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Role Of 25-Hydroxyvitamin D And Vitamin D Receptor In Hyperthyroidism: A Case-Control Study In A South Indian Population

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Abstract:

Background: *Hyperthyroidism is characterized by the thyroid gland's excessive production and release of thyroid hormones into the bloodstream. The global prevalence ranges between 0.2% and 2.5% in iodine-sufficient regions. Vitamin D has been implicated in the regulation of thyroid-related autoimmune and neoplastic disorders, primarily through its interaction with the vitamin D receptor (VDR). Notably, both vitamin D and thyroid hormones exert their effects via receptors belonging to the steroid hormone receptor family.*

Aim: *This study aims to investigate the role of the Vitamin D receptor (VDR) and 25-hydroxyvitamin D (25(OH)D) levels in the pathophysiology of hyperthyroidism by exploring their association in a South Indian population through a case-control design.*

Methods: *An observational study was conducted using a cross-sectional design involving 188 participants (80 hyperthyroid cases and 108 healthy controls) aged 18-70, matched for age and sex. Participants with a history of thyroidectomy, pregnant women, and individuals under 18 years were excluded. Blood samples were collected from all participants for necessary investigations. Thyroid profiles, thyroid antibodies, and Vitamin D levels were assessed using a fully automated chemiluminescent hormone analyzer, and VDR levels were measured using a commercially available human ELISA kit. All biochemical parameters were analyzed using a fully automated biochemistry analyzer. A p-value of <0.05 was considered statistically significant.*

Results: *The VDR levels among cases and controls were 0.49 ± 0.19 and 2.51 ± 0.67, and 25(OH) D3 levels were 14.58 ± 6.03 & 22.09 ± 9.75, respectively. A statistically significant difference in VDR and 25(OH) D3 levels was found between the case and control groups ($p < 0.05$).*

Conclusions: *Our findings reveal a notable relationship between the vitamin D receptor (VDR), 25(OH)D, and the levels of total T3 and total T4 in individuals with hyperthyroidism, suggesting that VDR may serve as a diagnostic marker for hyperthyroidism. Additional studies are needed to clarify the role of VDR in preventing and treating thyroid disorders, highlighting the need for more comprehensive research on VDR.*

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Keywords: *VDR: Vitamin D Receptor, ELISA: enzyme-linked immunosorbent assay, 1,25 (OH) D3: 1,25-dihydroxy vitamin D3.*

INTRODUCTION:

Hyperthyroidism is characterized by the thyroid gland's excessive production and release of thyroid hormones into the bloodstream. In iodine-sufficient regions, the global prevalence ranges between 0.2% and 2.5% (1). Hyperthyroidism is typically categorized into two forms: subclinical and overt. Subclinical hyperthyroidism, marked by a suppressed thyroid-stimulating hormone (TSH) level with normal circulating thyroid hormones, affects approximately 0.7% to 1.4% of individuals. Overt hyperthyroidism, defined by low TSH accompanied by elevated levels of tr12eiiodothyronine (T3) and/or free thyroxine (T4), has a prevalence of 0.2% to 1.4% (1,2). Subclinical hyperthyroidism can resolve on its own, but in some cases, it progresses to overt hyperthyroidism—about 8% of patients within 1 year and approximately 26% over 5 years. (3) The risk of progression is higher in individuals with an undetectable TSH level at the time of diagnosis and in those with toxic multinodular goitre. (3,4)

Subclinical hyperthyroidism has been associated with an increased risk of cardiovascular mortality, atrial fibrillation, all-cause mortality, and coronary heart disease events. (5,6) A serum TSH level of less than 0.1 mIU/L is particularly linked to a higher incidence of atrial fibrillation and cardiovascular death. (7) Hyperthyroidism leads to increased bone resorption because elevated thyroid hormone levels stimulate both osteoblast and osteoclast activity, with a net effect favouring osteoclast-mediated bone breakdown. (8) In postmenopausal women, a thyroid-stimulating hormone (TSH) level of ≤0.1 mIU/L is associated with a 3- to 4-fold increased risk of hip and vertebral (spinal) fractures. (9) Subclinical hyperthyroidism is linked to a 36% higher risk of hip fractures, a 28% increased risk of fractures overall, and a 16% greater risk of non-spine fractures compared to individuals with normal thyroid function. It is also associated with reduced bone density in both men and women. (10)

Thyrotoxicosis is a clinical syndrome caused by elevated levels of circulating thyroid hormones, leading to systemic effects on multiple organ systems. While it is commonly due to hyperthyroidism, it may also result from other conditions such as thyroiditis or exogenous thyroid hormone intake. In rare cases, thyrotoxicosis may arise from extrathyroidal sources of hormone production, such as struma ovarii, an uncommon ovarian tumour composed predominantly of functional thyroid tissue. If left untreated, hyperthyroidism can lead to serious complications, including cardiac arrhythmias, heart failure, osteoporosis, metabolic imbalances, and poor pregnancy outcomes (11).

Vitamin D (25 (OH) D) refers to a group of steroidal compounds, primarily including VitD2 (ergocalciferol) and VitD3 (cholecalciferol) (12). Its primary role has traditionally been associated with regulating calcium and phosphorus balance and maintaining bone health. However, the broad distribution of Vitamin D receptors (VDR) and the enzymes involved in its metabolism throughout the body points to a wider, pleiotropic role for this vitamin, implicating it in the pathogenesis of various diseases (13,14). Notably, Vitamin D has been shown to exert immunomodulatory effects, and growing evidence suggests it may influence the onset and progression of autoimmune diseases (AIDs). Among these, autoimmune thyroid disease (AITD) stands out as the most prevalent organ-specific AID (14).

The vitamin D receptor (VDR), first cloned in 1987, is expressed in various tissues—including the thyroid gland—and plays a central role in mediating the biological effects of vitamin D. As a ligand-dependent transcription factor, VDR regulates gene expression and contributes to the genomic actions of vitamin D (15, 16). It is a nuclear receptor superfamily member and shares a receptor system with thyroid hormones, indicating possible crosstalk between vitamin D signalling and thyroid function, particularly in autoimmune thyroid disease (17). As part of the steroid-thyroid-vitamin D receptor gene superfamily (18), VDR functions as a nuclear transcription factor. Although previous research has produced mixed findings—some showing little to no link between vitamin D and hyperthyroidism—no studies to date have directly examined the specific role of VDR in hyperthyroid disorders.

This study investigates the association between Vitamin D receptor (VDR) expression and serum 25-hydroxyvitamin D [25(OH)D] levels in individuals diagnosed with hyperthyroidism, with a specific emphasis on a South Indian population. Utilizing a case-control design, the research compares vitamin D status and VDR

expression between hyperthyroid patients and healthy controls, aiming to elucidate the potential role of vitamin D in the development and progression of thyroid dysfunction within this demographic.

Materials and Methods

Study Design and Population

This cross-sectional study was conducted at the Central Diagnostic Laboratory, Department of Biochemistry, Kodagu Institute of Medical Sciences (KoIMS), associated with the Teaching Hospital, Madikeri, Kodagu. It included 188 participants, comprising 80 cases and 108 age and sex-matched controls aged between 18 and 70. The study was conducted from September 2022 to April 2024.

Ethical Approval

The purpose and study procedures were explained to all participants, and written informed consent was obtained. The study received ethical approval from the Institutional Ethics Committee (KoIMS/IEC/16/2021-22) of Kodagu Institute of Medical Sciences and the Central Ethics Committee (NU/CEC/2022/315) of Nitte Deemed to be University.

Inclusion and Exclusion Criteria

Samples were collected from participants aged 18 to 70 years, of both sexes, with an abnormal thyroid profile, and who were willing to provide informed consent. Exclusion criteria included individuals who had undergone thyroidectomy, pregnant women, children under 18, those with other autoimmune disorders, and individuals on medications known to affect thyroid hormone function.

Data Collection

A detailed medical history was obtained from all participants. Blood samples were collected from patients attending the outpatient departments (OPDs) of General Medicine, General Surgery, Obstetrics and Gynaecology (OBG), and Ear, Nose, and Throat (ENT) at KoIMS, Madikeri.

Sample Collection and Handling

A total of 3 mL of blood was collected from each participant. The blood was processed as follows:

- **Serum Collection**: 3 mL of blood was transferred to a plain tube (red vacutainer) for serum separation. The serum was utilized for biochemical tests, including thyroid profile assessments, vitamin D, and vitamin D receptor levels. The serum samples were stored at -40°C for further analysis.

Biochemical Analysis

Biochemical tests were conducted on the separated serum samples to evaluate thyroid function and related biochemical markers as per standard laboratory protocols.

Measurement of biochemical parameters:

The collected blood samples were centrifuged at 2500 rpm for 12 minutes and serum was separated and collected in a screw cap cup for the biochemical parameter analysis. Glucose, urea, creatinine, lipid profile, liver function test, and calcium were measured by a fully automated biochemistry analyzer (Cobas c-311). The test was performed only after the instrument was standardized. Ionized calcium was measured by an ISE electrolyte analyzer (Roche 9180 electrolyte analyzer).

Measurement of hormones:

Measurement of T3, T4, TSH, FT3, FT4, thyroid peroxidase antibody, and thyroglobulin antibody was estimated by a fully automated chemiluminescent hormone analyzer (Maglumi X3, Snibe China). Before the sample analysis, the instrument was standardized by processing the quality control and calibration. 25 (OH) vitamin D level was measured by the direct competitive chemiluminescence immune assay method, using a 25 (OH) vitamin D kit, a fully automated chemiluminescence analyzer (Maglumi X3 Snibe, China).

Measurement of vitamin D receptor (VDR):

The serum Vitamin D Receptor (VDR) level was measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (GENLISA™ Human Vitamin D Receptor, VDR ELISA; Catalogue number:

HVDR0423). Calibration was performed with serial dilutions of the standard solution provided in the kit, which contains 240 ng/ml of recombinant human VDR. Serum VDR detection followed the manufacturer's recommendations: standards and serum samples were combined with a biotin-labeled monoclonal VDR antibody and horseradish peroxidase (HRP)-tagged streptavidin solution, then added to a micro-ELISA plate coated with a monoclonal antibody specific for VDR. After a 60-minute incubation at 37°C, the plate was washed five times, and a chromogen solution was added. Following an additional 10-minute incubation, colour development was stopped by adding a stop solution. The optical density (OD) was measured at a wavelength of 450 nm, and calculations were performed. The detectable concentration of VDR ranged from 0.1 ng/ml to 8 ng/ml, with intra-assay and inter-assay coefficients of variation of less than 10% and 12%, respectively (information taken from the kit insert and not verified by our experiments). To minimize variation within an assay, measurements were performed in duplicate and simultaneously using the same ELISA kit, with a sensitivity of 0.05 ng/ml.

Statistical Analysis

Data analysis was performed using SPSS version 26.0 (trial version). Different statistical methods were employed depending on the data type and distribution:

- **Continuous Variables:**
  - For normally distributed data, comparisons between two groups were made using the independent samples t-test.
  - For data not following a normal distribution, the Mann-Whitney U test was applied.
- **Categorical Variables:**
  - Associations between categorical variables were assessed using the Chi-square test.
- **Group Comparisons:**
  - One-way ANOVA was used to compare normally distributed continuous variables across multiple groups.
  - The Kruskal-Wallis test was applied for non-normally distributed continuous variables when comparing more than two groups.
- **Correlation Analysis:**
  - Pearson's correlation coefficient was calculated to examine relationships among vitamin D, T3, T4, TSH, FT3, and FT4 levels in both normal and hypothyroid subjects.

A p-value < 0.05 was considered statistically significant for all analyses.

Result

In this study involving 188 participants, we analyzed demographic and biochemical parameters between hyperthyroid patients (n=80) and healthy controls (n=108). The hyperthyroid group consisted of 15 males (18.75%) and 65 females (81.25%), while the control group included 23 males (21.29%) and 85 females (78.70%). The demographic data analysis for the study group (Table 1) showed that the majority of hyperthyroid patients were aged between 27 and 50 years, whereas the control group primarily ranged from 26 to 49 years. Statistical analysis revealed significant differences ($p < 0.05$) in body mass index (BMI), creatinine, total cholesterol, ALP, SGPT, and total calcium between the hyperthyroid patients and the control group. In contrast, parameters such as glucose, urea, triglycerides, HDL, LDL, and SGOT showed no significant differences between the two groups.

Test parameters	Hyperthyroid (n=80)	Normal (n=108)	P value
Age (years)			
18-25	09	07	
26-33	26	51	Not applicable
34-41	21	25	
42-49	19	15	
50-57	02	05	
58-71	03	05	
BMI (kg/m^2)	21.59±2.86	23.56 ±4.62	0.0005
Glucose (mg/dL)	105.02± 25.75	98.33±12.89	0.179

Urea (mg/dL)	21.54±8.64	20.68±5.58	0.800
Creatinine (mg/dL)	0.74±0.18	0.83±0.25	0.025
T. Cholesterol (mg/dL)	171.4±39.23	187.99±52.94	0.049
Triglyceride (mg/dL)	145.75±66.67	167.73±75.29	0.671
HDL (mg/dL)	43.92±12.29	44.35±12.63	0.513
LDL (mg/dL)	115.81 ± 37.84	130.29± 44.19	0.532
ALP (IU/L)	105.09 ± 41.5	90.34 ± 32.85	0.013
AST (IU/L)	22.61 ± 8.36	24.13 ± 9.11	0.195
ALT (IU/L)	16.03 ± 9.6	19.59 ± 10.7	0.002
T. Calcium (mg/dL)	9.42 ± 0.63	9.65 ± 0.45	0.011

*Data expressed in Mean ± SD, Independent t-test used, p <0.05 is considered statistically significant.

Table 1: showing baseline characteristics such as age, body mass index (BMI), glucose, urea, creatinine, total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine transferase (ALT) among hyperthyroid cases and controls and p <0.05 is considered statistically significant.

Determination of thyroid profile and serum levels of vitamin D in hyperthyroid cases and controls

In a study evaluating hyperthyroidism, levels of T3, T4, TSH, FT3, and FT4 were analyzed. Independent t-tests and Mann-Whitney U tests revealed a highly significant increase ($p < 0.001$) in serum T3, T4, FT3, and FT4 levels in the hyperthyroid group compared to the control group. A significant decrease in TSH levels were also observed in hyperthyroid cases compared to the control group ($p < 0.05$). Based on thyroid hormone levels, hyperthyroidism was classified into two categories: subclinical hyperthyroidism (n = 22; 27.5%) and overt hyperthyroidism (n = 58; 72.5%). Autoimmune thyroid disease was confirmed through the measurement of thyroid antibodies, including anti-TPO and anti-TGA. Analysis via Mann-Whitney U tests indicated a significant increase in TPO antibody levels in hyperthyroid cases [655 (678-23)] compared to controls [14.19 (4.52–18.75)]. Similarly, TGA antibody levels were significantly elevated in the hyperthyroid group [490.3 (511.25-20.98)] compared to controls [29.25 (6.84–36.3)], both showing significant differences between hyperthyroid and control groups ($p < 0.05$).

Test Parameters	Hyperthyroid (N= 80)	Normal (N= 108)	*p* values (<0.05)
T3	3.6± 2.0	1.41±0.36	<0.0001
T4	120.21 ± 38.1	72.69 ± 14.42	<0.0001
TSH	0.51 (0.517 – 0.007)	2.63 ± 1.41	<0.0001
F T3	8.22 (311.8- 3.57)	3.03 ± 0.58	<0.0001
FT4	17.94 (13.86 -31.8)	12.12 ± 3.23	<0.0001
Anti-TPO	655 (678-23)	14.19 (4.52-18.75)	<0.0001
Anti-TGA	490.3 (511.25-20.98)	29.25 (6.84- 36.3)	<0.0001
25 (OH) D	15.99 ± 4.3	22.09 ± 9.75	<0.0001
VDR	0.49 ± 0.19	2.51± 0.67	<0.0001
I. Calcium	0.85 ± 0.18	1.20 ±0.72	<0.0001

* Data expressed in Mean ± SD, Median (IQR). Independent t-test and Mann-Whitney U test used; p <0.05 is considered statistically significant.

Table 2 shows a comparison of serum 25-hydroxy vitamin D, Vitamin D Receptor, Thyroid profile, thyroid peroxidase antibody, thyroglobulin antibody, and ionised calcium between the hyperthyroid case and control group, and p <0.05 is considered statistically significant.

Graph 1 shows a significant positive correlation in vitamin D levels between cases and controls, with a correlation coefficient of **r = 0.299** and a **p-value of 0.01**. However, the **median vitamin D concentration** was significantly lower in cases (**15.80 ng/mL**, interquartile range [IQR] 7.06) compared to controls (**19.77 ng/mL**, IQR 6.38). These findings suggest a potential association between **lower vitamin D levels and hyperthyroidism**, indicating that vitamin D deficiency may be linked to the development or presence of the condition.

Determination of 25 (OH) D and VDR

The level of vitamin D for all the participants was measured. This study classified the thyroid abnormal patients and controls into two groups according to the vitamin D level. Vitamin D deficient group (vitamin D level is < 20 ng/ml) and vitamin D insufficient group (vitamin D level is 21-29.5 ng/ml). The analysis by unpaired t-test revealed a highly significant reduction (<0.0001) of vitamin D levels in hyperthyroid patients (14.58 ± 3.19 n=80) compared to healthy controls (22.09 ± 9.75 n=108). The deficiency of vitamin D level compared with healthy controls (14.4±3.36 n = 66) vs (16.65 ± 2.4 n = 66) (p=0.0001). (Table 3)

The comparison between serum levels of vitamin D receptor (VDR) showed that hyperthyroid patients had very low concentrations of VDR in their serum (0.49 ± 0.19) compared to healthy controls (2.51± 0.67) (p < 0.0001). Another biochemical parameter, ionised calcium, showed considerably lower concentration in hyperthyroid patients (0.85 ± 0.18) than healthy controls (1.20 ±0.72) (p <0.0001). (Table 3)

Test parameters	Hyperthyroid (n=108)	Normal (n=108)	P value
25 (OH) D (ng/mL)	14.58 ± 3.19	22.09 ± 9.75	<0.0001
< 20 (ng/mL)	14.4±3.36 (n = 66)	16.65 ± 2.4 (n = 59)	0.0002
21-29 (ng/mL)	22.69±1.84 (n = 14)	23.4± 2.52 (n = 37)	0.453
> 30(ng/mL)	-	42.96±15.6 (n = 12)	-
VDR (ng/mL)	0.49±0.19	2.51± 0.67	<0.0001
I calcium (mmol/L)	0.85 ± 0.18	1.20 ±0.72	<0.0001

*Data expressed in Mean ± SD, Independent t-test used, *p* <0.05 is considered statistically significant.

Table 3 shows 25-hydroxy vitamin D (25(OH)D), Vitamin D Receptor (VDR), and Ionised Calcium (I. calcium) among study subjects, and data were expressed as mean ± SD; *p* value < 0.05 considered as statistically significant.

Graph 2 indicates that the median expression levels of VDR (Vitamin D Receptor) significantly differed between the case and control groups. In the case group, the median VDR value was 0.44 with an interquartile range (IQR) of 0.24, while in the control group, the median VDR value was 2.34 with an IQR of 0.94. These results indicate a marked difference in VDR expression between the two groups, with the control group exhibiting higher VDR levels than the case group (*p*=0.0001).

Discussion

Thyroid disorders rank among the most common endocrine diseases, with Autoimmune Thyroid Disease (AITD) being the leading autoimmune condition globally (19,20). Although previous studies have extensively investigated the associations between hyperthyroidism, vitamin D deficiency, and genetic variations in the Vitamin D Receptor (VDR), the diagnostic potential of circulating serum VDR levels remains relatively underexplored. This study aims to assess serum vitamin D receptor (VDR) levels in individuals with hyperthyroidism and investigate their relationship with vitamin D status, thyroid function parameters, and other relevant biochemical markers. The findings of this study demonstrate a significant correlation between serum VDR levels and hyperthyroid conditions, indicating that serum VDR could potentially serve as a valuable biomarker for the diagnosis of hyperthyroidism.

Our demographic analysis revealed that among individuals with hyperthyroidism, 81.75% (65 out of 80) were female and 18.75% (15 out of 80) were male. A similar pattern was observed in the control group, with females comprising 78.7% (85 individuals) and males 23.3% (23 individuals). Furthermore, research by Alicja Wierzbicka et al. highlights sex as a significant non-environmental determinant of vitamin D levels and their physiological impact. A growing body of evidence indicates that vitamin D concentrations vary between men and women, with women generally exhibiting a higher risk of deficiency. (21) In our study, we found that the highest number of hyperthyroid patients belongs to the age group of 25-49 years. In support of our study, Nermin A. Sheribaa et al. (22) showed that even young people can suffer from vitamin D deficiency. In contrast to our study, Arabi A et

al. and Vieth R et al. proposed that 25(OH) D levels were significantly lower in the elderly patients compared with young adults. (23,24)

The study demonstrated that individuals with hyperthyroidism have significantly lower levels of vitamin D receptors compared to healthy controls (0.49 ± 0.19 vs 2.51 ± 0.67; p = 0.0001). Additionally, serum 25(OH)D concentrations were markedly reduced in hyperthyroid patients. A strong inverse correlation was observed between 25(OH)D levels and both total T3 and total T4 ($p < 0.001$). Specifically, hyperthyroid patients had significantly lower 25(OH)D levels than controls (14.58 ± 3.19 vs. 22.09 ± 9.75; p = 0.0001). Notably, this negative association between 25(OH)D levels and hyperthyroidism remained significant even after adjusting for BMI, ionized calcium, and thyroid autoantibodies.

The findings of the present study align with those of Kivity et al., who reported significantly lower levels of 25(OH)D in patients with hyperthyroidism (Graves' disease (GD)) compared to healthy controls. (25) Some studies have found no significant difference in vitamin D levels between patients with Graves' disease (GD) and healthy controls. (26) Both preclinical and clinical research have identified a link between autoimmune thyroid disease (AITD) and low levels of vitamin D. [27,28]. In a cross-sectional study, Kim et al. reported that Graves' disease (GD) patients exhibited a higher prevalence of vitamin D insufficiency compared to healthy controls.[29]. Xu and colleagues conducted a comprehensive meta-analysis to explore the association between serum vitamin D levels and Graves' disease (GD), revealing that individuals with GD were significantly more likely to be deficient in vitamin D compared to healthy controls. (30)

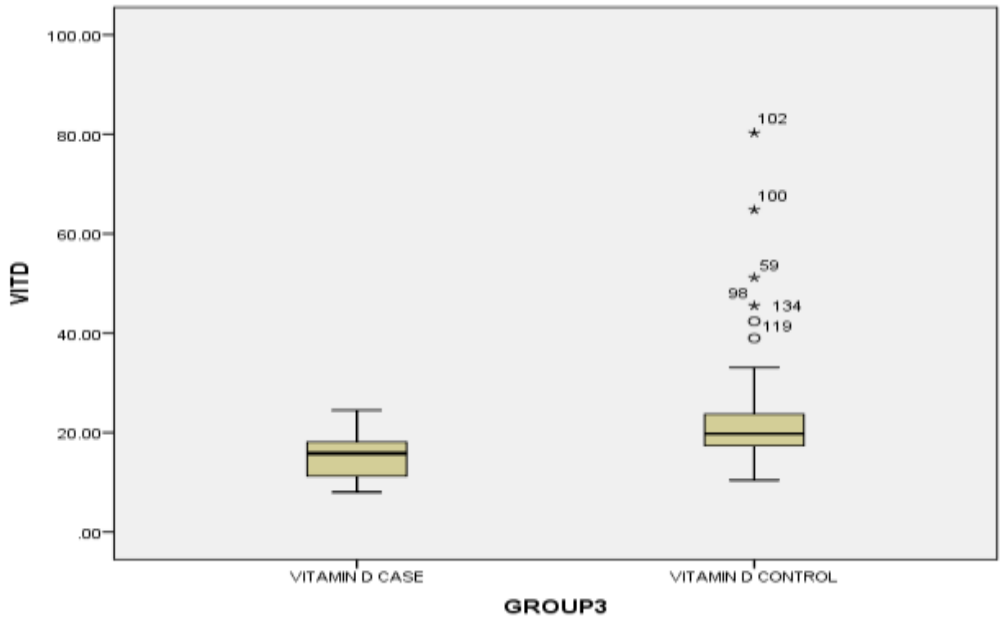
Our findings indicated an inverse relationship between vitamin D levels and the concentrations of anti-TPO and anti-TGA antibodies ($p< 0.001$). Zhang et al. observed that higher serum vitamin D levels were associated with lower TRAb concentrations. (31) The role of vitamin D in autoimmune thyroid disease remains controversial, with some studies supporting a connection (32,33), while others find no significant association (34, 35).

Expression of the vitamin D receptor (VDR) occurs in no fewer than 37 tissues. (36-38). Over 100 genomic promoter regions have been identified as containing VDR expression elements. (39-41). Furthermore, it is expected that intracellular VDR levels are influenced by various hormones and growth factors through both heterologous and homologous regulatory mechanisms. (42). Given that VDR is a member of the nuclear receptor superfamily and is also expressed on the cytoplasmic membrane, it is plausible that serum VDR levels may reflect the extent of its overall expression. McDonnell highlighted a compelling homology between the VDR and the thyroid hormone receptor. (43) Berg et al. demonstrated the VDR expression on follicular thyroid cells. (44)

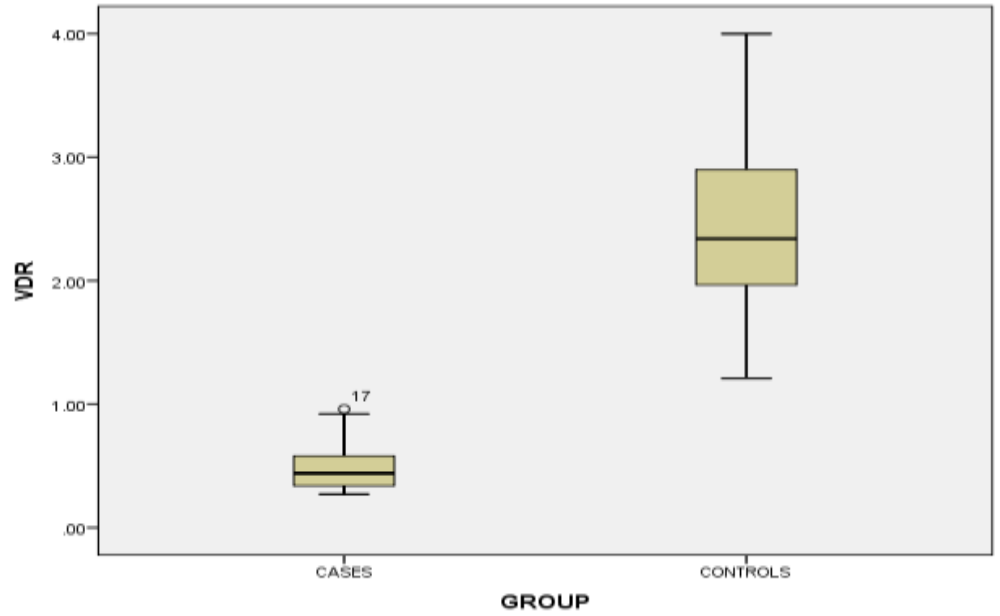
In the present study, VDR levels were significantly lower in hyperthyroid cases (0.49 ± 0.19) compared to controls (2.51 ± 0.67), with the difference being highly statistically significant ($p < 0.0001$). Supporting our study conducted in Saudi Arabia, Ayat B. Al Ghafari et al. (2020) (45) also found that serum vitamin D receptor levels were lower in colorectal cancer patients compared to healthy controls. (46). Unlike our findings, a study conducted in Antalya, Turkey by Seckin Ozgur Tekelli et al. reported higher serum VDR levels in gestational diabetes cases compared to controls. (47).

In individuals with hyperthyroidism, both total and ionized calcium levels were found to be significantly reduced compared to those in the control group. Hyperthyroid patients exhibited a total calcium level of 9.42 ± 0.63 mg/dL, which was significantly lower than the control group's level of 9.65 ± 0.45 mg/dL (p = 0.008). Ionized calcium levels were notably lower in hyperthyroid patients, averaging 0.85 ± 0.18 mmol/L, compared to 1.20 ± 0.72 mmol/L in the control group, showing a statistically significant difference ($p < 0.0001$). These findings are consistent with previous studies by Van Cromphaut et al. (2001) and Song et al. (2003) (48,49), which showed that intestinal vitamin D receptor (VDR) expression is essential for effective calcium absorption. Wang et al. (2015) (50) also emphasized the critical role of VDR in maintaining calcium balance within the kidney and bone.

This study investigates the association between vitamin D receptor (VDR), 25-hydroxyvitamin D [25(OH)D], and hyperthyroidism. Notably, it represents the first effort to measure serum VDR levels in patients diagnosed with hyperthyroidism. Furthermore, exploring polymorphisms in the VDR gene in hyperthyroid patients, along with examining serum levels of VDR and 25(OH)D, could offer important understanding into this persistent problem.



Graph 1: Comparison of vitamin D levels among cases and controls by box and whisker plot.



Graph 2: Comparison of VDR levels among cases and controls by box and whisker plot.

Conclusion:

This study reveals a notable relationship between the vitamin D receptor (VDR), 25(OH)D, and the levels of total T3 and total T4 in individuals with hyperthyroidism. It demonstrates an inverse correlation between VDR concentration and both T3 and T4 levels. Furthermore, the results show that serum VDR levels are reduced in hyperthyroid patients when compared to healthy individuals. Moreover, the analysis indicates possible positive association between VDR and various biochemical markers, highlighting the need for additional research. Nonetheless, the findings are constrained by the relatively small number of hyperthyroid cases included in the study. It highlights the importance of conducting larger and more thorough studies to gain a deeper understanding of the physiological mechanisms affected by these biochemical factors and their role in hyperthyroid disorders.

ABBREVIATION:

VDR: Vitamin D Receptor
ELISA: enzyme-linked immunosorbent assay
1,25 (OH) D3: 1, 25 dihydroxy vitamin D3
NIS: sodium/iodide symporter
T3: triiodothyronine thyroxine
T4: tetraiodothyronine
TPO: Thyroid Peroxidase
FT3: Free T3
FT4: Free T4
TSH: Thyroid Stimulating Hormone
AITD: Autoimmune Thyroid Diseases
HT: Hashimoto's thyroiditis
GD: Graves' disease
TFIIB: Transcription Factor IIB
VDRE: Vitamin D Responsive Elements
DNA: Deoxyribonucleic Acid
RXR-α: Retinoid X Receptor alpha
AF-1: Activation Function-1
NLS: Nuclear Localization Signals
ISE: Ion Selective Electrode
25(OH) D: 25-Hydroxy Vitamin D
HRP: Horseradish Peroxidase
TRAb: thyrotropin Receptor Antibody
OD: Optical Density
BMI: Body Mass Index
SGOT: serum glutamate-oxaloacetate transaminase
SGPT: Serum glutamate pyruvate transaminase
LDL: Low-Density Lipoprotein
HDL: High-Density Lipoprotein
ALP: Alkaline Phosphatase
I. Calcium: Ionised Calcium
T. Calcium: Total Calcium
SD: Standard Deviation
IQR: Interquartile Range
KoIMS: Kodagu Institute of Medical Sciences
IEC: Institutional Ethical Committee
CEC: Central Ethical Committee

Availability of data and material:
The data can be made available upon the author's approval

Competing interest:
The authors don't have a conflict of interest

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Authors contributions:
Conceptualization and study design: PN, RV, SKN. **Data collection:** PN, PKN, SKN. **Data analysis:** PN, RV, SKN, DDA, PKN. **Manuscript writing:** PN, RV, S, DDA **Manuscript editing and review:** PN, RV, S, DDA, PKN, SKN, SA, CKB, RH.

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