



ASSOCIATION OF VITAMIN D STATUS WITH THYROID FUNCTION AND BIOCHEMICAL PARAMETERS IN NEWLY DIAGNOSED PRIMARY HYPOTHYROIDISM: A CASE–CONTROL STUDY.

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Abstract

Background: Vitamin D plays an important role in immune modulation and endocrine regulation. Deficiency has been associated with autoimmune thyroid disorders and altered metabolic parameters. Data from Indian populations remain limited.

Objective: To assess serum vitamin D levels in newly diagnosed primary hypothyroidism and evaluate their association with thyroid function and biochemical parameters.

Methods: A hospital-based case–control study was conducted including 50 patients with newly diagnosed primary hypothyroidism and 50 age- and sex-matched healthy controls. Serum FT3, FT4, TSH, vitamin D, anti-TPO antibodies, and calcium were measured. Statistical analysis included comparison of means and correlation analysis.

Results: Mean serum vitamin D levels were significantly lower in cases (18.50 ± 12.20 ng/ml) compared to controls (37.14 ± 16.90 ng/ml) ($p < 0.001$). FT3 and FT4 levels were significantly lower, while TSH and anti-TPO antibody levels were significantly higher in cases. Correlation analysis showed a weak positive correlation between vitamin D and FT3 ($r = 0.134$, $p > 0.05$) and a moderate positive correlation between vitamin D and serum calcium ($r = 0.494$, $p < 0.05$).

Conclusion: Vitamin D deficiency is highly prevalent in hypothyroid patients and is associated with altered thyroid function and calcium metabolism. Screening and correction of deficiency may have clinical benefits.

Keywords: Hypothyroidism, Vitamin D deficiency, Thyroid function, Anti-TPO antibodies, Case–control study

Introduction

Hypothyroidism is one of the most common endocrine disorders, characterized by reduced production of thyroid hormones and elevated thyroid-stimulating hormone levels. Subclinical and overt hypothyroidism are associated with metabolic disturbances and increased cardiovascular risk, and early recognition and management are important in clinical practice.^{1–3}

Interpretation of thyroid function tests requires careful evaluation of TSH and thyroid hormone levels, particularly in early or minor thyroid dysfunction.⁴ Population-based studies have

demonstrated a significant prevalence of thyroid disorders and thyroid autoimmunity in different regions of the world.¹⁹

Vitamin D deficiency is highly prevalent globally and is considered an important public health issue affecting multiple organ systems.^{5–7} Vitamin D plays a key role in calcium metabolism, immune regulation, and cellular differentiation.^{6,9,10} In addition to its classical skeletal effects, vitamin D has been shown to influence several non-musculoskeletal systems, including endocrine and immune pathways.¹¹ Emerging evidence suggests a relationship between vitamin D status and thyroid disorders. Vitamin D receptors and activating enzymes have been identified in thyroid tissue, suggesting a potential biological role of vitamin D in thyroid function and autoimmunity.^{12,13} Several studies have reported a high prevalence of vitamin D deficiency in patients with hypothyroidism and autoimmune thyroid disease.^{14–18}

Vitamin D deficiency may contribute to thyroid dysfunction through immunomodulatory mechanisms, including altered T-cell activity, cytokine production, and autoantibody formation.^{10,12} Some interventional studies have also reported improvement in metabolic parameters and thyroid function following vitamin D supplementation, highlighting its possible therapeutic role.

Despite increasing evidence, data from Indian populations evaluating vitamin D status and its association with thyroid function and biochemical parameters remain limited. Therefore, the present study was conducted to assess serum vitamin D levels and their association with thyroid function tests and biochemical parameters in newly diagnosed primary hypothyroidism.

Aim

To evaluate serum vitamin D levels and their association with thyroid function and selected biochemical parameters in patients with newly diagnosed primary hypothyroidism.

Objectives

To compare serum vitamin D levels between patients with newly diagnosed primary hypothyroidism and healthy controls, to assess thyroid function parameters (FT3, FT4, and TSH), anti-TPO antibody levels, and serum calcium, and to evaluate the correlation between serum vitamin D levels and selected biochemical parameters.

Materials and Methods

Study Design and Setting

This hospital-based case–control study was conducted in the Department of Medicine at SMS Hospital, Jaipur over a period of 17 months from April 2014 to August 2015.

Study Population

The study included patients aged 20–50 years who were newly diagnosed with primary hypothyroidism and an equal number of age- and sex-matched healthy individuals serving as controls.

Inclusion Criteria

- Newly diagnosed primary hypothyroidism
- Age between 20 and 50 years
- Willingness to participate and provide informed consent

Exclusion Criteria

- Patients receiving vitamin D supplementation
- Pregnancy
- Chronic kidney disease or chronic liver disease
- Known metabolic bone disease
- Other endocrine disorders or serious systemic illness

Sample Size

A total of 100 subjects were included in the study, comprising 50 cases and 50 controls.

Data Collection

A detailed clinical history and physical examination were performed for all participants. Demographic details and relevant clinical information were recorded in a predesigned proforma.

Laboratory Investigations

Venous blood samples were collected under aseptic precautions. The following investigations were performed:

- Serum FT3
- Serum FT4
- Serum TSH
- Serum 25-hydroxyvitamin D
- Anti-thyroid peroxidase (Anti-TPO) antibodies
- Serum calcium

All biochemical investigations were carried out using standard laboratory methods in the institutional laboratory.

Definitions

Vitamin D status was classified as follows:

- Deficient: <20 ng/ml
- Insufficient: 20–30 ng/ml
- Sufficient: >30 ng/ml

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using statistical software. Continuous variables were expressed as mean $\pm$ standard deviation. Differences between cases and controls were analyzed using the independent Student's t-test. Correlation between vitamin D levels and biochemical parameters was assessed using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion in the study

Results

Table 1: Distribution of Cases and Controls According to Age and Sex

Age Group (years)	Cases Male	Cases Female	Total Cases	Controls Male	Controls Female	Total Controls
20–30	5	9	14	5	6	11
31–40	12	15	27	10	19	29
41–50	3	6	9	3	7	10
Total	20	30	50	18	32	50

A total of 100 subjects were included in the study, comprising 50 cases of newly diagnosed primary hypothyroidism and 50 healthy controls. The majority of participants in both groups belonged to the 31–40 years age group, and females constituted a larger proportion of cases as well as controls.

Table 2: Comparison of Mean Age Between Cases and Controls

Parameter	Cases (Mean $\pm$ SD)	Controls (Mean $\pm$ SD)	p-value
Age (years)	34.14 $\pm$ 6.95	35.28 $\pm$ 6.67	>0.05

The mean age of cases and controls was comparable, and the difference was not statistically significant, indicating proper matching of study groups.

Table 3: Comparison of Biochemical Parameters Between Cases and Controls

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	p-value
FT3	1.69 ± 0.60	2.70 ± 0.76	<0.001
FT4	0.90 ± 0.40	1.34 ± 0.28	<0.001
TSH	18.83 ± 7.41	2.12 ± 1.04	<0.001
Vitamin D	18.50 ± 12.20	37.14 ± 16.90	<0.001
Anti-TPO	266.2 ± 36.62	31.59 ± 8.23	<0.001
Calcium	8.43 ± 1.40	9.16 ± 0.97	<0.001

Serum FT3 and FT4 levels were significantly lower in cases compared to controls, while TSH levels were significantly higher, confirming thyroid dysfunction. Vitamin D levels were markedly reduced in hypothyroid patients. Anti-TPO antibody levels were significantly higher among cases, suggesting autoimmune thyroid disease in a substantial proportion of patients. Serum calcium levels were also significantly lower in cases compared to controls.

Table 4: Correlation of Vitamin D with Biochemical Parameters

Parameter	Correlation coefficient (r)	p-value	Interpretation
FT3	0.134	>0.05	Weak positive correlation
Serum Calcium	0.494	<0.05	Moderate positive correlation

Correlation analysis demonstrated a weak positive correlation between serum vitamin D and FT3 levels, which was not statistically significant. A moderate positive correlation was observed between vitamin D and serum calcium levels, which was statistically significant, indicating an association between vitamin D status and calcium metabolism.

Summary

Overall, the study demonstrated significantly lower vitamin D levels in patients with primary hypothyroidism compared to healthy controls. Thyroid function parameters and anti-TPO antibody levels showed statistically significant differences between cases and controls, and correlation analysis suggested an association of vitamin D with selected biochemical parameters.

Discussion

The present study demonstrated significantly lower serum vitamin D levels in patients with newly diagnosed primary hypothyroidism compared to healthy controls. Thyroid hormone levels (FT3 and FT4) were significantly reduced, while TSH levels were significantly elevated in cases, confirming thyroid dysfunction. These findings are consistent with previous studies describing biochemical alterations in hypothyroidism and the importance of accurate interpretation of thyroid function tests.^{3,4}

Vitamin D deficiency is highly prevalent worldwide and has been recognized as a major public health concern affecting multiple organ systems.^{5–7} In addition to its classical role in calcium and bone metabolism, vitamin D plays an important role in immune regulation and endocrine function.^{6,9,10} The non-skeletal effects of vitamin D, including its role in metabolic and endocrine pathways, have been increasingly recognized in recent years.¹¹

Several studies have suggested a relationship between vitamin D deficiency and thyroid dysfunction. Vitamin D receptors and activating enzymes have been identified in thyroid tissue, supporting a potential biological role of vitamin D in thyroid physiology and autoimmune mechanisms.^{12,13} Previous observational studies have also reported a higher prevalence of vitamin D deficiency in patients with hypothyroidism and autoimmune thyroid disease.^{14–18}

In the present study, anti-TPO antibody levels were significantly higher in hypothyroid patients, suggesting autoimmune etiology in a substantial proportion of cases. Vitamin D deficiency may contribute to autoimmune thyroid disease through immunomodulatory mechanisms, including altered T-cell activity and cytokine regulation.^{10,12}

Correlation analysis in this study demonstrated a positive association between serum vitamin D and calcium levels, which was statistically significant. This finding is consistent with the well-established physiological role of vitamin D in calcium homeostasis and mineral metabolism.⁶

Overall, the findings of the present study support the growing body of evidence indicating an association between vitamin D deficiency and thyroid dysfunction. Routine assessment of vitamin D status in hypothyroid patients may be beneficial, and further prospective studies are required to evaluate the long-term therapeutic effects of supplementation.

Conclusion

The present study demonstrated that serum vitamin D levels were significantly lower in patients with newly diagnosed primary hypothyroidism compared to healthy controls. Thyroid function parameters and anti-TPO antibody levels showed significant differences between cases and controls, and vitamin D levels were positively associated with serum calcium levels.

These findings suggest that vitamin D deficiency is common in hypothyroid patients and may play a role in thyroid dysfunction and metabolic alterations. Assessment of vitamin D status at the time of diagnosis may be beneficial in the comprehensive management of hypothyroidism

Limitations

1. The study was conducted at a single center, which may limit generalizability of the findings.
2. The sample size was moderate.
3. Follow-up of patients after vitamin D supplementation was not performed, so therapeutic outcomes could not be assessed.
4. Some biochemical correlations were limited to available parameters, and broader metabolic assessment was not included.

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Recommendations

1. Screening for vitamin D deficiency may be considered in patients with newly diagnosed hypothyroidism.
2. Larger multicentric studies are recommended to further evaluate the association between vitamin D status and thyroid dysfunction.
3. Prospective interventional studies are needed to assess the effect of vitamin D supplementation on thyroid function and clinical outcomes.
4. Public health strategies to address widespread vitamin D deficiency may contribute to improved endocrine and metabolic health.

References

1. Biondi B, Cappola AR, Cooper DS. Subclinical hypothyroidism: a review. *JAMA*. 2019;322(2):153-160.
2. Monteiro-Martins S, Sterenborg R, Borisov O, et al. New insights into the hypothalamic-pituitary-thyroid axis: a transcriptome- and proteome-wide association study. *Eur Thyroid J*. 2024;13:e240067.
3. Azim S, Nasr C. Subclinical hypothyroidism: when to treat. *Cleve Clin J Med*. 2019;86(2):101-110.
4. Andersen S, Karmisholt J, Bruun NH, et al. Interpretation of TSH and T4 for diagnosing minor alterations in thyroid function: a comparative analysis of two separate longitudinal cohorts. *Thyroid Res*. 2022;15:19.

5. Meshkin A, Badiie F, Salari N, Hassanabadi M, Khaleghi AA, Mohammadi M. The global prevalence of vitamin D deficiency in the elderly: a meta-analysis. *Indian J Orthop.* 2024;58(2):223-230.
6. Bikle D, Christakos S. New aspects of vitamin D metabolism and action—addressing the skin as source and target. *Nat Rev Endocrinol.* 2020;16(4):234-252.
7. Cui A, Zhang T, Xiao P, Fan Z, Wang H, Zhuang Y. Global and regional prevalence of vitamin D deficiency in population-based studies from 2000 to 2022: a pooled analysis of 7.9 million participants. *Front Nutr.* 2023;10:1070808.
8. Tracer H, West R. Screening for vitamin D deficiency in adults. *Am Fam Physician.* 2021;104(5):515-516.
9. Mazloom S, Kalayeh SMO, Najafpour A, Naeini SM, Esfandani A. The role of vitamin D in body organ systems: a systematic review. *Arch Pharm Pract.* 2020;11(1):169.
10. Ghaseminejad-Raeini A, Ghaderi A, Sharafi A, et al. Immunomodulatory actions of vitamin D in various immune-related disorders: a comprehensive review. *Front Immunol.* 2023;14:950465.
11. Zhang S, Miller DD, Li W. Non-musculoskeletal benefits of vitamin D beyond the musculoskeletal system. *Int J Mol Sci.* 2021;22(4):2128.
12. Babić Leko M, Jureško I, Rozić I, Pleić N, Gunjača I, Zemunik T. Vitamin D and the thyroid: a critical review of the current evidence. *Int J Mol Sci.* 2023;24(4):3586.
13. Khadzkou K, Buchwald P, Westin G, Dralle H, Akerström G, Hellman P. 25-hydroxyvitamin D3 1 α -hydroxylase and vitamin D receptor expression in papillary thyroid carcinoma. *J Histochem Cytochem.* 2006;54(3):355-361.
14. Tabrizi R, Moosazadeh M, Akbari M, et al. High prevalence of vitamin D deficiency among Iranian population: a systematic review and meta-analysis. *Iran J Med Sci.* 2018;43(2):125-139.
15. Elamawy M, Gouda Ameen S. Vitamin D deficiency in subclinical hypothyroid dysfunction patients: a case control study. *Benha Med J.* 2021;38:xxx-xxx.
16. Guo Y, Wu CY, Deng YH, Wu JL. Associations between serum 25-hydroxyvitamin D levels and thyroid function parameters in previously healthy children aged 6 to 24 months. *Risk Manag Healthc Policy.* 2020;13:1647-1653.
17. 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. *Open Access Maced J Med Sci.* 2017;5(2):126-130.
18. Aljohani NJ, Al-Daghri NM, Al-Attas OS, et al. Differences and associations of metabolic and vitamin D status among patients with and without subclinical hypothyroid dysfunction. *BMC Endocr Disord.* 2013;13:31.