



Autoimmune Hypothyroidism and Vitamin D Levels

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ABSTRACT

Objectives: Hypothyroidism is one of the commonest endocrine disorders. Autoimmunity has an important role in its etiology. The immunomodulatory role of vitamin D is emphasized in recent years. Vitamin D insufficiency/deficiency is seen to be associated with many autoimmune diseases like multiple sclerosis, SLE, Type 1 DM etc. This study was aimed to see the relation between serum vitamin D levels and serum TPO Ab levels in hypothyroid disease.

Materials and Methods: Serum vitamin D (25-OH) levels were measured in 25 patients with autoimmune positive hypothyroidism and 27 healthy subjects, utilizing the ELISA method (Calbiotech diagnostics, USA). Vitamin D deficiency was designated at levels lower than 20 ng/ml. Antithyroid peroxidase antibodies were assayed by ELISA. TSH, T3, T4 levels were evaluated in all patients.

Results: Serum 25(OH)D was significantly lower in hypothyroid patients [median value with interquartile range-14.3(12.65-17.90)] than in controls [median value with interquartile range- 26(21-32.8)]. Serum 25(OH)D values has shown weak inverse correlation with TPOAb titres.

Conclusion: The results of this study showed vitamin D deficiency in autoimmune hypothyroidism. The weak correlation between vitamin D and TPO Ab indicates the association but to prove it more extensive studies are required.

Keywords: Vitamin D; Hypothyroidism; TPO Ab; Thyroid autoantibodies, Autoimmune hypothyroidism.

Introduction

Vitamin D deficiency is a global health problem⁽¹⁾. Over a billion people worldwide are vitamin D deficient or insufficient⁽²⁾. The low levels of vitamin D have been attributed to reduced sun exposure and physical activity as well as obesity. Besides being a subtropical country vitamin D deficiency is prevalent in India⁽³⁾. 25(OH) D

deficiency has been associated with a wide range of non-skeletal effects including predisposition towards autoimmune disorders⁽⁴⁻⁷⁾. The demonstration of vitamin D receptor in monocytes, dendritic cells and activated T cells indicates significant interaction between vitamin D and the immune system⁽⁸⁾. Vitamin D mediates its effect though binding to vitamin D receptor

(VDR), and activation of VDR-responsive genes. VDR gene polymorphism was found to associate with autoimmune thyroid diseases (AITDs) ⁽⁹⁾. Though the molecular mechanisms of linking vitamin D with autoimmunity are under investigation, in vitro studies indicate an immunomodulatory effect of 1,25 (OH)D on Th1, Th2, T regulator and dendritic cells leading to a shift towards activation of Th2 cells ⁽¹⁰⁾. Autoimmune hypothyroidism has been estimated to be the most frequent endocrine autoimmune disorder ⁽¹¹⁾. Few studies were done to examine the correlation between vitamin D deficiency and autoimmune hypothyroidism and those that did yielded conflicting results. Goswami R et al ⁽¹²⁾ showed a significant inverse association between 25(OH)D levels and TPOAb positive autoimmune thyroid disease in Indian population. In a study done by Kivity et al ⁽¹³⁾ they showed that 79% of HT patients have 25(OH)D < 10ng/mL. A study by Zhang et al ⁽¹⁴⁾ has reported that a higher circulating 25(OH)D level was associated with lower TSH levels with negative serum thyroid autoimmunity titres independent of thyroid hormones levels. This study did not find a link between Vitamin D status and thyroid autoantibody positivity. The current study has been carried out to assess the relationship, if any, between thyroid autoimmunity and serum 25(OH)D levels in autoimmune hypothyroidism.

Materials and Methods

The present study included 25 cases of autoimmune hypothyroidism (age group:20-50yrs, both genders) and 27 age and gender matched clinically healthy individual as controls. The

ethical clearance for the study was obtained from institutional ethical committee. The cases were selected based on serum TSH levels >10 μ IU/ml(15) and serum TPO Ab levels > 34 IU/mL. Serum TSH levels in Controls was < 4.5 μ IU/mL, antibody negative. Subjects with any co-morbidities were excluded from study. After a written and informed consent, about 3mL of blood was collected in a gel separation tube, with due aseptic precautions, from each study subject. The blood samples were allowed to clot and were centrifuged at 4000 rpm for 8-10 minutes. The clear serum was used to analyze serum TSH, T4, T3 levels by ECLIA(Electro Chemiluminescence Immunoassay) on Cobas 6000 e601 automated analyzer. Serum 25(OH)D and serum TPOAb levels were analysed by ELISA (Enzyme Linked Immunosorbent Assay, Calbiotech Inc. assay ELISA kit, USA)

Results

Statistical analysis

Results were statistically analyzed by SPSS 20.0 for Windows. All the variables were presented as median with interquartile range (25th percentile-75th percentile) due to non-gaussian distribution of variables. The Kolmogorov- Smirnov method was used to test for normality of data distribution. Mann Whitney U test was used to compare the results between the studied groups. The associations between the variables in a group were analyzed using Spearman test as correlation coefficient (r) and their significance (p value). Results were considered significant when p value was <0.05.

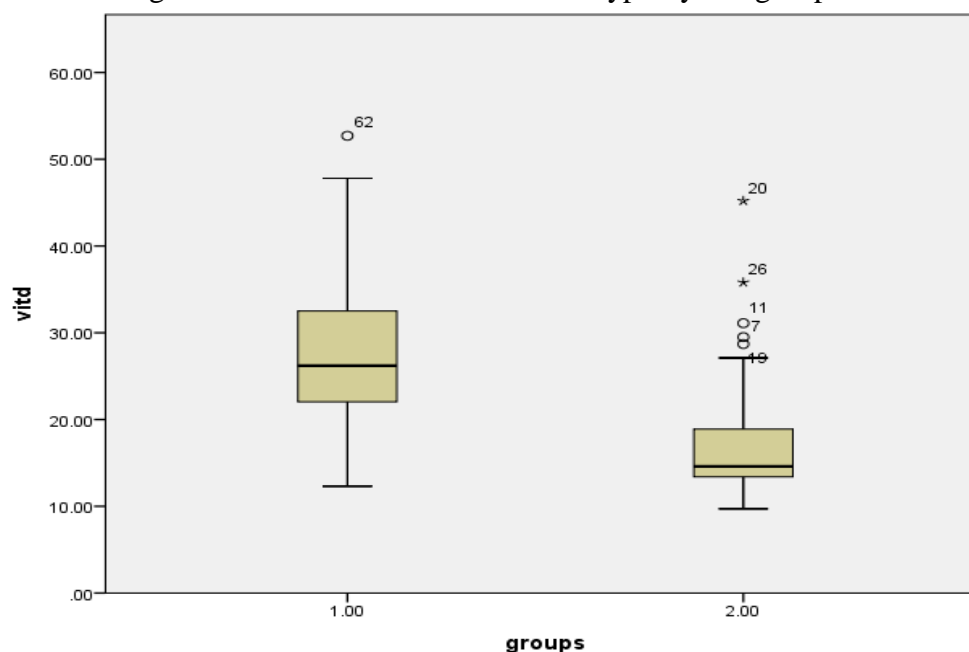
Results:

Table 1: Table showing the demographic data and laboratory parameters of the study group

	Control group (n=27)	Hypothyroid group (n=25)	
	Median(Interquartile range)	Median (Interquartile range)	p-value
Age (yrs)	31(27-34)	31(25- 38.5)	0.693
Total T ₃ (nmol/L)	1.79(1.54-1.96)	1.81(0.85-1.59)	<0.001*
Total T ₄ (nmol/L)	105.7(99.59- 120.00)	57.46(42.26-90.71)	<0.001*
TSH(μ IU/mL)	2.27(1.65- 2.92)	72.63(22.50-136.90)	<0.001*
Vitamin D(ng/mL)	26.2(21.00-32.8)	14.3(12.65-17.90)	<0.001*
TPO Ab (IU/mL)	9.7(6.25-15)	97.5(88.0-99.65)	<0.001*

Table 2: The correlation of different variables with Vitamin D in different groups

	Control group	Hypothyroid group
Total T ₃ (nmol/L)	r = 0.19 p = 0.33	r = 0.36 p = 0.07
Total T ₄ (nmol/L)	r = 0.12 p = 0.54	r = 0.60 p = 0.002*
TSH(μIU/mL)	r = 0.22 p = 0.91	r = -0.59 p = 0.002*
TPO Ab(IU/mL)	r = -0.18 p = 0.36	r = -0.37 p = 0.06

Figure 3: Box plots showing vitamin D levels in controls and hypothyroid group

*, ° - Outliers due to non-Gaussian data distribution.

Discussion

Thyroid diseases are among the most common endocrine abnormalities, and AITDs are perhaps the most prevalent autoimmune diseases⁽¹⁶⁾. The pathogenesis of AITDs, like other autoimmune diseases, is multifactorial, combining genetic, immune, environmental and hormonal influences such as vitamin D^(17,18). In the present study, an increased prevalence of vitamin D deficiency among patients with Hashimoto's thyroiditis was demonstrated. A significant association was also found between vitamin D deficiency and TSH levels. The results of the current study indicate the presence of an inverse association between 25(OH) D levels and thyroid autoimmunity as reflected in TPOAb titres. Though the relationship is not significant statistically, could be due to small sample size.

Vitamin D inhibits the production of Th1 polarizing cytokine (IL-12), thereby indirectly shifting the polarization of T cells from a Th1 toward a Th2 phenotype. Recently numerous studies have shown the relation of vitamin D and various autoimmune diseases. Vitamin D receptor (VDR) gene polymorphisms and vitamin D status are associated with different autoimmune diseases⁽¹⁹⁾. Various studies have shown a conflicting result on association between vitamin D and incidence of autoimmune thyroid diseases. A study conducted in Netherlands showed that Vitamin D deficiency is not associated with early stages of thyroid autoimmunity⁽²⁰⁾. Tamer et al⁽²¹⁾ had found vitamin D insufficiency in Hashimoto thyroiditis patients but that decrease was not significant.

The present study has few limitations, like the small number of patients, the heterogeneity of the study population, and lack of information on nutrition, social behavior (e.g., outdoor activity). Further studies with a larger number of subjects are needed to determine whether vitamin D deficiency is a casual factor in the pathogenesis of hypothyroidism or rather a consequence of the disease.

Conclusion

The present study showed vitamin D deficiency in autoantibody positive hypothyroid cases. The decrease is significant in patient group showing some association between vitamin D and hypothyroidism. No significant association was found between vitamin D levels and thyroperoxidase antibodies levels. Further randomized, controlled, prospective trials are needed in order to demonstrate the causality of vitamin D in AITD and consequently the role of vitamin D supplementation in prevention or improvement of AITD.

References

- Hollick MF, Chen TC. Vitamin D deficiency a worldwide problem with health consequences. *Am J Clin Nutr*. 2008; 87:10805–68.
- Naeem Z. Vitamin D Deficiency- An Ignored Epidemic. *Int J Health Sci (Qassim)*.2010; 4(1): 5–6.
- Goswami R, Mishra SK & Kochupillai N. Prevalence & potential significance of vitamin D deficiency in Asian Indians. *Indian J Med Res* 2008; 127, 229 – 238.
- Hypponen E, Laara E, Reunanen A, Jarvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. *Lancet* 2001; 358: 1500–1503.
- Merlino LA, Curtis J, Mikuls TR, Cerhan JR, Criswell LA, Saag KG. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. *Arthritis Rheum* 2004; 50: 72–77.
- Huisman AM, White KP, Algra A, Harth M, Vieth R, Jacobs JW et al. Vitamin D levels in women with systemic lupus erythematosus and fibromyalgia. *J Rheumatol* 2001; 28: 2535–2539.
- Baeke F, Takiishi T, Korf H, Gysemans C and Mathieu C. Vitamin D: modulator of the immune system. *Curr. Opin. Pharmacol.* 2010; 10 (4):482–96.
- Shoenfeld N, Amital H, Shoenfeld Y. The effect of melanism and vitamin D synthesis on the incidence of autoimmune disease. *Nat Clin Pract Rheumatol* 2009; 5: 99–105.
- Arnson Y, Amital H & Shoenfeld Y. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. *Ann Rheum Dis* 2007; 66, 1137– 1142.
- vanEtten E, Mathieu C. Immunoregulation by 1,25-dihydroxyvitamin D3: basic concepts. *J Steroid Biochem Mol Biol* 2005; 97: 93–101.
- Kochupillai N. Clinical endocrinology in India. *Curr Sci* 2000; 79, 1061 –1067.
- Goswami R, Marwaha RK, Gupta N et al. Prevalence of vitamin D deficiency and its relationship with thyroid autoimmunity in Asian Indians: a community-based survey. *Br J Nutr*. 2009; 102: 382-386.
- Kivity S, Agmon-Levin N, Zisappl M et al. Vitamin D and autoimmune thyroid diseases. *Cell Mol Immunol*. 2011; 8: 243-247.
- Zhang Q, Wang Z, Sun M, Cao M, Zhu Z, Fu Q et al. Association of high Vitamin D status with low circulating thyroid-stimulating hormone independent of thyroid hormone levels in middle-aged and elderly males. *Int J Endocrinol*. 2014; 63:18-22.
- Garber JR, Cobin RH, Gharib H, Hennessey JV, Mechanik JI et al. American Association of Clinical

- Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *EndocrPract.* 2012 Nov-Dec; 18 (6): 988-1028.
16. Shoenfeld Y, Zandman-Goddard G, Stojanovich L, Cutolo M, Amital H, Levy Y et al. The mosaic of autoimmunity: hormonal and environmental factors involved in autoimmune diseases—2008. *Isr Med Assoc J* 2008; 10: 8–12.
17. Penna G, Adorini L. 1 Alpha,25-dihydroxyvitamin D3 inhibits differentiation, maturation, activation, and survival of dendritic cells leading to impaired alloreactive T cell activation. *J Immunol* 2000; 164: 2405–2411.
18. Boonstra A, Barrat FJ, Crain C, Heath VL, Savelkoul HF, O'Garra A. 1alpha,25-Dihydroxyvitamin d3 has a direct effect on naive CD4+T cells to enhance the development of Th2 cells. *J Immunol* 2001; 167: 4974–4980.
19. Naderi N, Farnood A, Habibi M, Derakhshan F, Balaii H, Motahari Z, Agah M R et al. Association of vitamin D receptor gene polymorphisms in Iranian patients with inflammatory bowel disease. *J. Gastroenterol. Hepatol.* 2008; 23(12):1816–22.
20. Effraimidis G, Badenhoop K, Tijssen JG and Wiersinga WM. Vitamin D deficiency is not associated with early stages of thyroid autoimmunity. *Eur J Endocrinol.* 2012 Jul; 167(1):43-8.
21. Tamer G, Arik S, Tamer I and Coksert D. Relative vitamin D insufficiency in Hashimoto's thyroiditis. *Thyroid* .2011; 21(8):891–96.