

Vitamin D Status in Primary Hypothyroid Subjects Attending a Specialized Endocrine Center of Bangladesh

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Abstract

Background: Association between vitamin D deficiency and hypothyroidism has been reported by many authors though the study results are mixed. **Objective:** The study was conducted to observe vitamin D status among primary hypothyroid subjects. **Materials/Methods:** In this single-center cross-sectional study, 356 subjects with primary hypothyroidism (either new or previously diagnosed) were evaluated for serum thyroid stimulating hormone (TSH) and 25(OH) vitamin D levels. 25(OH)D levels were classified as normal (≥ 30 ng/ml), insufficient (>20 to 29.9 ng/ml), and deficient (≤ 20 ng/ml). **Results:** The mean age of the study subjects was 36.33 (± 12.44) years; majority of them were female (89.9%), homemaker (79.8%), residing in urban or suburban areas (64%), and literate (85.7%); almost half (48%) of them were obese. Their median TSH was 6.17 μ IU/ml and mean 25(OH)D was 25.16 (± 12.18) ng/ml. The frequencies of vitamin D deficiency and insufficiency were 39.6% and 34.3% respectively. No statistical differences were observed in 25(OH)D levels between males and females, obese and non-obese, new cases and previously diagnosed cases, new cases with subclinical and overt hypothyroidism, the previously diagnosed cases with controlled and uncontrolled hypothyroidism, and among subjects living in urban, suburban and rural areas. Serum 25(OH) vitamin D level showed no correlations with age, body mass index (BMI) and TSH levels of the study subjects. **Conclusion:** The observed frequency of hypovitaminosis D (deficiency and insufficiency) was high (73.9%) in primary hypothyroid subjects from Bangladesh.

Keywords

Primary Hypothyroidism, Vitamin D

1. Introduction

Vitamin D deficiency (VDD) is a global health problem affecting more than one billion people worldwide [1]. Despite enough sunshine, a high prevalence of vitamin D deficiency and insufficiency has been reported from the Indian subcontinent [2]. Vitamin D is a steroid hormone which exerts its physiological effects by binding with nuclear vitamin D receptor (VDR) and activating a cascade of genes. VDR is widely distributed in the human body present in more than 30 different tissues including pancreas, myocardium, lymphocytes, thyroid gland etc. Though the principal role of vitamin D is related to bone metabolism and in the regulation of intestinal absorption of minerals such as calcium and phosphorus, it has widespread and versatile effects on human organ systems [3]. The association of vitamin D deficiency and VDR polymorphisms with various chronic diseases including several endocrinopathies has been reported by many authors [4]. Hypothyroidism is a common endocrine disorder; the prevalence of hypothyroidism in Bangladesh is largely unknown, though the reported prevalence from neighboring countries is high (11%) [5]. Several studies have reported an association between vitamin D deficiency and hypothyroidism though the study results were mixed [6]-[12]. Vitamin D supplementation in hypothyroid patients has shown to reduce serum thyroid stimulating hormone (TSH) level [13].

Data are lacking for the frequency of VDD in hypothyroid patients from Bangladesh. This cross-sectional study was conducted to measure the frequency of VDD in subjects with primary hypothyroidism.

2. Materials/Methods

2.1. Study Area

In this cross-sectional study, 356 consecutive subjects with primary hypothyroidism attending a specialized endocrine center located at the district level of Bangladesh fulfilling the inclusion and exclusion criteria were investigated.

2.2. Study Subjects

The patients were either newly diagnosed or they were diagnosed earlier as primary hypothyroidism and had been receiving levothyroxine (LT4). Previous physician diagnosis of primary hypothyroidism and a TSH value ≥ 10 $\mu\text{IU/ml}$ in new patients were used as the diagnostic criteria for primary hypothyroidism in previously diagnosed and new patients respectively. New patients with a TSH value in between 5 - 10 $\mu\text{IU/ml}$ were categorized as subclinical hypothyroidism (SCH). Subjects having any acute illness, hepatic or renal dysfunction, debilitating chronic illness, and those who got vitamin D or calcium supplement in the previous 3 months were excluded. After taking informed written consent all patients were interviewed and examined for relevant clinical information. Anthropometric measurements were done for all. Obesity status was determined by

body mass index (BMI) categories applicable to the Asian Indians [14].

2.3. Study Assay

Venous blood was collected from each of the participants and serum 25(OH)D tests were performed by enzyme-linked fluorescent assay (ELFA) method by the autoanalyzer VIDAS (France). 25(OH)D levels were considered as normal (≥ 30 ng/ml), insufficient (>20 to 29.9 ng/ml), and deficient (≤ 20 ng/ml) as per Clinical Practice Guidelines, 2011 of The Endocrine Society [15]. Serum TSH was measured by Statfax 3300 Elisa plate reader, USA.

2.4. Statistical Analysis

Statistical analysis was done by using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA) software. The categorical variables were represented as percentages and measurable variables as mean \pm SD or median. Student's t-test, Chi-square test, and Oneway ANOVA were performed for comparing the variables between different groups as appropriate. Pearson's correlation test was used to observe correlation of vitamin D level with other variables. P value ≤ 0.05 was considered to be statistically significant.

3. Results

Majority of the participants were female, homemaker, residing in urban or suburban areas, and got an education at least up to the secondary level as shown in **Table 1**. Almost half of them were obese. Their median TSH was 6.17 μ IU/ml and mean 25(OH)D was 25.16 ng/ml. The vitamin D categories of the study subjects are depicted in **Figure 1**. Comparison of 25(OH)D levels among the subclasses of the variables is shown in **Table 2**. Correlations of serum 25(OH)D with other variables are shown in **Table 3**.

4. Discussions

In this study, 356 subjects with primary hypothyroidism were investigated for vitamin D status. The mean 25(OH)D in the study subjects was 25.16 ng/ml (± 12.18 SD). 39.6% of them were vitamin D deficient, 34.3% were insufficient and 26.1% had normal 25(OH)D.

Although the well known primary role of vitamin D is linked with bone and mineral metabolism, recently the association of vitamin D deficiency with many diseases of several other organ systems including obesity, cardiovascular disease, diabetes, cancer, and infectious diseases has been discovered. The causal role of vitamin D deficiency in several autoimmune diseases also has been proved [2]. Though there is still debate, an association of autoimmune thyroid diseases (Hashimoto's thyroiditis and Graves' disease) with vitamin D deficiency has been observed by many researchers [9] [10] [11] [12] [16]. Hashimoto's thyroiditis is the most common cause of hypothyroidism worldwide [17]. Despite the fact that vitamin D deficiency is prevalent worldwide including Indian

Table 1. Demographic characteristics of the study subjects (N = 356).

Variable	Subcategories	Value
Age (years), mean \pm SD		36.33 \pm 12.44
Gender (%)	Male	36 (10.1%)
	Female	320 (89.9%)
Residence (%)	Urban	121 (34.0%)
	Suburban	107 (30.0%)
	Rural	128 (36.0%)
Occupation (%)	Home maker	284 (79.8%)
	Business	17 (4.8%)
	Student	20 (5.6%)
	Service	33 (9.3%)
	Day labor	2 (0.6%)
Education level (%)	Illiterate	27 (7.6%)
	Can sign only	24 (6.7%)
	Primary	28 (7.9%)
	Secondary	97 (27.2%)
	Higher secondary	137 (38.5%)
	Graduation or above	43 (12.1%)
BMI (kg/m ²)		27.33 \pm 4.09
BMI category (%)	<27.5	185 (52%)
	\geq 27.5	171 (48%)
S. TSH (μ IU/ml), median		6.17 (3.00 - 12.35)
Patient category (%)	<i>New cases</i>	63 (17.7%)
	Overt Hypothyroidism	34 (54%)
	Subclinical Hypothyroidism	29 (46%)
	<i>Under treatment</i>	293 (82.3%)
	TSH within target	147 (50.2%)
	TSH not within target	146 (49.8%)
S. 25(OH) Vitamin D (ng/ml)		
Mean \pm SD		25.16 \pm 12.18
Median (IQR)		22.67 (16.82 - 30.61)

BMI: Body mass index; IQR: Inter-quartile range.

subcontinent, lower vitamin D level has been observed in hypothyroid subjects in comparison to healthy adults in this area [6] [7] [9].

Though it is not well established, 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 to poor absorption of vitamin D from the intestine; secondly, the body may not activate vitamin D properly. Both vitamin D and thyroid hormone exert their physiological effects through binding with steroid hormone receptors located in the nucleus. Vitamin D receptor (VDR) gene polymorphisms have

Table 2. Comparison of 25(OH)D among different subclasses of the variables (N = 356).

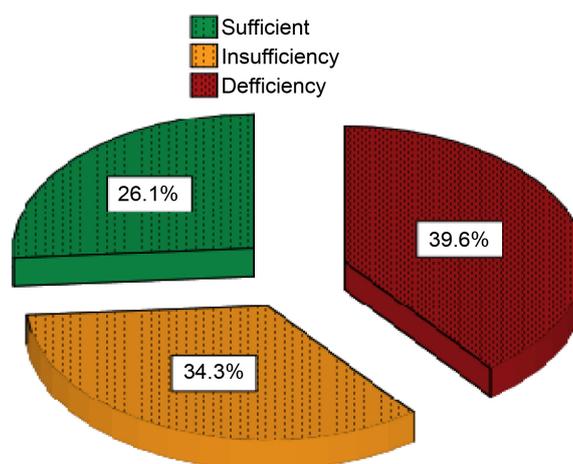
Variable	Subcategories	25(OH)D Level (ng/ml, mean \pm SD)	P
Gender	Male (n = 36)	24.04 \pm 12.26	0.563 ^a
	Female (n = 320)	25.29 \pm 12.18	
Residence	Urban (n = 121)	26.30 \pm 12.61	0.440 ^b
	Sub-urban (n = 107)	24.74 \pm 11.72	
	Rural (n = 128)	24.43 \pm 12.16	
BMI category	<27.5 (n = 185)	26.05 \pm 12.84	0.154 ^a
	\geq 27.5 (n = 171)	24.20 \pm 11.39	
Patient category	New cases (n = 63)	25.08 \pm 12.59	0.952 ^a
	Under treatment (n = 293)	25.18 \pm 12.11	
New cases	Overt Hypothyroidism (n = 34)	24.69 \pm 10.16	0.795 ^a
	Subclinical Hypothyroidism (n = 29)	25.53 \pm 15.14	
Cases on treatment	TSH within target (n = 147)	26.00 \pm 11.75	0.244 ^a
	TSH not within target (n = 146)	24.34 \pm 12.45	

^aby Student's *t*-test; ^bby Oneway ANOVA.

Table 3. Correlations of serum 25(OH)D with other variables.

Variable	r	P
Age	0.039	0.465
BMI	-0.035	0.513
S. TSH	-0.047	0.380

p-value by Pearson correlation.

**Figure 1.** Vitamin D status of the study subjects (N = 356).

been found to be associated with different autoimmune diseases including autoimmune thyroid diseases [8].

More than two-thirds (79.3%) of the subjects with primary hypothyroidism in this study had either deficiency or insufficiency of vitamin D (39.6% deficient,

34.3% insufficient). The frequency is lower than the observations of Indiculla *et al.* (96%) [6] and Tamer *et al.* (92%) [10]. Though the prevalence of vitamin D deficiency in the general population of Bangladesh is largely unknown, several small scale studies have found high frequencies of vitamin D insufficiency and/or insufficiency. A recent study conducted in Dhaka city among 212 patients presenting with generalized body ache and pain found all of them to have subnormal vitamin D (<30 ng/ml) [18]. In another study in Dhaka, hypovitaminosis D (≤ 40 nmol/L) was observed in 77.7% of 121 women aged 18 - 60 years [19]. Another study also found 100% of women of reproductive age to have either D deficiency or insufficiency [20]. Above observations reveals the fact that the majority of the healthy population of this area have vitamin D deficiency. So it is very hard to reach a decision that the frequency of subnormal vitamin D primary hypothyroid subjects in this study is higher than the population prevalence. We have to wait till the results of larger studies including healthy controls are known.

The current study found no difference in vitamin D levels between males and females, which is in accordance with the finding of Mackawy *et al.* [8]. On the contrary, lower vitamin D levels have been observed in hypothyroid females in comparison to hypothyroid males by Prasad *et al.* [9]. Among the new cases, overt and subclinical hypothyroid subjects in this study had similar vitamin D levels; Tamer *et al.* also had similar observation [10]. No difference in vitamin D level was observed between obese and non-obese hypothyroid subjects in this study and BMI showed no correlation with vitamin D level. Obesity was an independent risk factor for hypovitaminosis D in the study done by Hossain *et al.* [16], though another study found no correlation between these two in healthy Bangladeshi women of reproductive age [20]. Though the literature revealed that rural subjects working in the field and spending more time outdoors in the sunlight have higher vitamin D levels [18], this study found no difference in vitamin D levels among subjects from urban, suburban or rural areas.

Serum TSH level showed no correlation with serum 25(OH)D level in the study subjects. Vitamin D level found to be negatively correlated with TSH in previous studies by Koch *et al.* [6], Mackawy *et al.* [8], and Prasad *et al.* [9].

5. Conclusion

The observed frequency of hypovitaminosis D (deficiency and insufficiency) was high in primary hypothyroid subjects from Bangladesh. Large multicenter studies with the inclusion of healthy controls are needed to establish the actual association of vitamin D and hypothyroidism and determine the benefit of vitamin D supplementation in these subjects.

6. Limitations of the Study

The main limitation of the current study is that it had no healthy control group for comparison. Thyroid autoantibodies were also not measured limiting the eti-

ological diagnosis of hypothyroidism and establishing the association of Hashimoto's thyroiditis with vitamin D deficiency. The extent of sun exposure was not quantified and the seasonal variations in vitamin D level were also not considered. The study subjects were recruited from only one center, so the study result may not be generalizable. Nevertheless, this one is the first study that assessed vitamin D status in hypothyroid subjects in Bangladesh and served as a baseline for future research in this field.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Mitchell, D.M., Henao, M.P., Finkelstein, J.S. and Burnett-Bowie, S.A. (2012) Prevalence and Predictors of Vitamin D Deficiency in Healthy Adults. *Endocrine Practice*, **18**, 914-923. <https://doi.org/10.4158/EP12072.OR>
- [2] Ritu, G. and Gupta, A. (2014) Vitamin D deficiency in India: Prevalence, Causalities and Interventions. *Nutrients*, **6**, 729-775. <https://doi.org/10.3390/nu6020729>
- [3] Nair, R. and Maseeh, A. (2012) Vitamin D: The "Sunshine" Vitamin. *Journal of Pharmacology & Pharmacotherapeutics*, **3**, 118-126.
- [4] Agmon-Levin, N., Theodor, E., Segal, R.M. and Shoenfeld, Y. (2013) Vitamin D in Systemic and Organ-Specific Autoimmune Diseases. *Clinical Reviews in Allergy & Immunology*, **45**, 256-266. <https://doi.org/10.1007/s12016-012-8342-y>
- [5] Bagechi, S. (2014) Hypothyroidism in India: More to Be Done. *The Lancet Diabetes & Endocrinology*, **2**, 778. [https://doi.org/10.1016/S2213-8587\(14\)70208-6](https://doi.org/10.1016/S2213-8587(14)70208-6)
- [6] Idiculla, J., Prabhu, P., Pradeep, R., Khadilkar, K. and Kannan, S. (2018) Vitamin D and Primary Hypothyroidism: Is There an Association? *Thyroid Research and Practice*, **15**, 34-37. https://doi.org/10.4103/trp.trp_49_17
- [7] Koch, N., Kaur, J., Mittal, A., Gupta, A., Kaur, I.P. and Agarwal, S. (2016) Status of Vitamin D Levels in Hypothyroid Patients and Its Associations with TSH, T3 and T4 in North Indian Population of Meerut, a Cross Sectional Study. *International Journal of Clinical Biochemistry and Research*, **3**, 295-298. <https://doi.org/10.5958/2394-6377.2016.00057.5>
- [8] Mackawy, A., Al-ayed, B. and Al-rashidi, B. (2013) Vitamin D Deficiency and Its Association with Thyroid Disease. *International Journal of Health Sciences*, **7**, 267-275. <https://ijhs.org.sa/index.php/journal/article/view/523>
<https://doi.org/10.12816/0006054>
- [9] Prasad, I., Kumari, R. and Saran, A. (2016) Vitamin D Evaluation in Autoimmune Thyroid Diseases. *International Journal of Contemporary Medical Research*, **3**, 3415-3418. https://www.ijcmr.com/uploads/7/7/4/6/77464738/ijcmr_1111_dec_21.pdf
- [10] Tamer, G., Arik, S., Tamer, I. and Coksert, D. (2011) Relative Vitamin D Insuffi-

ciency in Hashimoto's Thyroiditis. *Thyroid*, **21**, 891-896.

<https://doi.org/10.1089/thy.2009.0200>

- [11] Yasmeh, J., Farpour, F., Rizzo, V., Kheradnam, S. and Sachmechi, I. (2016) Hashimoto Thyroiditis Not Associated with Vitamin D Deficiency. *Endocrine Practice*, **22**, 809-813. <https://doi.org/10.4158/EP15934.OR>
- [12] Wang, J., Lv, S., Chen, G., Gao, C., He, J., Zhong, H. and Xu, Y. (2015) Meta-Analysis of the Association between Vitamin D and Autoimmune Thyroid Disease. *Nutrients*, **7**, 2485-2498. <https://doi.org/10.3390/nu7042485>
- [13] Talaei, A., Ghorbani, F. and Asemi, Z. (2018) The Effects of Vitamin D Supplementation on Thyroid Function in Hypothyroid Patients: A Randomized, Double-Blind, Placebo-Controlled Trial. *Indian Journal of Endocrinology and Metabolism*, **22**, 584-588. https://doi.org/10.4103/ijem.IJEM_603_17
- [14] WHO Expert Consultation (2004) Appropriate Body-Mass Index for Asian Populations and Its Implications for Policy and Intervention Strategies. *The Lancet*, **363**, 157-163. [https://doi.org/10.1016/S0140-6736\(03\)15268-3](https://doi.org/10.1016/S0140-6736(03)15268-3)
- [15] Holick, M.F., Binkley, N.C., Bischoff-Ferrari, H.A., Gordon, C.M., Hanley, D.A., Heaney, R.P., Murad, M.H. and Weaver, C.M. (2011) Evaluation, Treatment and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*, **96**, 1911-1930. <https://doi.org/10.1210/jc.2011-0385>
- [16] Yasuda, T., Okamoto, Y., Hamada, N., Miyashita, K., Takahara, M., Sakamoto, F., *et al.* (2012) Serum Vitamin D Levels Are Decreased and Associated with Thyroid Volume in Female Patients with Newly Onset Graves' Disease. *Endocrine*, **42**, 739-741. <https://doi.org/10.1007/s12020-012-9679-y>
- [17] Kostoglou-Athanassiou, I. and Ntalles, K. (2010) Hypothyroidism—New Aspects of an Old Disease. *Hippokratia*, **14**, 82-87. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2895281>
- [18] Hossain, H.T., Islam, Q.T., Khandaker, M.A.K. and Ahasan, H.N. (2018) Study of Serum Vitamin D Level in Different Socio-Demographic Population—A Pilot Study. *Journal of Medicine*, **19**, 22-29. <https://doi.org/10.3329/jom.v19i1.34836>
- [19] Islam, M.Z., Akhtaruzzaman, M. and Lamberg-Allardt, C. (2006) Hypovitaminosis D Is Common in Both Veiled and Nonveiled Bangladeshi Women. *Asia Pacific Journal of Clinical Nutrition*, **15**, 81-87. <https://www.ncbi.nlm.nih.gov/pubmed/16500882>
- [20] Kamrul-Hasan, A.B., Aalpona, F.Z., Chanda, P.K., Ariful-Islam, M., Palash-Molla, M., Rabaya-Akter, M., Talukder, R.K. and Siddiqui, N.I. (2018) Vitamin D Status in Polycystic Ovarian Syndrome Patients Attending a Tertiary Hospital of Bangladesh. *Mymensingh Medical Journal*, **27**, 730-736. <https://www.ncbi.nlm.nih.gov/pubmed/30487487>