RESEARCH PAPER

Exploring The Role Of Vitamin D Receptor And 25(Oh) Vitamin D In The Pathophysiology Of Hypothyroidism

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ABSTRACT

Background: Thyroid hormone disorders are among the most prevalent diseases, significantly impacting public health in India and worldwide. Vitamin D has been associated with modulating thyroid neoplastic and autoimmune diseases, with the vitamin D receptor (VDR) acting as the primary receptor for vitamin D3.

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 hypothyroidism 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 216 participants (108 with thyroid abnormalities and 108 healthy controls), aged 18-70, who were 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 0.72 ± 0.30 and 2.26 ± 0.97, and 25(OH) D3 levels were 17.04 ± 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 indicate that serum VDR levels are significantly lower in patients with thyroid abnormalities than in healthy controls, suggesting that VDR may serve as a diagnostic marker for thyroid dysfunction..

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

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INTRODUCTION

Thyroid hormone disorders pose a major public health issue, impacting roughly 32% of the population in India and contributing to a considerable global burden (1). These hormones are crucial for regulating metabolism, growth, body temperature, the menstrual cycle, and the functioning of vital organs, including the lungs and heart (2). The production of thyroid hormones, triiodothyronine (T3), and thyroxine (T4) depends on the active transport of iodide through the sodium/iodide symporter (NaIS) and the iodination of thyroglobulin by thyroid peroxidase (TPO). The thyroid gland primarily secretes T4 in a ratio of about 14:1 relative to T3, with most T4 being converted into T3 in peripheral tissues (3, 4). Only around 0.03% of these hormones are present in their free form, while the rest are attached to plasma proteins. emphasizing the significance of free T3 and T4 in biological activity (5).

Hypothyroidism is a common endocrine disorder characterized by an underactive thyroid gland. The condition is associated with a variety of clinical manifestations, including fatigue, slow heart rate, sensitivity to cold, constipation, tiredness, weight gain, and depression. Recent investigations have revealed that the emergence of autoimmune thyroid diseases (AITD), such as

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Hashimoto's thyroiditis (HT), is driven by T-cell-mediated autoimmunity. (2)

Although iodine deficiency has long been recognized as a primary cause of thyroid disorders, recent research has highlighted other potential contributors, including vitamin D deficiency. Vitamin D, a fat-soluble vitamin, 25-hydroxyvitamin D [25(OH)D], the primary circulating form of vitamin D, serves as an important biomarker for vitamin D status in the body and plays a critical role in calcium metabolism, immune system regulation, muscle health, and bone development. Its deficiency has been linked to several autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and type 1 diabetes mellitus (6). The latest research has increasingly focused on the potential role of vitamin D in thyroid function. Emerging evidence suggests a possible interaction between vitamin D metabolism and thyroid function, especially in individuals with hypothyroidism. While the exact mechanisms through which vitamin D and its receptor influence thyroid function are not yet fully understood, several studies have proposed a link between low vitamin D levels and hypothyroidism. Notably, a 2011 study by Temer et al. was the first to document reduced vitamin D levels in patients with Hashimoto's thyroiditis (7).

The vitamin D receptor (VDR), identified through cloning in 1987, is present in various tissues, including the thyroid gland, mediates the biological effects of vitamin D, and functions as a ligand-dependent transcription factor, mediating the genomic effects of vitamin D (6, 8). VDR belongs to the nuclear receptor superfamily and shares a receptor system with thyroid hormones, suggesting potential interactions between these hormones and autoimmune thyroid disease (9). The VDR is a key member of the steroid-thyroid-vitamin D receptor gene superfamily (10), acting as a nuclear transcription factor. Previous studies have yielded inconsistent results, with some suggesting a weak or no significant association between hypothyroidism and vitamin D. To date, no studies have specifically investigated the relationship between VDR and hypothyroid conditions.

The current study aims to explore the relationship between the Vitamin D receptor (VDR) and 25-hydroxyvitamin D [25(OH)D] in individuals with hypothyroidism, with a particular focus on a South Indian population. A case-control design was employed to compare the levels of vitamin D and VDR expression between hypothyroid patients and healthy controls, aiming to better how vitamin D status contributes to the pathogenesis of hypothyroidism in this regional cohort.

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. The study included a total of 216 participants, comprising 108 cases and 108 age- and sex-matched controls, aged between 18 and 70 years. 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

Participants aged 18 to 70, of either sex, diagnosed with hypothyroidism (including both subclinical and overt forms), and willing to provide informed consent were eligible for inclusion in the study. 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 Gynecology (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 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 chemiluminescence hormone analyzer (Maglumi X3, Snibe China). Before the sample analysis, the instrument was standardized by processing the quality control and calibration. The direct competitive chemiluminescence immune assay method measured 25 (OH) vitamin D level. 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 was performed according to the manufacturer's recommendations: standards and serum samples were combined with a biotin-labeled monoclonal VDR antibody and a 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 were analyzed using SPSS version 26.0 (trial version). Continuous variables were assessed for normality before analysis. Normally distributed continuous variables were compared using the independent samples *t*-test, while non-normally distributed data were analyzed using the Mann–Whitney *U* test. For comparisons involving more than two groups, one-way analysis of variance (ANOVA) was applied to normally distributed continuous variables, whereas the Kruskal – Wallis' test was used for non-normally distributed continuous variables.

Categorical variables were analyzed using the Chi-square test to assess associations between groups. Pearson's correlation coefficient was employed to evaluate the relationship between vitamin D and thyroid function parameters (T3, T4, TSH, FT3, and FT4) in both normal and hypothyroid subjects. A *p*-value of less than 0.05 was considered statistically significant for all analyses.

RESULT

In this study involving 216 participants, we analyzed demographic and biochemical parameters between hypothyroid patients (n=108) and healthy controls (n=108). The hypothyroid group consisted of 14 males (12.96%) and 94 females (87.03%), while the control group included 23 males (21.29%) and 85 females (78.70%). The demographic data analysis for the study group (**Table 1**) revealed age distribution, indicating that most hypothyroid patients were between 27 and 50 years old, whereas controls were primarily aged 27 to 44 years. Statistical analysis revealed significant differences ($p < 0.05$) in body mass index (BMI), total cholesterol, triglycerides, SGPT, LDL, and total calcium between the hypothyroid patients and the control group. In contrast, parameters such as glucose, urea, creatinine, HDL, ALP, and SGOT showed no significant differences between the two groups

Test parameters	**Hypothyroid (n=108)**	**Normal (n=108)**	**P value**
Age (years) 18-26 27-35 36-44 45-53 54-62 63-71	 17 29 28 22 07 05	 07 51 25 15 05 05	Not applicable
BMI (kg/m^2)	25.37 ± 5.45	23.56 ±4.62	0.010
Glucose (mg/dL)	105.38± 23.68	98.33±12.89	0.075
Urea (mg/dL)	21.41±4.98	20.68±5.58	0.936
Creatinine (mg/dL)	0.86±0.23	0.83±0.25	0.131
T. Cholesterol (mg/dL)	207.7±54.64	187.99±52.94	0.003
Triglyceride (mg/dL)	175.17±80.39	167.73±75.29	0.004
HDL (mg/dL)	45.08±12.6	44.35±12.63	0.535
LDL (mg/dL)	139.11 ± 44.25	130.29± 44.19	0.001
ALP (IU/L)	91.96 ± 32.21	90.34 ± 32.85	0.548
AST (IU/L)	24.1 ± 9.26	24.13 ± 9.11	0.952
ALT (IU/L)	11.77 ± 5.58	19.59 ± 10.7	<0.001
T. Calcium (mg/dL)	9.28 ± 0.76	9.65 ± 0.45	0.008

Table 1: Showing various baseline characteristics among hypothyroid cases and controls.
*Data expressed in Mean ± SD, Independent t-test used, $p < 0.05$ is considered statistically significant.

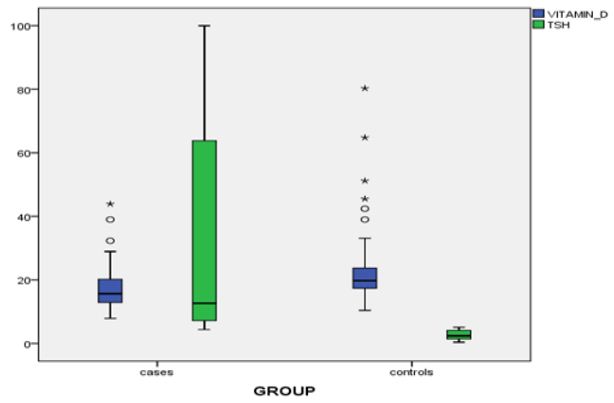
Determination of thyroid profile and serum levels of vitamin D in hypothyroid cases and controls

In a study evaluating hypothyroidism, levels of T3, T4, TSH, free T3 (FT3), and free T4 (FT4) were analyzed. Independent t-tests and Mann-Whitney U tests revealed a highly significant reduction in T3, T4, FT3, and FT4 levels in the hypothyroid group compared to the control group, along with a considerably elevated TSH level in the hypothyroid cases ($p < 0.05$). Hypothyroidism was classified into two categories based on thyroid hormone levels: subclinical hypothyroidism (n = 71, 65.74%) and overt hypothyroidism (n = 37, 34.26%). Autoimmune thyroid disease was confirmed through the measurement of thyroid antibodies, including anti-TPO and anti-TGA.

Analysis via Mann-Whitney U tests revealed a significant increase in TPO antibody levels in hypothyroid cases (890 [32.8–922.9]) compared to controls (14.19 [4.52–18.75]). Similarly, TGA antibody levels were significantly elevated in the hypothyroid group [277.81 (18.45–296.25)] compared to controls [29.25 (6.84–36.3)], both showing significant differences between hypothyroid and control groups ($p < 0.05$)

Test parameters	Hypothyroid (N= 108)	Normal (N= 108)	*p* values (<0.05)
T3	1.24 ± 0.36	1.41±0.36	0.002
T4	54.18 ± 23.78	72.69 ± 14.42	<0.001
TSH	57.63 (7.07 – 64.7)	2.63 ± 1.41	<0.001
F T3	0.83 (2.41-3.25)	3.03 ± 0.58	0.002
FT4	4.52 (7.70 - 12.22)	12.12 ± 3.23	<0.001
Anti-TPO	890 (32.8-922.9)	14.19 (4.52-18.75)	<0.001
Anti-TGA	277.81 (18.45-296.25)	29.25 (6.84-36.3)	<0.001
25 (OH) D	17.04 ± 6.03	22.09 ± 9.75	<0.0001
VDR	0.84 ± 0.3	2.51± 0.67	<0.0001
I. Calcium	0.79 ± 0.19	1.20 ±0.72	<0.0001

Table 2 shows a comparison of serum 25 (OH) D, Vitamin D Receptor, Thyroid profile, thyroid peroxidase antibody, thyroglobulin antibody, and ionized calcium between the hypothyroid case and the control group
*Data expressed in Mean ± SD, Median (IQR). Independent t-test and Mann-Whitney U test used; *p* <0.05 is considered statistically significant.



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

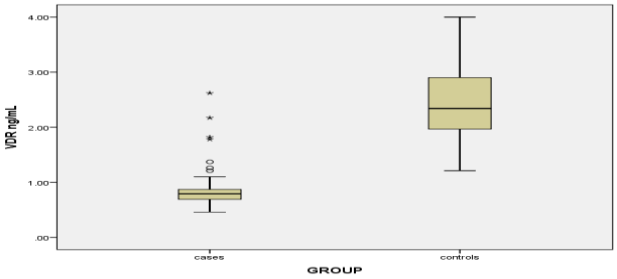
The results from **Graph 1** indicate a significant negative correlation between vitamin D and TSH levels in cases, with a correlation coefficient of r = -0.230 (p = 0.017), suggesting that lower vitamin D concentrations are associated with higher TSH levels in the case group. In contrast, no significant correlation was observed in the control group (r = -0.075, p = 0.464), indicating that vitamin D and TSH levels are not related in this group. The median vitamin D concentration was lower in the cases (15.65 ng/mL, interquartile range 7.36) compared to the controls (19.77 ng/mL, interquartile range 6.38), and similarly, the median TSH value was markedly higher in the cases (12.64 µU/mL, interquartile range 57.63) than in the controls (2.37 µU/mL, interquartile range 2.73). These findings highlight a significant association between vitamin D and TSH in cases, which was not evident in the control group.

Determination of 25 (OH) D and VDR

The level of vitamin D for all the participants was measured. In this study, according to the vitamin D level, the abnormal thyroid patients and controls were classified into two groups. 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 hypothyroid patients (17.04 ± 6.03 n=108) 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 = 76) vs (16.65 ± 2.4 n = 59) (p=0.0001). (Table 3) The comparison between serum levels of vitamin D receptor (VDR) showed that hypothyroid patients had very low concentrations of VDR in their serum (0.84 ± 0.3) compared to healthy controls (2.51± 0.67) (p < 0.001). Another biochemical parameter, ionised calcium, showed a considerably lower concentration in hypothyroid patients (0.79 ± 0.19) than in healthy controls (1.20 ±0.72) (p <0.0001). (Table 3)

Test parameters	Hypothyroid (n=108)	Normal (n=108)	P value
25 (OH) D (ng/mL)	17.04 ± 6.03	22.09 ± 9.75	<0.0001
< 20 (ng/mL)	14.4±3.36 (n = 76)	16.65 ± 2.4 (n = 59)	0.0001
21-29 (ng/mL)	23.09±2.44 (n = 29)	23.4± 2.52 (n = 37)	0.3082
> 30(ng/mL)	38.4±5.82 (n = 03)	42.96±15.6 (n = 12)	0.3172
VDR (ng/mL)	0.84±0.3	2.51± 0.67	<0.0001
I. calcium (mmol/L)	0.79 ± 0.19	1.20 ±0.72	<0.0001

Table 3 shows 25-hydroxy vitamin D (25(OH)D), Vitamin D Receptor (VDR), and Ionised Calcium (I. calcium) among study subjects.
*Data expressed in Mean ± SD, Independent t-test used, *p* <0.05 is considered statistically significant.



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

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 0.79 with an interquartile range (IQR) of 0.18, 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 abnormalities represent one of the most common forms of endocrine dysfunction, with Autoimmune Thyroid Disease (AITD) being the most prevalent autoimmune disorder globally (11,12). Existing research has predominantly focused on the relationships between hypothyroidism, vitamin D deficiency, and Vitamin D Receptor (VDR) mutations. However, there is a notable lack of studies examining circulating serum VDR levels as a potential diagnostic marker for hypothyroidism. This study aims to investigate serum VDR levels in hypothyroid patients and assess their correlation with vitamin D levels, thyroid profiles, and various biochemical parameters. Our findings suggest a significant association between serum VDR levels and hypothyroid conditions, highlighting the potential of serum VDR as a valuable diagnostic tool in managing thyroid dysfunction.

In our demographic findings, we observed that hypothyroidism affects 87.3% (94) of the total population (108), a trend that was also evident in the control group, where 78% (85) of individuals were affected. Additionally, as demonstrated by Alicja Wierzbicka et al., sex is a crucial non-environmental factor influencing the levels and effects of vitamin D. Numerous studies have shown that vitamin D levels differ between men and women, with females being more susceptible to vitamin D deficiency. (13)

The study found that vitamin D receptor levels are lower in hypothyroid cases than in controls. Moreover, 25 (OH) D level is also decreased in hypothyroid patients compared to controls. There is a significant negative correlation between 25 (OH) D level and TSH, with p-value <0.001. Compared to the control, the hypothyroid patients exhibited significantly lower 25 (OH) D levels, 17.04 ± 6.03 vs 22.09 ± 9.75 (p = 0.0001). This negative correlation between hypothyroidism and 25(OH)D level is independent of BMI, ionized calcium, and thyroid antibodies.

The current study is supported by Bozkurt et al., who demonstrated that 25 (OH) D levels in hypothyroid (Hashimoto's thyroiditis) patients were significantly lower than those of controls. (14) Another study by Hoda A. et, al. (2019) demonstrated that vitamin D levels are lower in hypothyroid cases than in controls (15) contrary to our result, Goswamy et, al. conducted a study on the prevalence of vitamin D deficiency and its relationship with thyroid hormones and thyroid abnormality, but they observed no significant difference between thyroid hormones in AITD and vitamin D levels. (16) A case-control study conducted in Saudi Arabia by Musa et al. (2017) found an insignificant difference in the level of vitamin D among women with hypothyroidism in comparison with the control. One more cross-sectional study conducted in Portugal in 2017 also showed a result contradictory to our study. They did not find any significant association or correlation between vitamin D, TSH, FT3, and FT4 levels after adjustment for sex and age. The difference between these studies and our study may be due to different sample sizes, populations, and geographical areas. (17,18)

We also revealed the fact that vitamin D was inversely proportional to anti-TPO and anti-TGA, p< 0.001. About the role of vitamin D in autoimmune thyroid disease, the data available is still controversial. Some authors support the data (19-20), and some do not support it (16, 21).

Vitamin D receptor (VDR) is expressed in at least 37 different tissues. (22-24). More than 100 genomic promoter regions have also been found to contain VDR expression. (25-27). Moreover, it is not surprising that intracellular VDR concentration is regulated by other hormones and growth factors. Both homologous and heterologous regulation (28). The fact that VDR is a member of the nuclear receptor superfamily, which is also expressed on the cytoplasmic membrane, suggests that the amount of VDR in serum may be directly proportional to VDR expression. In the current study the VDR level is low in the hypothyroid case (0.8±0.3) vs control (2.51±0.67) (p<0.0001) by supporting our study conducted in Saudi Arabia by Ayat B Al Ghafari et, al. (2020) (30) demonstrated that serum vitamin D receptor level is low in the case (colorectal cancer) than controls (29). In contrast to our study, a study conducted in Antalya, Turkey, by Seckin Ozgur Tekelli et al. showed that serum VDR level is higher in the case (Gestational Diabetes) than in the control (31).

In cases of hypothyroidism, both total calcium and ionized calcium levels were significantly lower compared to controls. The total calcium level in hypothyroid patients was found to be 9.28 ± 0.76 mg/dL, which is a significant decrease compared to the control group's level of 9.65 ± 0.45 mg/dL (p = 0.008). Similarly, ionized calcium levels were also significantly reduced in hypothyroid cases, with measurements of 0.79 ± 0.19 mmol/L compared to 1.20 ± 0.72 mmol/L in the control group (p < 0.0001). These findings are supported by previous studies, including those by Van Cromphaut et al. (2001) and Song et al. (2003) (32,33), which demonstrated that vitamin D receptor (VDR) levels in the intestine play a crucial role in regulating efficient calcium absorption. Furthermore, Wang et al. (2015) (34) highlighted the importance of VDR in calcium homeostasis at the level of the kidney and bone.

This study is the first to estimate serum Vitamin D Receptor (VDR) levels in individuals with hypothyroidism, providing valuable insight into the relationship between vitamin D, VDR, and hypothyroidism. Examining both serum VDR and 25-hydroxyvitamin D [25(OH)D] levels, it offers a comprehensive understanding of the interplay between vitamin D metabolism and thyroid function. However, as the study is purely case-control and not longitudinal, it can only suggest an association, rather than establish causation, between vitamin D levels and hypothyroidism. The lack of a longitudinal design limits the ability to assess the long-term effects of changes in VDR or 25(OH)D levels on the progression of hypothyroidism or treatment outcomes

CONCLUSION:

This study highlights a significant association between vitamin D receptor (VDR) levels and thyroid-stimulating hormone (TSH) levels in hypothyroid patients, demonstrating a negative correlation between VDR concentration and TSH. The findings indicate that VDR levels are decreased in the serum of hypothyroid patients compared to healthy controls. Additionally, the analysis suggests potential positive correlations between VDR and other biochemical parameters, which warrant further investigation. However, this study is limited by the relatively small sample size of hypothyroid cases. It emphasizes the need for larger, more comprehensive studies to better understand the physiological processes influenced by these biochemical factors and their contributions to hypothyroid conditions.

Future scope: This research could serve as a foundation for future studies investigating the broader implications of VDR and vitamin D in thyroid health, especially given the increasing interest in personalized medicine. A longitudinal study design allows for assessing the long-term effects of changes in VDR or 25(OH)D levels on the progression of hypothyroidism or treatment outcomes. Examining VDR gene polymorphisms in hypothyroid individuals could uncover genetic variations that may explain variations in vitamin D metabolism or susceptibility to hypothyroidism

ABBREVIATION:

VDR: Vitamin D Receptor
ELISA: enzyme-linked immunosorbent assay
1,25 (OH) D3: 1, 25 dihydroxy vitamin D3
NaIS: 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
DNA: Deoxyribonucleic Acid
ISE: Ion Selective Electrode
25(OH) D: 25 Hydroxy Vitamin D
HRP: Horseradish Peroxidase
OD: Optical Density
BMI: Mass Index
SGOT: serum glutamic-oxaloacetic transaminase
SGPT: Serum glutamic pyruvic transaminase
LDL: Low-Density Lipoprotein
HDL: High-Density Lipoprotein
ALP: Alkaline Phosphatase
I. Calcium: Ionised Calcium
T. Calcium: Total Calcium
SD: Standard Deviation
IQR: Inter Quartile Range
KoIMS: Kodagu Institute of Medical Sciences
IEC: Institutional Ethical Committee
CEC: Central Ethical Committee

Availability of data and material:

The data can be available upon the author's approval

Competing interest:

The authors don't have a conflict of interest

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Author's contributions:

Conceptualization and study design: PN, RV. **Data collection:** PN, PKN, **Data analysis:** PN, RV, DDA, PKN, **Manuscript writing:** PN, RV, S, DDA, **Manuscript editing and review:** PN, RV, S, DDA, PKN.

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