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ESTIMATION OF VITAMIN D IN HYPOTHYROID FEMALES OF DIFFERENT AGE GROUPS AND ITS CORRELATION WITH TSH

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ABSTRACT

Background- Hypothyroidism and vitamin D deficiency are common worldwide. Vitamin D is not simply a vitamin but also a steroidal hormone, which acts through nuclear receptors. Hypothyroidism may be caused by immune or non-immune causes, Autoimmune thyroiditis being the most common cause.

The aim of the study is to estimate the levels of vitamin D in the hypothyroid females of different age groups so as to establish a correlation between TSH and Vitamin D. Method: The study was conducted in Govt. Medical College, Kota and attached group of hospitals. Duration of study is from January 2015 to July 2015.. A total of 65 hypothyroid females age group between 25-65 years, presenting with overt hypothyroidism(TSH>20) were included in the study. Levels of Vitamin D and Thyroid Stimulating Hormone(TSH) was measured by chemiluminescence in Hormonal Assay Lab, Department of Biochemistry, Govt. Medical College, Kota. Result: Statstical Analysis was done by Microsoft Excel. Mean ± SD of Vitamin D and TSH were calculated in all cases. The results were compared by One Way ANOVA and the significant negative correlation between TSH and Vitamin D was found by Pearson's correlation (r= - 0.49). P value was < 0.05, which is highly significant. Conclusion: We found that vitamin D deficiency is prevalent in hypothyroidism, showing its increased probability as the age advances. There is an inverse association between Vitamin D and TSH.

KEYWORDS: Hypothyroidism, Menopause, TSH (Thyroid Stimulating Hormone), Vitamin D, VDR (Vitamin D Receptor)

INTRODUCTION

Vitamin D deficiency is a global health problem. Over a billion people worldwide are vitamin D deficient or insufficient(1). It is recognized to be involved in various immune functions as well as bone and muscle development(2).Vitamin D is a steroidal hormone, introduced in the body through food, but major synthesis occurs through exposure of skin to solar ultraviolet light(3). Vitamin D obtained from skin or diet, is converted by the liver to 25(OH)D and is metabolized in the kidneys by the enzyme 25-hydroxyvitamin D-1α-hydroxylase (CYP27B1) to its active form 1,25-dihydroxyvitamin D(4). Vitamin D mediates its effect through binding to vitamin D receptor(VDR), and activation of VDR-responsive genes(5,6). Apart from its main function in regulation of calcium absorption and homeostasis, it also has

a role in regulating cell proliferation and differentiation(7). Many tissues and cells in the body express the vitamin D receptor, resulting in growing interest in extra-skeletal conditions like cancers, cardiovascular diseases and auto-immune diseases(8,9,10,11).Recent studies indicate that 1,25(OH)2D, the biologically active form of vitamin D, is a modulator of both the innate and adaptive immune system. Immune cells such as monocytes, macrophages, dendritic cells,T-lymphocytes, and B-lymphocytes are targets for the active vitamin D(11). Low vitamin D intake and vitamin D deficiency have been identified as a risk factor for type 1 diabetes, multiple sclerosis, Crohn's disease, and rheumatoid arthritis (12,13,14,15,16,17).

Hypothyroidism occurs due to reduced functioning of thyroid gland which may be primary(disease of thyroid gland) or less commonly secondary to hypothalamic or pituitary disease, seen more common in females with its incidence increasing as the age advances. Most common cause of hypothyroidism is autoimmune thyroiditis. (18). Measurement of plasma TSH concentration is the principal test for biochemical evaluation of hypothyroidism. Normal level of TSH is 0.3 – 3.5 mU/l and > 10 mU/l is observed in hypothyroidism (19). Importantly, both vitamin D and thyroid hormone bind to receptors which are similar in structure(6). A different gene in vitamin D receptor was shown to predispose people to autoimmune thyroid disease including Grave's disease and Hashimoto's thyroiditis. thus it becomes essential to understand how the vitamin D system works. VDR gene polymorphism was found to associate with autoimmune thyroid diseases(5). In hypothyroidism, intestinal absorption of nutrients is affected both by reduction in rate of absorption, so vitamin D deficiency is commonly seen(19). Reports have proved a correlation between vitamin D and TSH, especially in patients with thyroid diseases(20).

Menopause is cessation of menstrual cycle. It is strictly defined as 1 year without menses and is caused by reduced secretions of ovarian hormones, estrogen and progesterone(21). It naturally occurs at the age of 45 – 55 years. Symptoms of menopause are loss of bone density (osteoporosis), vaginal dryness, depression, weight gain and hot flushes (22). Estrogen enhance the activity of the enzyme responsible for activating vitamin D. End organ response to 1,25 $(OH)_2D$ is also impaired in post menopause. The resulting vitamin D resistance can be attributed to decrease in number of vitamin D receptor and its activity due to decline in oestrogen level (23,24). Hypovitaminosis is more common in post menopausal women.(25)

Serum concentration of 25(OH)D is the best indicator of vitamin D status(26). It has a half life of 15 days(27). Whereas, circulating 1,25$(OH)_2D$ is not a good indicator of Vitamin D status due to its short half life of 15 hours and its level being regulated by parathyroid hormone, calcium and phosphate(28).

Levels of vitamin D more than 30ng/ml is considered to be normal, levels of 20-29ng/ml(< 50nmol/L) is insufficient and if it is less than 10 ng/ml(12.5nmol/L) signifies severe deficiency(29).

AIM: To estimate the levels of vitamin D in the hypothyroid females of different age groups so as to establish a correlation between TSH and Vitamin D. Thus helpful for public health and clinical practice.

MATERIALS AND METHODS

Study Population

The study was carried out in Govt. Medical College and attached group of hospitals, Kota, Rajasthan. The study period was from January 2015 to July 2015. A total of 65 immune and non immune hypothyroid females age group

between 25-65 years, presenting with overt hypothyroidism(TSH>20mU/L) were included in the study. These females were further divided into four groups,Group 1 of ages between 25-35 years, Group 2 includes age group of 36-45 years, Group 3 includes age group of 46-55 years and Group 4 includes 56-65 years.

The patients with parathyroid disease, prior history of metabolic bone disease and vitamin D deficiency, diabetes mellitus, liver disease, malignancy, chronic kidney disease, chronic drug use like antiepileptic agents, steroids and history of calcium or vitamin-D supplementation in the last one year, which are likely to interfere with vitamin-D metabolism and the patients who did not give the consent were excluded.

Sample Collection

A sample of 2 ml was collected after the overnight fasting, following the consent of the patient. The samples were left standing for one hour and then the serum was obtained after centrifugation at 3000 rpm for 10 minutes. There after the samples were analyzed for TSH and Vitamin D by chemiluminescence technique on Cobas e 411 in Hormonal Assay Lab, Department of Biochemistry, Govt. Medical College, Kota.

Statistical Analysis

Statistical Analysis was done on Microsoft excel. Continuous parameters were expressed as Mean± SD. The results were obtained by One way ANOVA. The Correlation between TSH and Vitamin D was established by Pearson coefficient of correlation(r).P value <0.05 was considered statistically significant.

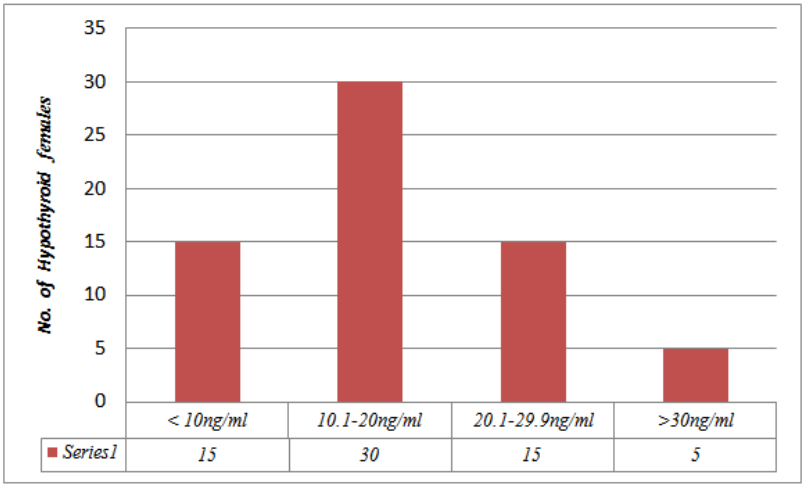
RESULTS

During the 6 months study period from January 2015 to July 2015, a total of 65 hypothyroid females were studied and were categorized into 4 Groups based on their ages. Group 1 includes age group of 25-35years, Group 2 of 36-45 years, Group 46-55years and Group 4 of age group 56-65 years. The Mean± SD of age is 47.23± 11.77.

On comparing the vitamin D levels in 4 groups, we found that vitamin D insufficiency(20.1-29.9ng/ml) was prevalent among the Group 3 and 4. Vitamin D deficiency(<10 ng/ml) is seen in all groups of hypothyroid females, but the prevalence was relatively high among the Group 4 females. Among the total hypothyroid females, severe deficiency of vitamin D (<10ng/ml) was seen in 15(23%) cases, moderate deficiency(10.1-20ng/ml) was seen in 30(46.2%), insufficiency(20.1-29.9ng/ml) was seen in 15(23%) cases and normal levels(>30ng/ml) were seen in 5(7.6%) cases.

Table 1: Comparison of Vitamin D Levels in All 4 Groups

Vitamin D Levels (In Ng/Ml)	Group 1 (25-35yrs)	Group 2 (36-45yrs)	Group 3 (46-55yrs)	Group 4 (56-65yrs)	Total
< 10 (Severe Deficiency)	2	1	5	7	15 (23.1%)
10.1 – 20 (Moderate Deficiency)	5	4	9	12	30 (46.2%)
20.1 – 29.9 (Insufficiency)	6	3	4	2	15 (23.1%)
>30 (Normal)	1	2	0	2	5 (7.6%)



Graph 1: Showing No. of Hypothyroid Females with Respect to their Vitamin D Levels

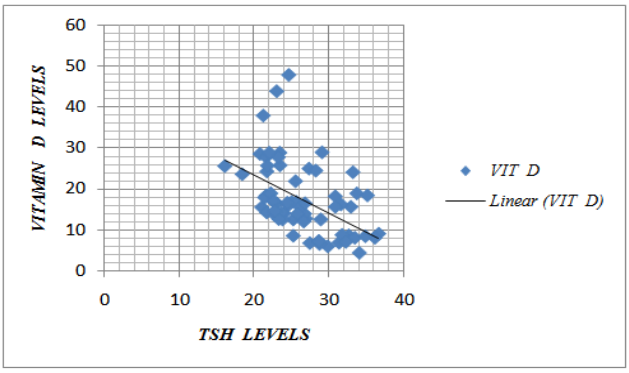
The Mean± SD of Vitamin D of Group 1 is 22.3± 9.70, Group 2 is 22.61± 11.71, Group 3 is 15.06± 6.79 and Group 4 is 15.63±9.10. Similarly, the Mean± SD of TSH of Group 1 is 21.99± 2.45, Group 2 is 23.61± 1.63, Group 3 is 28.38± 4.01 and Group 4 is 29.66±4.28.

Table 2: Showing Mean ± Sd of Vitamin D and Tsh of Females of Different Ages

Parameter	Group 1 (25-35yrs)	Group 2 (36-45yrs)	Group 3 (46-55yrs)	Group 4 (56-65yrs)	P Value
VITAMIN D (MEAN± SD) (ng/ml)	22.3± 9.70	22.61±11.71	15.06±6.79	15.63±9.10	0.034(highly significant)
TSH (MEAN± SD) (mU/L)	21.99±2.45	23.36±1.63	28.38±4.01	29.66±4.28	0.001(highly significant)

Correlation between Vitamin D and TSH

There is a negative correlation between Vitamin D and TSH,represented by r= - 0.49, which shows that Vitamin D level decreases with increase in TSH levels.



Graph 2: **Correlation between Vitamin D and TSH**

DISCUSSIONS AND CONCLUSIONS

Vitamin D is not just a vitamin, but also a hormone and a substance with pleiotropic effects on the optimal functions of the cardiac, skeletal, reproductive and endocrine systems. It is also an important immunomodulator. The elevated TSH levels as observed in hypothyroidism causes metabolic changes and functions of specific organs which leads to bone disorders and other endocrine related disorders. Estimation of vitamin D is important in all age groups, due to its versatile role in human body. Vitamin D deficiency is the common condition throughout the world(30). India has a noteworthy burden of both hypothyroidism and hypovitaminosis. Females are more prone to vitamin D deficiency due to their life style, cultural practices and excessive use of cosmetics. Several studies have established a relationship between low Vitamin D and autoimmune thyroid disorders. According to Journal of Cellular and Molecular Immunology (2011), Vitamin D deficiency was more common in patients with autoimmune thyroid disorders, but the deficiency was also seen in non- immune hypothyroid patients. Autoimmune diseases are basically caused by genetic polymorphism. Thus even a minor change at genetic level, affects the structure and functions of various cells of body. This genetic polymorphism also affects VDRs. This polymorphism of VDRs leads to decreased biological activity even when the levels of vitamin D are normal. Our results revealed that although Vitamin D deficiency is seen in majority of the hypothyroid females but is profound in postmenopausal hypothyroid females as a result of additional effect of decreased level of oestrogens. One of two mechanisms may explain the low levels of vitamin D in patients with hypothyroidism. First, low levels of vitamin D may be due poor absorption of vitamin D from the intestine. Secondly, the body may not activate vitamin D properly(5). The study by Amal Mackway et al also goes in favour of our study(31). In the developing country like India, females generally suffer from hypovitaminosis, in which vitamin D deficiency is more frequently seen. In an experimental study by Byron Richards (2008) studied the effect of vitamin D deficiency on thyroid gland, he reported that a lack of vitamin D contributed to the possibility of low thyroid hormones(32). The significant negative correlation between Vitamin D and TSH indicates the association between TSH and Vitamin D.

LIMITATION

Further studies are needed to explore, whether Vitamin D deficiency is a causative factor in pathogenesis of hypothyroidism or a consequence of the disease.

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