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Original Research Article

A Population-based Assessment of the Association between Vitamin D Deficiency and Hypothyroidism

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Abstract

Aim: To evaluate the relationship between hypothyroidism and vitamin D levels.

Material & Methods: For this study, a total of 250 patients were selected. This study was conducted in the Department of Pathology, Government Medical College, Bettiah, Bihar, India. All participants who were ≥ 18 years of age had signed a written informed consent following an extensive and detailed description about the survey including the interview, medical examination and laboratory evaluation.

Results: A total of 250 participants were included in this study, of which 25 (10%) were having hypothyroidism. The man age of this cohort was 47.2 years and 53.4% were females. About 55.8% of the participants had more than 12 years of formal education. Comparison of clinical characteristics between hypothyroid patients and normal controls also showed significant difference in majority of the factors. There was a significant association ($P < 0.001$) between vitamin D categories and hypothyroid state.

Conclusion: Low vitamin D levels are associated with autoimmune hypothyroidism. Healthcare initiatives such as mass vitamin D deficiency screening among at-risk population could significantly decrease the risk for hypothyroidism in the long-term.

Keywords: Hypothyroidism, Low vitamin D, Autoimmune, Thyroid peroxidase, Thyroglobulin

Introduction

Vitamin D deficiency is a global health problem. [1] Over a billion people worldwide are vitamin D deficient or insufficient. [1] Yet no international health organization or governmental body has declared a health emergency to warn the public about the urgent need of achieving sufficient vitamin D blood levels. [2] Understanding of the role of vitamin D has been evolving since its discovery in the early 20th century from being a simple vitamin to a steroid pro-hormone. [3] It has been recognized to be involved in various immune functions as well as bone and muscle development. [3] Vitamin D deficiency has been shown to be associated with autoimmune diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD),

multiple sclerosis (MS) and type 1 diabetes (T1DM), and that vitamin D supplementation prevents the onset and/or development of these autoimmune diseases. [4] Furthermore, it was reported that patients with Hashimoto's thyroiditis, an autoimmune thyroid disease had lower vitamin D levels. [5] Vitamin D plays an essential role in calcium homeostasis and the development and maintenance of the skeleton. [6]

Many autoimmune diseases, such as pernicious anemia, myasthenia gravis, idiopathic hypoparathyroidism, vitiligo, celiac disease, type 1 diabetes mellitus, autoimmune liver diseases, primary biliary cirrhosis, multiple sclerosis, Addison's disease, rheumatoid arthritis, and systemic lupus erythematosus, may accompany HT [7]. Vitamin B12 (vit-B12) deficiency has been reported frequently in autoimmune thyroid patients [8]. This association is probably due to impaired absorption of vit-B12 by atrophic gastritis and/or pernicious anemia associated with autoimmune thyroid disease [9].

Hypothyroidism (HT) is an autoimmune disease and studies suggest that vit-D deficiency has an effect on the etiopathogenesis of the disease. In addition, vit-B12 deficiency is frequently seen in this disease [8].

Hence, we aim to evaluate the relationship between hypothyroidism and vitamin D levels using a population-based data.

Material & Methods:

For this study, a total of 250 patients were selected. This study was conducted in the Department of Pathology, Government Medical College, Bettiah, Bihar, India for five months. All participants who were ≥ 18 years of age had signed a written informed consent following an extensive and detailed description about the survey including the interview, medical examination and laboratory evaluation. Details of the methods and protocols for the questionnaires, laboratory, and examination can be found elsewhere.

Vitamin D status:

For this study, we categorized participants into three clinically relevant categories based on the serum 25(OH) D levels following the Endocrinology Society Clinical Practice Guidelines. The three categories are optimal (≥30 ng/mL), intermediate (20 to < 30 ng/mL) and deficient (< 20 ng/mL) vitamin D levels.

Hypothyroidism:

We used the laboratory reference range of thyroid stimulating hormone (TSH), 0.34–5.60 mIU/L, from manufacturer's studies, for diagnosing hypothyroidism. Participants were defined as hypothyroid if their TSH was more than 5.60 mIU/L or were on levothyroxine. Participants were categorized as normal controls if their TSH was between 0.34–5.60 mIU/L and they were not taking any thyroid medication.

Statistical analysis was performed using SAS (version 9.4, SAS Institute, Cary, North Carolina), which accounted for the complex survey design and clustering. Demographic and socioeconomic measures were compared between hypothyroid patients and normal controls using independent samples t test for continuous variables and Chi-square test for categorical variables. Similarly, clinical characteristics of hypothyroid patients and normal controls were compared. Weighted multivariable logistic regression analyses were used to calculate the odds of being hypothyroid based on vitamin D status, after adjusting for covariates such as age, education, income, smoking, alcohol consumption, body mass index (BMI), physical activity, hypertension, diabetes, dyslipidemia, blood urea nitrogen, creatinine and magnesium levels.

Results:

A total of 250 participants were included in this study, of which 25 (10%) were having hypothyroidism. The man age of this cohort was 47.2 years and 53.4% were females. About 55.8% of the participants had more than 12 years of formal education. More than half of the participants (57.3%) reported that they had engaged in some form of physical activity and 74.8% never smoked and 78.9% currently consumed alcohol. Significant differences were observed in all demographics and socioeconomic factors between hypothyroid patients and normal control (Table 1).

Comparison of clinical characteristics between hypothyroid patients and normal controls also showed significant difference in majority of the factors. There was a significant association ($P < 0.001$) between vitamin D categories and hypothyroid state. Nearly 26.1% of hypothyroid patients had vitamin D deficiency, compared to 21.3% in normal controls. [Figure 1]

All regression models are shown in Table 2 and 3. Table 3 shows correlation between variables included in the regression models.

Table 1: Demographic and socioeconomic characteristics of the participants, (n = 250)

Variables	Hypothyroidism N = 25 (10%)	Normal Control N = 225	P value	Total N = 250
Age, mean years (SE)	50.5	45. 7	< 0.001	47.2
Female, % (SE)	74.7%	47.9%	< 0.001	53.4%
Education, % (SE)			0.05	
Less than 12	16.9%	18.0%		19.1%
12	23.4%	24.8%		22.5%
More than 12	62.2%	58.2%		55.8%
Physical activity, % (SE)	46.9%	57.2%	0.001	57.3%
Smoking, % (SE)			0.001	
Current	12.1%	22.5%		20.2%
Former	2.6%	2.7%		2.8%
Never	82.5%	74.8%		74.8%
Alcohol use, % (SE)			0.01	
Never	12.4%	9.3%		10.3%
Former	12.2%	11.4%		11.7%
Current	74.8%	78.3%		78.9%

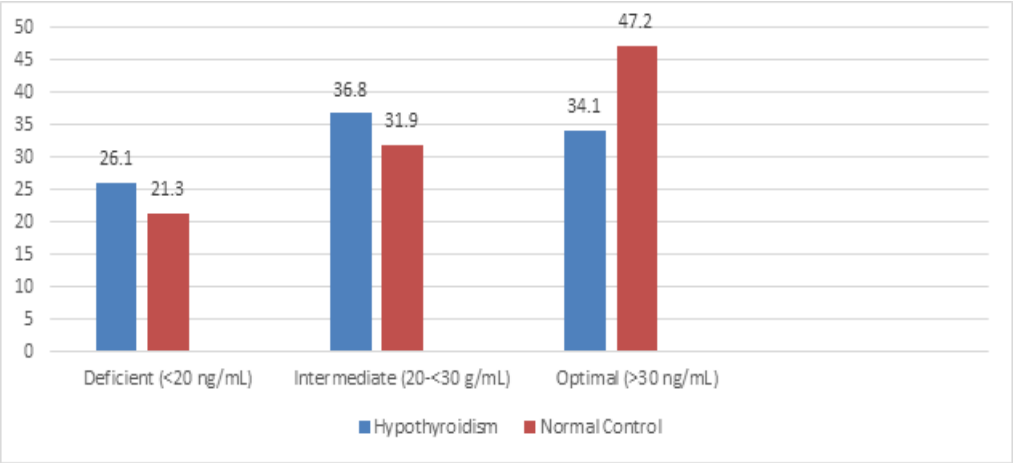

Figure 1: Comparison of vitamin D categories by hypothyroidism and normal control

Table 2 Multivariable logistic regression results showing association between vitamin D and hypothyroidism (N = 250)

Models	Optimal	Intermediate	Deficient
	(≥30 ng/mL)	(20 to < 30 g/mL)	(< 20 ng/mL)
Model 1 Reference	Reference	1.5 (0.7–1.8)	1.1 (0.7–1.5)
Model 2	Reference	1.1 (0.6–1.7)	1.3 (0.6–1.8)
Model 3	Reference	1.2 (0.5–1.6)	1.2 (0.5–1.3)
Model 4	Reference	1.3 (0.9–1.4)	1.2 (0.4–1.5)
Model 5	Reference	1.1 (0.6–1.5)	1.3 (0.2–1.8)
Model 6	Reference	1.5 (0.8–1.5)	1.5 (0.4–1.9)
Model 7	Reference	1.6 (1.5–1.9)	1.6 (1.6–1.9)

Model 1: Unadjusted
Model 2: Adjusted for age, sex, education, and income
Model 3: Adjusted for age, sex, education, income, smoking, alcohol consumption, BMI and physical activity
Model 4: Adjusted for age, education, income, smoking, alcohol consumption,
BMI, physical activity, hypertension, and diabetes
Model 5: Adjusted for age, education, income, smoking, alcohol consumption,
BMI, physical activity, hypertension, diabetes, dyslipidemia, and blood urea nitrogen
Model 6: Adjusted for age, education, income, smoking, alcohol consumption,
BMI, physical activity, hypertension, diabetes, dyslipidemia, blood urea nitrogen, and creatinine
Model 7: Adjusted for age, education, income, smoking, alcohol consumption,
BMI, physical activity, hypertension, diabetes, dyslipidemia, blood urea nitrogen, creatinine, and magnesium

Table 3 Correlation between variables included in the regression models

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Age	–													
2. Education	0.163	–												
3. Income	0.248	0.262	–											
4. Smoking	0.132	0.017	0.147	–										
5.Alcoholconsumption	0.271	0.174	0.151	0.253	–									
6. Body mass index	0.234	0.201	0.137	0.427	0.461	–								
7.Physical activity	0.538	0.066	0.127	0.046	0.138	0.355	–							
8. Hypertension	0.054	0.271	0.268	0.342	0.010	0.433	0.256	–						
9. Diabetes	0.133	0.154	0.271	0.252	0.158	0.164	0.148	0.152	–					
10. Dyslipidemia	0.372	0.249	0.338	0.458	0.128	0.164	0.078	0.143	0.120	–				
11.Blood ureanitrogen	0.448	0.139	0.328	0.328	0.333	0.148	0.343	0.248	0.162	0.255	–			
12. Creatinine	0.340	0.288	0.181	0.132	0.338	0.177	0.462	0.749	0.364	0.121	0.233	–		
13. Magnesium	0.087	0.378	0.442	0.124	0.428	0.129	0.220	0.098	0.348	0.149	0.334	0.112	–	
14. Vitamin D	0.164	0.458	0.139	0.312	0.358	0.049	0.369	0.133	0.476	0.439	0.340	0.301	0.322	–
15. Hypothyroidism	0.342	0.139	0.160	0.132	0.143	0.090	0.144	0.248	0.164	0.229	0.482	0.373	0.088	0.363

Discussion:

Vitamin D is known for its primary role in bone and mineral homeostasis, and it has been shown recently that its deficiency is associated with various diseases such as cardiovascular disease, cancer, infection, and adiposity as well as osteoporosis. [10] Interestingly, it has been shown recently that vitamin D has potent immunomodulatory effects and plays important roles in the pathogenesis of autoimmune diseases. [11] Serum concentration of 25(OH) D is the best indicator of vitamin D status. It reflects vitamin D produced cutaneously and that obtained from food and supplements [12] and has a fairly long circulating half-life of 15 days. [13] In contrast to 25(OH) D, circulating 1, 25(OH) 2D is generally not a good indicator of vitamin D status because

it has a short half-life of 15 hours and serum concentrations are closely regulated by parathyroid hormone, calcium, and phosphate [13].

Mazokopakis et al. [14] showed that serum levels of 25(OH)D were inversely related to anti-TPO levels in patients with HT. Anti-TPO levels were also significantly higher in HT patients with vit-D deficiency (< 75 nmol/L) than those HT patients without vit-D deficiency. In another study, a significant decrease in serum anti-TPO levels was reported after 4 months of oral vit-D3 supplementation (1,200–4,000 IU/day) in patients with vit-D deficiency [14]. Screening for vit-D deficiency and replacement therapy if necessary has been recommended [15]. Levels of vit-D were observed to be significantly lower in children with HT [16]. A negative correlation between vit-D and TPO antibodies was found in our study. HT disease activity has been reported to decrease with vit-D treatment [17].

Vitamin D inhibits the production of Th1 polarizing cytokine (IL-12), thereby indirectly shifting the polarization of T cells from a Th1 toward a Th2 phenotype. In the CD4+ T cell response, vitamin D directly inhibits the production of Th1 cytokines (IL2 and IFN-c), and enhances Th2 cytokine (IL-4) production. [18]

In addition, recent numerous studies have shown the relation of vitamin D and various autoimmune diseases. Vitamin D receptor (VDR) gene polymorphisms and vitamin D status are associated with different autoimmune diseases. [18-19] Furthermore, vitamin D supplementation prevented the onset and/or development of several kinds of autoimmune diseases in humans and animal models. [20] These results suggested that vitamin D deficiency might cause the onset and/or development of several kinds of autoimmune diseases. [21]

Conclusion:

Low vitamin D levels are associated with autoimmune hypothyroidism. Healthcare initiatives such as mass vitamin D deficiency screening among at-risk population could significantly decrease the risk for hypothyroidism in the long-term.

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