptor was shown to predispose people to autoimmune thyroid disease including Graves' disease and Hashimoto's thyroiditis.

In the present study, vitamin D deficiency was found to be maximum i.e. 62.5% in hypothyroidism. In cases of hyperthyroidism the deficiency was 47.5% whereas in controls it was only 40%.

It has been found by Evliyaoğlu et al[4] and Camurdan et al [5] that in pediatric and adolescent cases, there is higher prevalence (71.1%) of vitamin D deficiency in HashimotosThyroiditis patients than that in the control group. Kivity et al[6] reported that patients with autoimmune thyroid disease had higher vitamin D deficiency as compared to patients with non-autoimmune thyroid disease and healthy controls. Mackawy et al[7] have also shown that vitamin D levels were significantly lower in hypothyroid patients than in controls. Its level was insignificantly decreased in females than male patients.

Tamer et al[8] has reported that the prevalence of vitamin D insufficiency in Hashimoto Thyroiditis cases was significantly higher than that observed in healthy controls. Among Hashimoto Thyroiditis cases, the prevalence rate of vitamin D insufficiency showed a trend to be higher in patients with overt hypothyroidism or subclinical hypothyroidism as compared to patients with euthyroidism with insignificant differences.

Bozkurt et al[9] demonstrated that serum vitamin D levels of HashimotoThyroiditis patients were significantly lower than controls, and severity of vitamin D deficiency was correlated with duration of HashimotoThyroiditis, thyroid volume, and antibody levels Yamashita et al[10] found that there were relatively low concentrations of serum vitamin D in Graves' disease patients. In female Graves' patients vitamin D levels were lower than their male counterparts. The concentrations were lowest in females in their twenties and highest in females in their fifties and sixties. This was explained in part, by the fact that females tend to avoid ultraviolet rays and use sunscreen mainly because of cosmetic concern, and that males tend to have more outdoor occupations. In the study of newly diagnosed Grave's disease female patients, Yasuda et al[11] observed that vitamin D levels were significantly lower in patients in comparison to control subjects. The prevalence of vitamin D deficiency in Grave's Disease patients was significantly higher compared to control subjects. It was suggested that decreased vitamin D levels may cause the onset and/or development of Grave's disease, however further study would be necessary to conclude it. Alhuzaim et al[12] postulated that vitamin D deficiency may exacerbate the onset and/or development of Grave's disease and correction of the deficiency may be able to reverse it.

Misharin et al[13] has suggested that vitamin D deficiency is related to the pathogenesis of Grave's disease. Mackawy et al[7] indicated that patients with hypothyroidism suffered from low levels of vitamin D with hypocalcemia, which was significantly associated with the degree and severity of the hypothyroidism. Łacka et al[14] postulated that there is a relationship between vitamin D deficiency and the risk of autoimmune thyroiditis development. Sudha K et al[15] in their study had established that 76% of the adults with subclinical hypothyroidism were in suboptimal vitamin D status. MacFarlane IA et al[16] found in their study that in hyperthyroid patients, 1,25(OH)2D3 concentrations were decreased. While Karsenty G et al[17] found that the metabolic clearance rate (MCR) of 1,25(OH)2D3 was elevated in hyperthyroidism. Yasuda T et al[11] postulated that vitamin D levels in female patients with newly onset Grave's disease were decreased and significantly associated with thyroid volume.

Xu MY et al[18] in their analysis of 26 studies involving 1748 cases and 1848 controls conclude that the patients with Graves' disease were more likely to be deficient in vitamin D compared to the controls They further confirmed that low vitamin D status may increase the risk of Graves' disease. Lin WY et al[19] have shown that vitamin D receptor polymorphisms are associated with susceptibility to autoimmune thyroid disease (AITD). Vitamin D is an immunomodulator and may affect autoimmune thyroid diseases. Mariani et al[20] postulated that by binding to vitamin D Receptors (VDR) on immune cells, vitamin D can prevent them from triggering autoimmune destruction of cells. Their results showed that low levels of vitamin D and the thyroid hormones increased the population of NK cells. However, only vitamin D level was found to be linked to the cell-destroying activity of the innate immune system. Kivity S et al[6] documented significantly low levels of vitamin D in patients with AITDs and postulated that the low levels were related to the presence of anti thyroid antibodies and abnormal thyroid function tests, suggesting the involvement of vitamin D in the pathogenesis of AITDs and the advisability of supplementation. Tamer G et al[8] found 92% prevalence of vitamin D deficiency in their study involving 161 cases of Hashimoto's disease which was significantly higher than that of healthy controls where it was 63%. Bozkurt NC[9] et al demonstrated that vitamin D levels of Hashimoto's thyroiditis patients were significantly lower than the controls, and vitamin D deficiency severity correlated with duration of Hashimoto's thyroiditis, thyroid volume, and antibody levels.

Vitamin D has also been shown to influence thyrocytes directly by attenuating TSH stimulated iodide uptake and cell growth, this was shown in their study by Jonklaas J et al[21].

Until recently, vitamin D deficiency was considered rare in India because of abundant sunshine. However, a systematic study carried out by Goswami et al[22] in Delhi showed the presence of low 25-hydroxy vitamin D in a majority of subjects including newborns, their mothers, healthy physicians, nurses, soldiers and those with vitiligo and albinism. They also postulated that there was an inverse association between vitamin D and thyroid autoimmunity as reflected in anti-TPO titers. Subsequently, a series of studies have documented widespread hypovitaminosis D in north as well as south India[23,24]. Dutta D et al[25] in their study of various papers on Vitamin D and thyroid have agreed with Goswami et al[24] that there is high prevalence of vitamin-D deficiency and thyroid autoimmunity among Indians. They concluded that the relation between vitamin-D status and thyroid dysfunction is more relevant in the Indian contex. But, in a study published in the European Journal of Endocrinology in 2012, Effraimidis et al[26] concluded that early stages of thyroid autoimmunity are not associated with low vitamin D levels . They also found that the prevalence of vitamin D deficiency was not different between AITD patients (both Hashimoto's and Graves' disease) and non-AITD patients (72 vs 52%); abnormal thyroid function (not specified further) in these groups occurred in 44 and 15% respectively An important limitation of the present study is small sample size and heterogeineity of dietary habits and socioeconomic status.

CONCLUSION

In our study it was found that vitamin D was lower in thyroid disorders statistically significant in hypothyroid cases and ATA positive status. All hypothyroid cases should be screened for vitamin D status and treated accordingly.

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