

Serum Vitamin D Status in Newly Diagnosed Hypothyroid Patients

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ABSTRACT

More than billion people worldwide are vitamin D deficient. It is recognized to have function in bone and muscle development by regulating calcium and phosphorus metabolism. Its role as an immune modulator has recently been discovered. Deficiency of vitamin D has been discovered to be associated with various cardiovascular, infectious, malignant, hypothyroidism and autoimmune thyroid diseases. Prevalence of hypothyroidism and hypovitaminosis D in Bangladesh is not known but supposed to be high because our neighbor country India has high prevalence. Vitamin D mediates its effect through binding to vitamin D receptor (VDR) and activation of VDR- responsive genes. VDR gene polymorphism was found to be associated with autoimmune thyroid diseases. On the other way hypothyroidism either decreases the metabolism of vitamin D or prevents to activate it. A total of 38 adult hypothyroid otherwise healthy patients and age, sex, BMI, socioeconomic status matched euthyroid adults were included in the study. The mean age in the hypothyroid group was 37.82 ± 7.95 years and in the euthyroid group was 34.84 ± 8.61 years. Male participants were 14 and female participants were 24 in each group. The mean value of serum vitamin D of healthy group was 17.11 ± 5.62 ng/ml and in hypothyroid patients was 13.16 ± 4.29 ng/ml. Hypothyroid patients had significantly lower levels of serum Vitamin D₃ as compared to controls ($p = 0.037, < 0.05$).

Negative correlation was observed between serum TSH and serum vitamin D ($r = -.119, p = .034$), moderate positive correlation was observed between serum FT₄ and serum vitamin D ($r = 0.457, p = 0.01, P < 0.05$).

Keywords: Hypothyroidism, Euthyroid status, Vitamin D status

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INTRODUCTION

Vitamin D deficiency is an emerging global health problem. More than billion people worldwide are vitamin D deficient (1, 2). Prevalence is not yet estimated in Bangladesh but in our neighbor country India 70-100% of general population are deficient in vitamin D (3). Inadequate vitamin D still remains one of the most common and untreated medical conditions. Deficiency of

vitamin D gives rise the symptoms of unexplained tiredness, musculoskeletal pain, poor wound healing, hair loss, repeated respiratory tract infection, depression, bone loss (1, 4). People are unaware about achieving sufficient blood level of vitamin D because there is no warning from any international health organization (5). In the early 20th century it is discovered that it is not a simple vitamin rather a steroid pro-hormone (6). It is recognized to have function in bone and muscle development by regulating calcium and phosphorus metabolism. Its role as an immune modulator has recently been discovered (6). Deficiency of vitamin D has been discovered to be associated with various cardiovascular, infectious, malignant and autoimmune diseases (7, 8). Insufficient serum vitamin D is associated with autoimmune diseases including type 1 diabetes, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis and systemic lupus erythematosus. Studies in animal model have shown that vitamin D supplementation prevents the onset and/or development of these autoimmune diseases specially type 1 diabetes mellitus, multiple sclerosis and inflammatory bowel disease (2). Vitamin D deficiency has been found to be related with an increased risk of hypothyroidism and autoimmune thyroid disease, though the findings are still under evaluation (9-11). Low serum 25-hydroxyvitamin D concentration is associated with the development of both Hashimoto's thyroiditis and Grave's disease (12, 13). In Hashimoto's thyroiditis supplementation with vitamin D has shown to decrease serum TSH level as well as anti TPO antibody (14).

Both vitamin D and thyroid hormone bind to similar receptors called steroid hormone receptor. Vitamin D

mediates its effect through binding to vitamin D receptor (VDR) and activation of VDR- responsive genes. VDR gene polymorphism was found to be associated with autoimmune thyroid diseases (15). On the other way hypothyroidism either decreases the metabolism of vitamin D or prevents to activate it. Hypothyroid patients suffer from fatigue, weakness, weight gaining, coarse- dry hair, rough skin, muscle cramp, depression, irritability, memory loss which are similar to hypovitaminosis D(16). Hypovitaminosis D and hypothyroidism have common symptoms, their symptoms mask each other. Their cause effect relationship is needed to be clearly defined for better management of hypothyroid patients.

PATIENTS AND METHODS

The cross sectional observational study was carried out at National Institute of Nuclear Medicine & Allied Sciences (NINMAS), from July 2017 to June 2018. In this study 38 newly diagnosed hypothyroid patients who were referred to NINMAS from all over Bangladesh for thyroid status evaluation (Hypothyroid group) and age, sex, BMI, socio economic status and sun exposure matched euthyroid subjects (Euthyroid group) who were known to free from any thyroid disease were included. After taking informed written consent, detailed clinical history and laboratory findings (TSH, FT4, vitamin D3) were collected on pre-formed data collection sheet. Vitamin D3 status of the two groups was tested statistically. Correlation between different thyroid hormones and serum vitamin D3 was observed.

RESULTS

The mean ± SD age was found 37.82 ± 7.955 years in hypothyroid group and 34.84 ± 8.6 years in the euthyroid group. The mean age difference was not statistically significant (p>.05) between two groups (Table 1). Majority of the patients belonged to age group 30-50 years. Male and female were equally distributed among hypothyroid and euthyroid groups. In both groups 14 were males and 24 were females. Among the study population 31.4% was overt hypothyroid patients and 68.4% was subclinical hypothyroid patients.

Among 38 hypothyroid patients 18 (47.4%) participants were positive for TPO Ab and 20 (52.6%) patients were negative for TPO Ab.

Table 1: Age distribution of participants according to Thyroid hormone status

	Hypothyroid (n=38)	Euthyroid (n=38)	p-value
Age in years			
Mean ± SD	37.82 ± 7.955	34.84 ± 8.610	0.402 ^{ns}

(p-value reached from independent t-test)

Serum vitamin D deficiency was found in 36 (94.7%) hypothyroid participants and 32 (84.2%) euthyroid participants; insufficiency was observed in two (5.3%) hypothyroid participants and 05 (13.2%) euthyroid participants. None of the hypothyroid patient had sufficient serum vitamin D and only one (2.6%) euthyroid participant had sufficient serum vitamin D (Figure 1).

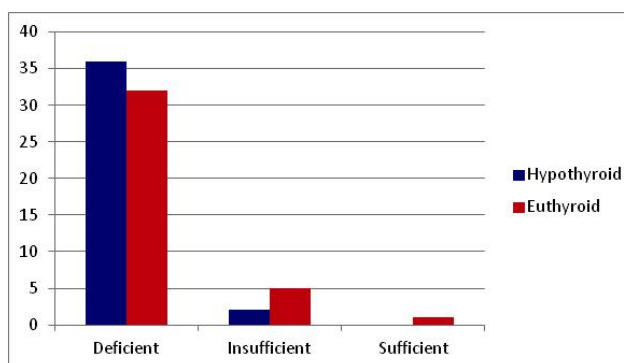


Figure-1: Bar diagram showing serum vitamin D among the study participants

It was observed that the mean value of serum vitamin D was low in hypothyroid patients (13.16 ± 4.29 ng/ml) than that of euthyroid subjects (17.11 ± 5.62 ng/ml), the difference was statistically significant, p-value 0.037 (<.05) (Table 2).

Table 2: Comparison of mean serum Vit D between hypothyroid and euthyroid group

	Hypothyroid (n=38)	Euthyroid (n=38)	p-value
Serum Vit D ng/ml Mean ± SD	13.16 ± 4.29	17.11 ± 5.62	.037 ^s

(p-value reached through independent 't' test)

Difference between serum vitamin D in overt and subclinical hypothyroid patients were shown in Table 3. Overt hypothyroid patients had slightly lower serum vitamin D with a mean value of 10.94 ± 4.9 ng/ml than the subclinical hypothyroid patients with a mean value of 14.19 ± 3.36 ng/ml. The difference was not statistically significant (*p-value* .05).

Table 3: Difference between serum vitamin D in overt and subclinical hypothyroid patients

Serum Vit D ng/ml	Overt (n=12)	Subclinical (n=26)	<i>p- value</i>
Mean \pm SD	10.94 ± 4.9	14.19 ± 3.36	.05 ^{ns}

Serum vitamin D level in TPO Ab positive and negative hypothyroid participants is shown in Table 4. The mean value of serum vitamin D in TPO Ab positive patients was 12.50 ± 4.81 ng/ml and 13.75 ± 3.56 ng/ml in TPO Ab negative patients, the difference between two groups was not statistically significant (*p- value* .462).

Table 4: Distribution of serum vitamin D on the basis of TPO Ab

Serum Vit D ng/ml	TPOAb positive (n=18)	TPO Ab Negative (n=20)	<i>p- value</i>
Mean \pm SD	12.50 ± 4.81	13.75 ± 3.56	.462 ^{ns}

(*p-value* reached through independent t test).

Difference in serum vitamin D between male and female participants is shown in Table 5. The mean serum vitamin D among hypothyroid male participants was 14.11 ± 4.74 ng/ml and in female participants was 12.48 ± 3.83 ng/ml; the difference was not statistically significant, *p-value* .105. The mean serum vitamin D among euthyroid male and female participants was 19.43 ± 5.98 ng/ml and 15.33 ± 4.23 ng/ml, respectively; the difference was statistically significant *p-value* was 0.015 ($P < 0.05$).

Table 5: Difference in serum vitamin D between male and female

	In Hypothyroid	In Euthyroid	<i>p-value</i>
In Hypothyroid	14.11 ± 4.74	12.48 ± 3.83	.105 ^{ns}
In Euthyroid	19.43 ± 5.98	15.33 ± 4.23	.015 ^s

(*p-value* reached from independent t-test)

Figure 2 demonstrates the correlation between serum TSH and serum vitamin D. It is shown that there was steady decrease in serum vitamin D with raising serum TSH; a negative correlation was observed between the two variable which was statistically significant ($r = -.119$ and $p = .034$).

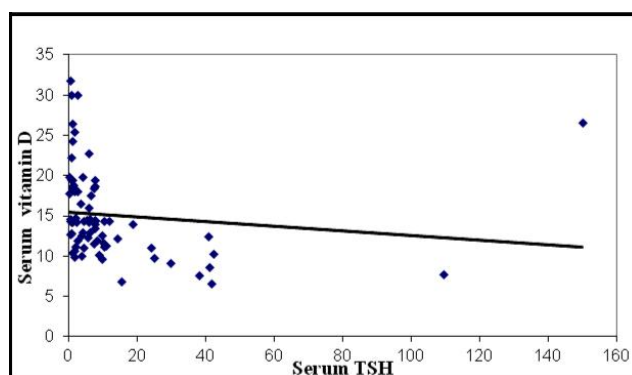


Figure2: Scatter diagram showing negative correlation between serum TSH

Correlation between serum FT₄ and serum vitamin D was shown in figure 3. Moderate positive correlation was observed between serum FT₄ and serum vitamin D. The variables moved in same direction with the raising of the other ($r = .453$, $p = .000$).

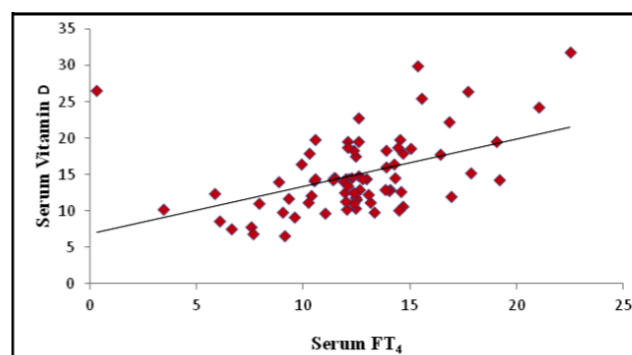


Figure 3: Scatter diagram showing moderate positive correlation between serum FT₄ and serum vitamin D.

DISCUSSION

The symptoms of hypothyroidism and serum vitamin D merges each other like unexplained tiredness, musculoskeletal pain, poor wound healing, hair loss, repeated respiratory tract infection, depression, bone loss (1, 4). Few studies have been conducted in order to find any significant association between the levels of vitamin D

and hypothyroidism and to determine whether vitamin D deficiency involves in the pathogenesis of hypothyroidism or rather a consequence of the disease and those studies yielded ambiguous and inconclusive results (9-11). Some researchers examined the prevalence of Vitamin D deficiency in different populations worldwide but this study was aimed to examine the association of Vitamin D level with hypothyroidism in Bangladeshi population. This current study was undertaken to evaluate the levels of vitamin D among patients with hypothyroidism compared to healthy controls with normal serum TSH and FT₄ level. The study population was 38 newly diagnosed hypothyroid patients and age, sex, BMI, sun exposure, socioeconomic status matched 38 euthyroid subjects. Each group consisted of 14 male and 24 female participants. Serum TSH, FT₄, serum 25 (OH)₂D₃ was evaluated in all participants and tested statistically. All participants were adult between 19-51 years of age. The mean age in the hypothyroid and euthyroid groups were matched. Most of the participants as well as hypothyroid patients belonged to 30-50 years of age. This finding was also observed in different studies that the prevalence of hypothyroidism increases with age (9, 17). Women suffer from hypothyroidism more than men worldwide (18). This study also shows higher number of female hypothyroid patients in comparison to male. There were 12 (31.6%) overt hypothyroid and 26 (68.4%) subclinical hypothyroid patients in the hypothyroid group. World-wide the prevalence of subclinical hypothyroidism is 10 to 20 times more than the overt disease. The prevalence of subclinical hypothyroidism in India is 9.4% (19). The Colorado thyroid prevalence survey reported 8.5% of subclinical disease and 0.4% overt disease in the united states (20, 21). TPO antibody was found positive in 47.4

% of hypothyroid patients. In India 46.3% hypothyroid patients were found positive for anti-TPO antibody (22) and in another population based study in Cochin it was about 53% (17). Among Indian population, about 70-100% of Indian populations are deficient in vitamin D₃. It is suspected that Bangladeshi population might have the same picture due to same geographical region and same food habit. This study revealed that 84.2% of

euthyroid, otherwise healthy adult had deficiency in serum vitamin D, 13.2% of healthy euthyroid had insufficient vitamin D and only 2.6% of euthyroid participants had sufficient serum vitamin D (Figure 1). In healthy euthyroid mean serum vitamin D was 17.11 ± 5.62 ng/ml, which was at vitamin D deficiency level. Dark skin color, changing lifestyle, office work, lack of sunlight in home and most importantly clothing plays an important role in low serum vitamin D level in our population. It was observed in this study that vitamin D does have a role to play in hypothyroidism, hypothyroid patients had significantly lower levels of serum Vitamin D as compared to controls ($p = 0.037 < 0.05$; Table 2). The mean value of serum vitamin D of healthy group 17.11 ± 5.62 ng/ml, which was higher in comparison to hypothyroid patients with a mean value of 13.16 ± 4.29 ng/ml. This outcome was supported by Tamer et al (12) that illustrated deficiency of serum Vitamin D levels were significantly associated with degree and severity of hypothyroidism, conducted in Turkish population. Koch et al (9) also reported that low thyroid hormones lead to a lack of Vitamin D, deficiency increases with disease progression and severity. In this current study mean of serum vitamin D observed between overt and subclinical hypothyroid patients was 10.94 ± 5.21 and 14.18 ± 3.2 , respectively although the difference was not statistically significant, p -value 0.05 (Table 3). No significant difference of serum vitamin D was observed between TPO Ab positive and TPO Ab negative patients with a p -value 0.462 (Table 4). This finding agrees with the findings of Amsterdam study, 803 subjects were investigated in a longitudinal study who showed that 25(OH)₂D levels were not lower in hypothyroid cases compared to controls, nor in subjects with a genetic susceptibility for AITD or patients who later became anti-TPO antibody positive. The authors concluded that vitamin D deficiency is not associated with the early stages of thyroid autoimmunity (23). Female participants had significantly lower serum vitamin D than male participants in the euthyroid group, 15.33 ± 4.13 ng/ml vs. 19.43 ± 6.4 ng/ml, with a p -value 0

.01 (Table 5). This result matches the result of other researchers (17, 24) {Mackawy, 2013 #2864; Rockell,

2006 #2880}. They found significant difference of serum vitamin D between healthy male and female. Differences in the dietary intake of vitamin D, selection of patients, clothing and exposure to sunlight could be responsible for the discrepancies among these studies. This present study showed a negative correlation of serum 25(OH)₂ Vitamin D levels with TSH in hypothyroid patients on Pearson's correlation analysis which was statistically significant ($r = -0.119$, $P = 0.034$) (Figure 2) as well as moderate positive correlation between FT₄ and Vitamin D in the participants ($r = 0.457$, $p = 0.01$, $P < 0.05$) (Figure 3). These findings suggest an inter relationship that is presumed to exist between vitamin D deficiency and hypothyroidism with progression of the disease. Koch et al (9) and Mackawy et al (17) showed significant negative correlation between serum TSH and serum vitamin D. Positive correlation between FT₄ and serum vitamin D was also observed in participants in studies by Goswami et al (25) and Mackawy et al (17).

CONCLUSION

There are few reports on association between hypovitaminosis D and hypothyroidism with conflicting results. Their cause effect relationship is needed to be clearly defined for better management of hypothyroid patients. This study revealed that our population is deficient in vitamin D. Women are more deficient than men in our country. There is an interrelationship observed between hypothyroidism and hypovitaminosis D. Study indicated that patients with hypothyroidism may have overshadowed hypovitaminosis D. Vitamin D deficiency increases with progression of the disease which encourages screening of Vitamin D levels and supplementation in hypothyroid patients.

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