Is there any Association between Serum 25 (OH) Vitamin D3 Level and Hypothyroidism among Females: A Cross Sectional Study

Meenakshi Shankar¹, Mukul Singh²

¹Senior Resident, ²Professor, Department of Pathology, Vardhman Mahavir Medical College& Safdarjung Hospital, New Delhi, India,

Corresponding Author: Mukul Singh

ABSTRACT

Background: Hypovitaminosis D is a global health problem where over a billion people are affected. Few studies have been done in past to assess the association between vitamin D status and hypothyroidism but yielded conflicting results. The aim of this study was to investigate correlation of serum (25-OH) D3 level among females with hypothyroidism and healthy controls.

Materials and Methods: This was a cross sectional study and total of 90 women were enrolled in it for analysis. 45 recently diagnosed hypothyroid female patients were included in group I (case) and 45 healthy females were recruited in group II (control). Serum 25(OH) D3, T3, T4 and TSH were measured in all participants.

Results: While there was no significant difference in the age compared with the controls. Cases had significantly higher TSH, had significantly lower T4 and there was no significant difference in T3 levels. We found significant difference in the mean 25(OH) Vitamin D levels in hypothyroid females than in healthy females (15.44 ± 4.65 vs 20.91 ± 7.98 , p=0.000). Furthermore, 100% hypothyroid and 79.9% healthy females had vitamin D levels <30ng/ml. We found inverse insignificant correlation between 25(OH)D3 and TSH in the hypothyroid group was also seen with (r = -0.060, p 0.695).

Conclusion: We conclude that there is no correlation of serum (25-OH)D3 levels among females with hypothyroidism and healthy controls.

Keywords: Females, hypothyroidism, vitamin D deficiency.

1. INTRODUCTION

Hypovitaminosis D is a global health problem where over a billion people are affected. ^[1, 2] The main function of vitamin D is the regulation of bone metabolism and helps calcium and phosphorus in homeostasis. Vitamin D is steroid hormone and its functions by acting on vitamin D receptors (VDR), which are found in all the organs of body.^[3] But recently its role as immune modulator has been emerging.^[4] Moreover, researchers are emphasizing the role of vitamin D in the regulation of proinflammatory cytokines, regulatory T cell, and immune response. ^[5] According to them hypovitaminosis D leads to an increase in the risk of various autoimmune diseases. Vitamin D also involve in the pathogenesis of DCs cells, macro- phage, CD4 + T, CD8+ T, and B cells in development of immunity.^[6,7] Thyroid gland also has VD receptor and these are member of a group of receptors called nuclear receptors, which also belong to the thyroid hormones receptor. ^[6] Furthermore, hypovitaminosis D seems to be involved in many diseases like cardiovascular disease, diabetes mellitus, kidney disease and infections. ^[8-11] Vitamin D deficiency has also been associated with autoimmune thyroid diseases (AITD) such as Hashimoto's thyroiditis and Graves' disease. [12,13]

Hypothyroidism is a common health problem in India, most of which may be results of Hashimoto's thyroiditis. Incidence of which increases with age and females are at higher risk (8-15 times). ^[14] Thyroid disorders may reduce vitamin D levels as observed in autoimmune thyroid disease. ^[15] Few studies have examined the association between the levels of vitamin D and hypothyroidism but found conflicting results. ^[16-22]

AIM: Therefore, we undertook this study to evaluate the role of vitamin D status among females with hypothyroidism compared to healthy controls.

2. MATERIAL AND METHODS

A total of 90 subjects were included in this study. They were recruited in Lab medicine department of Pathology, at our hospital, during the period from March 2020 to June 2020. Written informed consent was taken from all participants in this study.

Inclusion criteria: Age >18 years, nonpregnant, no history of old thyroid problem (only newly diagnosed hypothyroid females not on any medications), no history of chronic illness.

Exclusion criteria: Age <18 years, pregnancy, history of thyroidectomy, radio-Iodine ablation, history of malabsorption disorder, H/o chronic kidney, liver, thyroid vitamin D and calcium disease. on supplementation, H/o diabetes mellitus, dermatological disease, rheumatological disease, alcoholics. After exclusion & inclusion criteria, two groups were formed. Group I "Hypothyroid patients": included 45female patients, their age mean±SD was 40.57±12.57 years. They were diagnosed as hypothyroid patients if TSH level was higher than 6.2mlU/ml with lower levels of T3 (Ref.range =0.69-2.02ng/ml) and T4 (Ref. range = $4.4-11.6\mu g/ml$) than normal value.

Group II "Control group": It included 45 healthy females subjects their age mean \pm S.D was 38.6 \pm 13.49 years.

After complete history, examination, Laboratory investigations (serum 25(OH)D3 and thyroid profile) was done.

Laboratory investigations: For measuring serum TSH, T3, T4 and 25(OH)D3: After aseptic precaution, blood sample was collected by venepuncture at the fasting state(overnight fasting for 10-12 hrs).The serum was separated by centrifugation and then stored at -80°C for a week until analysed. Vitamin D status was evaluated by measurement of serum 25(OH)D3 levels with a chemiluminescent immunoassay method (Seimens Adivacenture CP system). Serum 25(OH) D3 levels were considered as deficient when it is <10ng/ml and insufficient between 10-30ng/ml.

STATISTICAL ANALYSIS: Data were statistically analysed by SPSS version-23 for Windows. The mean and the standard deviation (SD) for all the variables were calculated. Student's t-test and Mann-Whitney test were used to compare the continuous parametric and non-parametric (thyroid hormones and 25 (OH) vitamin D) data, respectively between the two groups. Spearman correlation analysis was used in the evaluation of relationships between variables. Results considered significant when p value is < 0.05.

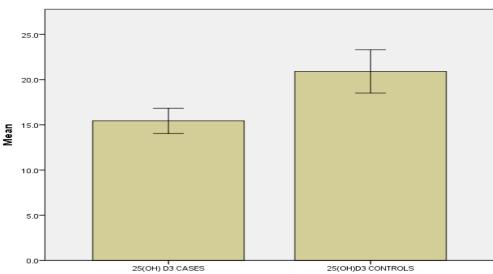
3. RESULTS

There was no significant difference in the mean \pm SD of age 40.57 \pm 13.04 vs 38.38 \pm 12.99 years (p =0.471) levels between the two groups. Compared with the controls, cases, had significantly lower T4 and 25 (OH) vitamin D3 levels and had significantly higher TSH(p<0.05).There was no significant difference in T3 between controls and case group.(Table 1)

The spearman test was used to investigate correlation of vitamin D levels in hypothyroid patients. Insignificant positive correlation was seen with age,T3,T4 and nonsignificant inverse correlation was found in TSH in Hypothyroid and Control.(Table: 2)

VARIABLES	GROUP 1 (CASES)	GROUP II (CONTROLS)	t TEST	P value
	n=45	n=45		
	Mean±SD	Mean±SD		
AGE (Years)	40.57±12.57	38.80±13.09	0.712	0.471
T3 (pg/dl)	1.03±0.50	1.31±0.94	-1.750	0.087
T4 (ng/dl)	7.24±2.66	8.4±1.88	-2.457	0.018
TSH (mlU/ml)	12.96±9.59	1.85±1.08	7.610	0.000
25(OH)D3 (ng/ml)	15.44±4.65	20.91±7.98	-3.910	0.000
VitD sufficiency [n (%)]				
Deficient <10ng/ml	3(6.6%)	1(2.2%)		
Insufficient(10-30ng/ml)	42(93.3%)	35(77.7%%)		
Sufficient(>30ng/ml)	0(0%)	9(20%%)		

Table 1: Clinicopathological parameters of both groups



Error Bars: 95% CI

Figure 1 Comparison of 25 (OH) vitamin D3 levels between hypothyroid females and control group.

 Table 2: Correlation between 25 (OH) vitamin D3 and other variables in patients group

Variables	r (correlation coefficient)	p value
Age	0.106	0.488
T3	0.042	0.786
T4	0.124	0.415
TSH	-0.060	0.695

DISCUSSION

Recent studies have shown hypovitaminosis is a risk factor for many diseases like autoimmune diseases, cardiovascular disease, diabetes mellitus, kidney disease and infections etc. ^[8-11] It also plays essential role in autoimmune thyroid diseases (AITD) such as Hashimoto's thyroiditis and Graves' disease. ^[12-13] Hypothyroidism is a common health problem in India, most of which may be results of endemic goitre and AITD.^[14] It's incidence increases with age and females are at higher risk (8-15 times).^[15]

In the present study, there was no significant difference in the mean \pm SD of age 40.57 ± 12.57 vs 38.80 ± 13.09 years

(p=0.471) levels between the two groups. Hypothyroid females had significantly lower T4 and significantly higher TSH (p<0.05). There was no significant difference in T3 levels between controls and case groups.(Table 1)

In current study, we found significant difference in the mean 25(OH) Vitamin D3 levels in hypothyroid females than in healthy females (15.44±4.65 vs 20.91±7.98, p=0.000)respectively. Furthermore, 100% hypothyroid and 79.9% healthy females had vitamin D levels <30ng/ml. The community-based Indian studies done on apparently healthy controls reported a prevalence of hypovitaminosis D is ranging from 50% to 94%. Prevalence of 25(OH)D3 estimated in urban population was 75% in females whereas the prevalence of Vitamin D deficiency was slightly lower in a rural area as 70% in females. ^[28] Our results are in agreement with these studies.

This high prevalence of 25(OH) Vitamin D3 deficiency in females may be attributed to clothing habits leads to inadequate exposure of the skin to the UV B portion of sunlight. There is recent trend in increases use of sunscreen lotions by females for protection against skin cancer and cosmetic reasons which may lead to a significant decrease in solar induced previtamin D production, leading to [29] insufficient levels of vitamin D. Research done by Goswami et al and Pallavi et al also found lower levels of 25(OH) vitamin D in females, but the value was not significant (p=>0.05). [17,18]

In the study inverse insignificant correlation between 25(OH)D3 and TSH in the hypothyroid group was also seen (r = -0.060, p 0.695). Our results are in agreement with the study by Musa IR et al. they found no correlation between 25(OH)D3 and TSH in the hypothyroid group (r = -0.002, p=0.814).^[23]

Contrary to our results Amal Mohammed Husein Mackawy et al, Colbay M et al, Mackawy et al , Fawzy et al and Pallavi et al, who all in their research work found significant correlation between TSH and vitamin D level in hypothyroid subjects. [19-22]

In our study, we found a positive correlation but insignificant between serum vitamin D and T4,T3 levels in the hypothyroid group these results are in concordance with study by Fawzy et al and Musa IR et al. ^[22,23] In the study by Zhang et al concluded that vitamin D is involved in binding of thyroid hormone to the nuclear receptor thus lack of vitamin D may contribute to decreased levels of thyroid hormones and increased levels of TSH. ^[30] According to Byron Richards experimental study hypovitaminosis D contributed to the possibility of low thyroid hormones. ^[31]

Our results indicated that female patients with hypothyroidism suffered from hypovitaminosis D. Moreover, no significant correlation between serum vitamin D and thyroid hormones is found which may be attributed to small sample size of study.

CONCLUSION

We conclude that there is no correlation of serum (25-OH)D3 level among females with hypothyroidism and healthy controls.

Limitations and Recommendations

The limitations of this study are firstly, small number of subjects. Secondly calcium, phosphorous, parathyroid hormones and thyroid antibodies were not investigated. Therefore, further prospective large clinical studies required to examine the direct role of vitamin D in the patients with thyroid disorders.

Conflicts of Interest

There are no conflicts of interest.

REFERENCE

- 1. Holick MF. Vitamin D Deficiency. New England Journal of Medicine. 2007; 357: 266–281.
- Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. The American journal of clinical nutrition. 2008; 87:1080S–6S.
- Lemire JM, Adams JS, Sakai R, Jordan SC. 1 alpha,25- dihydroxyvitamin D3 suppresses proliferation and immunoglobulin production by normal human peripheral blood mononuclear cells. Journal of Clinical Investigation. 1984; 74(2):657-661.
- Rigby WF, Stacy T, Fanger MW. Inhibition of T lymphocyte mitogenesis by 1, 25-dihydroxyvitamin D3 (calcitriol). The Journal of clinical investigation. 1984; 74:1451–5.
- Thacher TD, Clarke BL. Vitamin D insufficiency. Mayo Clinic Proc. 2011; 86(1): 50–60
- 6. Dankers W, Colin EM, van Hamburg JP, Lubberts E. Vitamin D in autoimmunity: molecular mechanisms and therapeutic potential. Front Immunol. 2017;7:697.
- Haussler MR, Haussler CA, Jurutka PW, Thompson PD, Hsieh JC, Remus LS, Selznick SH, Whitfield GK. The vitamin D hormone and its nuclear receptor:

molecular actions and disease states. J Endocrinol. 1997;154(3 Suppl):S57-73.

- Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, Benjamin EJ, D'Agostino RB, Wolf M, Vasan RS. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008; 117(4):503–11.
- Berridge MJ. Vitamin D deficiency and diabetes. Biochem J. 2017;474(8): 1321– 32
- Al-Badr W, Martin KJ. Vitamin D and kidney disease. Clin J Am Soc Nephrol. 2008;3(5):1555–60.
- Yamshchikov A, Desai N, Blumberg H, Ziegler T, Tangpricha V. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. EndocrPract. 2009;15(5):438–49. 15.Tamer G, Arik S, Tamer I, Coksert D. Relative vitamin D insufficiency in Hashimoto's thyroiditis. Thyroid. 2011;21(8):891–6.
- Bozkurt N, Karbek B, Ucan B, Sahin M, Cakal E, Ozbek M, Delibasi T. The association between severity of vitamin D deficiency and Hashimoto's thyroiditis. EndocrPract. 2013;19(3):479–84.
- 13. Mosekilde L, Lund, Sorensen OH, Christensen MS, Melsen F. Serum-25 hydroxycholecalciferol in hyperthyroidism. The Lancet. 1977; 309:806–7
- 14. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J Endocrinol Metab. 2013;17(4):647-52.
- 15. Kostoglou-Athanassiou I, Ntalles K. Hypothyroidism - new aspects of an old disease. Hippokratia. 2010;14(2):82-7.
- Alhuzaim ON, Aljohani N. Effect of Vitamin D3 on Untreated Graves' Disease with Vitamin D Deficiency. Clinical Medicine Insights Case Reports. 2014; 7:83-5.
- 17. Goswami R, Marwaha RK, Gupta N, Tandon N, Sreenivas V, Tomar 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(3):382-6

- 18. Pallavi, Runi Devi, Sarita Choudhary, Kavita Choudhary: A Comparative Study on Vitamin D levels among Hypothyroid and Euthyroid Patients, Indian Journal of Basic and Applied Medical Research; December 2018: Vol.-8, Issue- 1, P. 154-9
- 19. Amal Mohammed HuseinMackawy,Bushra Mohammed Alayed, Bashayer Mater Al-rashidi; Vitamin D Deficiency and Its Association with Thyroid Disease. International Journal of Health Sciences, Qassim University, Vol. 7, No.3 (Nov 2013)
- 20. Colbay M, Altay M, Akturk M, Cakir N, Yetkin I, Arslan M. Vitamin D levels are associated with serum TSH levels but not with thyroid autoantibodies. In: 13th European Congress of Endocrinology, BioScientifica. 2011;26.
- 21. Mackawy AMH, Al-ayed BM ,Al-rashidi BM. Vitamin D Deficiency and Its Association with Thyroid Disease. Int J Health Sci (Qassim)2013;7(3):267-75
- 22. Fawzy E , Mohamed SA , Shebl M, El-Rabat AM. Hypovitaminosis D In Autoimmune Hypothyroidism. Journal of American Science.2013;9(11).
- 23. Musa IR, Gasim GI, Khan S, Ibrahim IA, Abo- alazm H, Adam I. No Association between 25 (OH) Vitamin D Level And Hypothyroidism among Females. Maced J Med Sci. 2017 Apr 15; 15(2):126- 30.
- 24. Marwaha RK, Tandon N, Garg MK, Kanwar R, Narang A, Sastry A, et al. Vitamin D status in healthy Indians aged 50 years and above. J Assoc Physicians India. 2011;59:706–9.
- 25. Goswami R, Kochupillai N, Gupta N, Goswami D, Singh N, Dudha A, et al. Presence of 25(OH) D deficiency in a rural North Indian village despite abundant sunshine. J Assoc Physicians India. 2008; 56:755–7.
- 26. Sofi NY, Jain M, Kapil U, Seenu V, Ramakrishnan L, Yadav CP, et al. Status of serum Vitamin D and calcium levels in women of reproductive age in national capital territory of India. Indian J Endocrinol Metab. 2017;21:731–3.

- Bawaskar PH, Bawaskar HS, Bawaskar PH, Pakhare AP. Profile of Vitamin D in patients attending at general hospital Mahad India. Indian J Endocrinol Metab. 2017; 21:125–30.
- Mehlawat U, Singh P, Pande S. Current status of Vitamin-D deficiency in India. Innov Pharm Pharmacother 2014;2: 328-35.
- 29. Lips P. Vitamin D physiology. Prog BiophysMol Biol. 2006; 92(1):4–8.
- 30. ZhangQ, WangZ, SunM, CaoM, ZhuZ, FuQ, 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;2014:631819.

31. Byron Richards. Low Vitamin D Contributes to Thyroid Problems. Health news 2008.

How to cite this article: Shankar M, Singh M. Is there any association between serum 25 (OH) vitamin D3 level and hypothyroidism among females: a cross sectional study? International Journal of Science & Healthcare Research. 2020; 5(3): 180-185.
