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Association between Serum 25 (OH) Vitamin D level and Thyroiditis in Western Saudi Arabian Population.

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ABSTRACT

Background: The association of low vitamin D status with Autoimmune Thyroid Disease (AITD), which includes Hashimoto's Thyroiditis (HT), is controversial. (HT) is a chronic autoimmune thyroid disease caused by an interaction between genetic factors and environmental conditions, both of which are yet to be fully understood. The management of HT depends on its clinical manifestations, commonly including diffuse or nodular goiter with euthyroidism, subclinical hypothyroidism and permanent hypothyroidism. The aim of this study was to investigate mainly the correlation between vitamin D deficiency and HT. **Methods:** This study was carried out in tertiary hospitals, included patients who visited the hospital for thyroid evaluation or follow-up. **Results:** A total of 310 subjects were included, of whom 84 participants were healthy, and 226 patients with hypothyroid disease, 119 subjects were diagnosed as having HT (AITD), 107 Non-AITD. Conclusion: The prevalence of vitamin D deficiency was significantly higher in HT group than in non AITD (48.9 % vs. 37.4 %, p=0.013). Among HT cases, patients with overt hypothyroidism had a significantly higher prevalence of vitamin D insufficiency than HT with euthyroidism, subclinical hypothyroidism (60.4% vs. 44.1%, 29.7%, respectively, p 0.009, 0.017, 0.026). **Conclusion:** Considering current evidence, presented in this study, screening for vitamin D deficiency and careful vitamin D supplementation, when required, may be recommended for patients with HT.

Keywords: Autoimmune Thyroid Disease, Hashimoto's Thyroiditis, 25-Hydroxyvitamin D and Thyroid Peroxidase Antibodies.

INTRODUCTION

Hashimoto's thyroiditis (HT), also called chronic lymphocytic or autoimmune thyroiditis (AITD), is part of the spectrum of chronic autoimmune thyroid diseases and is associated with various degrees of thyroid hypofunction, thyroid autoantibodies production [the most common, Thyroid Peroxidase Antibodies (TPO-Ab) and Thyroglobulin Antibodies (Tg-Ab)], and with lymphocytic infiltration.[1,2]

The incidence of this disease is 2% with a peak in women 30-50 years-old, Genetic and environmental factors are considered the main triggers of the disease.[3] Vitamin D is a steroid molecule that is mainly produced in the skin and regulates the expression of many genes.[4] 25-hydroxyvitamin D (25(OH) D) this form is mainly converted in the liver and the kidneys to the active form of 1, 25(OH) D3 and is commonly used as an indicator of vitamin D status.[5]

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Vitamin D deficiency can be caused by low sun exposure, lack of vitamin D fortified foods and malabsorption. Impaired hydroxylation of vitamin D in liver or kidney can also cause deficiency.[2] The main role of vitamin D is to control bone metabolism, calcium and phosphorus homeostasis. Vitamin D is also associated with non-skeletal roles, including autoimmune diseases, infectious diseases, metabolic syndrome and its components, cardiovascular diseases, cancers, and all-cause mortality.[2-4]

Vitamin D acts as an immunomodulator in autoimmune diseases such as Hashimoto's thyroiditis (HT).[6] Despite the fact that it was initially described as a vitamin", vitamin D is now considered as both a fat-soluble vitamin and a steroid hormone that plays a central role in the regulation of calcium/phosphate homeostasis and bone intensity.[7]

Vitamin D has major effects on nearly all cells of the immune system. Antigen presenting cells, such as dendritic cells, macrophages, T and B cells, express the vitamin D receptor. As an immune modulator, vitamin D reduces activation of the acquired immune system.[8-11] Vitamin D also inhibits generation of cytokine which plays an important role in developing autoimmune thyroiditis.[12]

Although several studies have revealed low serum 25-hydroxyvitamin D (25(OH) D) levels, among patients with HT as vitamin D deficiency is correlated with the presence or high levels of antithyroid antibodies, abnormal thyroid function, increased thyroid volume, and increased thyroid stimulating hormone (TSH) levels,[8-10] but it is unclear if this association is the result of the autoimmune disease process or part of its cause.[4,6]
Considering the potential role of vitamin D in autoimmune diseases, the aim of this study is to examine vitamin D levels in patients with hypothyroid diseases and its correlation with HT.

MATERIALS AND METHODS

The study group is choosen from patients who visited the endocrinology outpatient clinic of Prince Mishiri Bin Saud Hospital ((PMSH) Hospital for thyroid evaluation or follow-up by endocrinologist from July 2015 To August 2017.
Although subjects with normal 25(OH) D concentrations are rare in our region the control group in this study is a real healthy group with a normal 25(OH) D concentrations.
A venous blood sample was collected in the morning after overnight fasting. Patients underwent a thyroid function tests, anti-thyroid antibodies, and serum 25(OH) D levels. Thyroid antibodies were TPO-Ab and Thyroglobulin Antibody (TgAb) and ultrasound patterns (diffusely enlarged thyroid gland with a heterogeneous echo texture and occasionally hypervascularity on color Doppler study) suggestive of HT. Serum Parathyroid Hormone (PTH), Other biochemical parameters were blood glucose, hepatic transaminases (AST, ALT), urea, creatinine, calcium and phosphorus were also measured in these patients.
Participants who had a history of another autoimmune disease, diabetes mellitus, malignancy, chronic renal or liver disease, metabolic bone disorders, primary hyperparathyroidism as well as those with epilepsy treated by anticonvulsants or taking any medication that could affect 25(OH) D levels were excluded from the study, subjects who had transient thyroid dysfunction but negative thyroid autoantibodies, such as subacute thyroiditis or nonthyroidal illness, were excluded.
Among imaging techniques, a thyroid and kidney ultrasound (US) performed by an experienced radiologist was used to confirm HT patterns and detect nephrolithiasis (kidney stones in urinary tract).
A total of 310 were selected, Of these, 84 displayed normal thyroid function and negative thyroid auto-antibodies as well as having no evidence of thyroid disease (control). The other 226 patients were placed in the AITD or non-AITD group according to the presence of antithyroid antibodies, 119 subjects were diagnosed as having HT (AITD), 107 Non-AITD .
The diagnosis of patients with HT was based on TPO-Ab (>34 mIU/L) or Tg-Ab positivity (>115 mIU/L). Patients with HT were also classified into three groups according to their thyroid function status at the time of sampling. Overt hypothyroid patients were those with serum TSH >10 mIU/L and free thyroxine (fT4) < 12 pmol/L, or those with levothyroxine replacement regardless of thyroid function status. Subclinical hypothyroid patients were those with normal serum fT4 12.0–22 pmol/L and with elevated serum TSH levels within the range of 4.2-10 mIU/L. Euthyroid patients were those with normal serum fT4 and TSH levels (0.27-4.2 mIU/L).
Laboratory parameters were measured using a Roche cobas e 411, 501 Analyzer which is electrochemiluminescence immunoassay (ECLIA; Roche Diagnostics®, Penzberg, Germany).

Statistical analyses

Results were statistically analyzed by SPSS 11.5 for Windows. The mean and the standard deviation (SD) for all the variables were calculated. Analysis of variance F test (ANOVA) was used to compare the results of all examined cases in all studied groups.
The correlations between serum Vit D, calcium and TSH were presented by correlation coefficient (r2). Results considered significant or non-significant when P > or < 0.05, respectively.

RESULTS

A total of 226 subjects (181 females and 45 males). The overall mean serum 25(OH) D level was 13.7 ng/mL. The prevalence of vitamin D deficiency is significantly different in study and control group was 43 % and 11 %, respectively (p= 0.0001). [Table 1].
Serum TSH, FT4 concentrations of control and study group were statistically different (p = 0. 0.001, 0.005, respectively) but FT3 were not statistically different(p = 0.690) . Study group had a lower serum 25(OH)D concentration than control group (13.7 ± 5.4 vs 35.5 ± 7.3 , p < 0.0001) [Table 1].
PTH concentration was high, calcium and phosphorus levels were low in study group. The differences were statistically significant (p = 0.005, 0.0004, 0.004, respectively) [Table 1].
The mean age of study and control groups were 38.2 ± 6.1, 39.1 ± 6.4, respectively. The difference was not statistically significant (p = 0.466). Blood glucose, AST, ALT and creatinine levels of groups were also similar (p = 0.122, 0.143, 0.059, 0.131, respectively) [Table 1].
Anti TPO antibodies and TG antibodies were significantly higher in study group than control one (p= 0.000 for both). [Table 1].
Serum calcium levels had a negative significant correlation with serum TSH (r = − 0.39, P =0.036). Otherwise it was non-significantly correlated with either T3and T4 in hypothyroid patients.

Among the 226 patients, 119 subjects were diagnosed as having AITD (HT) and 107 as non-AITD. The baseline characteristics of AITD and non-AITD patients are compared in Table 2. Patients with AITD were significantly younger and higher serum PTH levels than those with non-AITD. The mean serum 25(OH)D levels in patients with AITD (HT) 11.8± 4.7 ng/mL had a tendency to be lower than in those with non-AITD 15.6 ± 6.1 ng/mL, but the difference was not significant (p >0.05). The prevalence of vitamin D defficiency in patients with AITD was significantly higher than in those with non-AITD (58.9% vs. 41.1 %, p=0.013; [Table 2]).

Table 1: Characteristics of the study and control groups.

	Reference values	Study group (N=226)	Control group (N=84)	P value
Age		38.2±6.1	39.1±6.4	0.466
Glucose (mmol/L)	3.6-6.1	5.1±0.45	5.4±0.67	0.122
Creatinine(umol/L)	71-115	81.6±13.6	87.7±15.1	0.143
AST (IU/L)	<40	17.0±8.3	17.9±6.7	0.059
ALT (IU/L)	<40	16.3±5.2	17.2±5.1	0.131
TSH (µlU/mL)	0.27-4.2	4.6±6.4	1.8±0.9	0.001
FT3(pmol/L)	3.1-6.8	4.69±3.7	4.4±1.7	0.690
FT4 (pmol/L)	12.0-22	12.96±1.68	16.92±3.94	0.005
PTH(pg/mL)	15-65	73.0±39.7	61.2±30.7	0.005
Calcium(mmol/L	2.15-5.5	2.23±0.21	3.1±0.18	0.0004
Phosphorus(mmol/L)	0.81-1.45	0.96±0.22	1.15±0.24	0.004
25(OH)D(ng/mL) Prevalence of vitamin D defficiency (%)	30-70	13.7±5.4 43 %	35.5±7.3 11%	<0.0001 <0.0001
TPO-Ab (IU/ml)	.0-34	213±245.1	12.3±2.0	0.000
Tg Ab(IU/ml)	0-115	539±463.5	19.3±4.2	0.000

Table 2: The characteristics based on the presence of autoimmune thyroid disease (AITD)

	HT (n=119)	Non-AITD (n=107)	P-value
Age (years)	34.8 ± 63	39.8± 6.4	0.000
Female gender [n (%)]	58..9 %	41.7 %	0.013
25 (OH)D (ng/mL)	11.8 ± 4.7	15.6±6.1	0.011
Prevalence of vitamin D defficiency (%)	58.9 %	41.1 %	0.013
PTH (pg/ml)	76.0 ± 39.9	70.1± 40.2	0.012
Calcium (mmol/L)	2.18 ± 0.11	2.28± 0.13	0.000
Phosphorus (mmol/L)	0.93± 0.23	1.09± 0.21	0.051
fT4 (pmol/L)	11.2± 6.7	13.5 ± 3.9	0.005
TSH (mIU/L)	5.4 ± 11.9	3.8± 6.6	0.000
TPO-Ab (IU/ml)	543.2±123.5	19.1±13.8	0.000
Tg-Ab (IU/ml)	731.3± 210.4	28.7± 15.3	0.000

Table 3: The characteristics based on vitamin D defficiency

	Vitamin D deficiency [25(OH)D < 30 ng/mL]	Vitamin D sufficiency [25(OH)D ≥30 ng/mL]	P-value
Age (years)	35.7± 13.2	38.7± 15.4	0.004
Female gender [%]	34.07 %	8.84 %	0.000
PTH (ng/L)	78.1± 18.6	67.9± 12.4	0.000
Calcium (mmol/L)	2.26± 0.12	2.27± 0.11	0.395
Phosphorus (mmol/L)	1.68± 0.22	1.79± 0.21	0.162
fT4 (pmol/L)	19.7± 13.3	19.1± 12.0	0.501
TSH (mIU/L)	5.2 ± 12.0	3.2± 7.3	0.006
TPO-Ab (IU/ml)	420.8±143.	299±93.2	0.000
Tg-Ab (IU/ml)	642.5±164.1	493± 124.1	0.005
Prevalence of TPO-Ab or Tg-Ab positivity [%]	57.3 %	37.1 %	0.019

Table 4: Serum 25(OH)D levels and the prevalence of vitamin D defficiency according to the presence and the severity of Hashimoto's thyroiditis (HT).

	25(OH)D (ng/mL)	Vitamin D defficiency(%)
Non-AITD	15.6 ± 6.1	37.1
HT	11.8 ±4.7	48.9
HT with ET	9.3 ± 3.2	44.1
HT with SCH	13.3 ± 4.9	29.7
HT with OH	8.1 ± 4.7*	60.4

AITD, autoimmune thyroid disease; ET, euthyroidism; SCH, subclinical hypothyroidism; OH, overt hypothyroidism P value < 0.026

Table 5: Correlations of 25(OH) D with thyroid auto antibodies, TSH and T4.

25(OH) D	AntiTg	AntiTPO	TSH	T4	Correlation
Study group (N=226)	- 0.482	- 0.335	- 0.423	0.045	r
	0.005	0.019	0.013	0.05	p

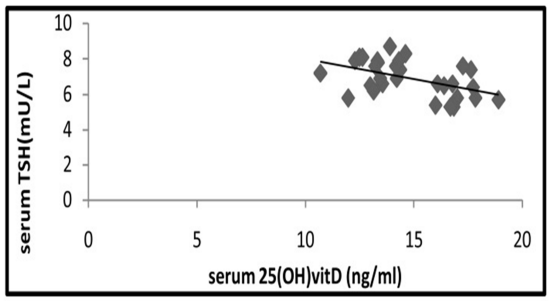

Figure 1: Correlations between 25(OH)vit D and serum TSH levels in hypothyroid patients

Anti TPO antibodies and TG antibodies, TSH in Patients with AITD were significantly higher than those with non-AITD. (p= 0.000 for all). While calcium and FT4 were significantly lower (p= 0.000, 0.005 respectively).[Table 3].

Patients with vitamin D defficiency were significantly younger (p=0.004) and more predominantly female (34.07 % vs 8.84 % , p=0.000) . The serum PTH levels in patients with vitamin D defficiency were significantly higher than those with vitamin D sufficiency (78.1 vs 67.9 p=0.000) , but there were no significant differences in serum calcium and phosphorus levels (p=0.395 , p= 0. 162) respectively . The vitamin D defficiency group had a significantly higher TSH level (5.2 vs 3.2 p= 006) and prevalence of thyroid autoantibody positivity (TPO-Ab 57.3%, vs Tg-Ab 37.1 %), higher thyroid autoantibody titres (TPO-Ab, and Tg-Ab titres) (p=0.000 , p= 0. 005) respectively, than the vitamin D sufficiency group but there were no significant differences in fT4 (p= 0. 501).

Patients with HT were further classified into three groups according to their thyroid function status at the time of sampling: euthyroid (n=52), subclinical hypothyroid (n=20) , and overt hypothyroid patients (n=47). There were significant differences between the 25(OH)D levels of the HT groups and the non-AITD group (p =0.011). Overt hypothyroid patients with HT had significantly lower 25(OH)D levels than those with non-AITD (p=0.008), but there were no differences in 25(OH)D levels between other groups. Similarly, the prevalence of vitamin D defficiency was significantly higher in overt hypothyroid patients with HT than in euthyroid and subclinical hypothyroid patients with HT and in those with non-AITD (60.4% vs. 44.1%, 29.7%, respectively, p 0.009 , 0.017 , 0.026) ; [Table 4])

Correlation analyses have shown that Serum 25(OH)D levels were also significantly negatively correlated with serum TSH levels (r= -0.423 , p=0.013) with non-significant positive correlation with T4 (r = 0.045, P > 0.05)., 25(OH) D concentrations has negative correlation with thyroid auto antibodies (p < 0.05 , [Table 5]).

A significant positive correlation persisted between Anti Tg and TSH (p < 0.001), and between TSH and Anti TPO (p < 0.001)

DISCUSSION & CONCLUSION

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 and has a fairly long circulating half-life of 15 days. 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 . Levels of 1, 25(OH)2D do not typically decrease until vitamin D deficiency is severe. Therefore, in the present study we measured serum 25(OH)D rather than 1,25(OH)2D to ensure we are getting more accurate results .[13]

Numerous studies have confirmed that when Vit D deficiency exists, the risk factors of autoimmune diseases, malignant cancer, or other diseases are significantly increased.[14]

The ages of the subjects in our study were between the most appropriate age's ranges for Hashimoto's thyroiditis because the incidence of the disease is higher in age between 30-50 years. Additonally, severe vitamin D deficiency is also common in reproductive age of women.[15,16]

The prevalence of vitamin D deficiency (serum 25(OH)D levels <30 ng/mL) in the study group (43 %) was significantly higher than that observed in healthy controls (11 %; P<0.0001). also in agree with Bozkurt et al. (2013) our study demonstrated that serum 25(OH)D levels of study group were significantly lower than controls (13.7± 5.4 ng/mL versus 35.5±7.3 ng/mL, P< 0.0001).[17]

Wang et al 2015 found that patients with hypothyroid disease compared to healthy control individuals had lower levels of 25(OH)D and were more likely to be deficient in 25(OH)D, suggesting a role of vitamin D deficiency in the pathological process of AITD.[5] Moreover, serum calcium levels recorded a significant decrease in hypothyroid patients when compared to controls (P = 0.0004) this is in agreement with Amal et al 2013.[13] There was a significant decrease in the levels of Vitamin D amongst hypothyroid patients.[18]

Furthermore, the present study showed that vitamin D and calcium serum levels were significantly lower in hypothyroid patients compared to the controls. We recorded a significant positive association between Vit D and calcium levels in both groups.

Vit D and calcium serum levels had negative correlation when compared to TSH levels. These results suggested that there may be a significant association between vitamin D deficiency and hypothyroidism. Our results were in harmony with the previous studies that showed the prevalence of vitamin D defficiency in Hashimoto's cases (92%) was significantly higher than that observed in healthy controls (63%, p < 0.0001).[19]

Our study showed a high prevalence (of vitamin D deficiency [serum 25(OH)D levels <30 ng/mL] among HT patients compared to patients with non-AITD (48.9 % % versus 37.4 %; P<0.05), such as an inverse correlation between serum 25(OH)D and anti-TPO thyroid antibodies Indicating association of vitamin D deficiency and autoimmune process or may be part of its cause . Several studies, as ours, have shown low serum 25(OH) D levels in patients with HT indicating an association between vitamin D deficiency and thyroid autoimmunity.[5,6] Bozkurt et al. (2013) demonstrated that serum 25(OH)D

levels of HT patients were significantly lower than controls.[17]

Kivity et al. reported that the prevalence of vitamin D deficiency was higher in patients with HT compared to patients with non-AITD, and vitamin D deficiency was also correlated with the presence of antithyroid antibodies and abnormal thyroid function tests, suggesting the involvement of vitamin D in the pathogenesis of AITD.[19]

Our findings are supported by other studies which showed lower serum 25(OH)D levels or a higher prevalence of vitamin D defficiency in AITD or HT and a negative correlation between 25(OH) D and TPO-Ab levels in AITD or HT.[9,10,20,21]

Some studies, however, have failed to find an association between low vitamin D status and AITD or HT. Goswami et al., revealed no association of vitamin D deficiency (<25 nmol/L) and anti-TPO positivity, but only a weak inverse correlation between serum 25(OH)D and anti-TPO levels in 642 students, teachers, and staff from India ($r = 0.08$; $p = 0.04$).[22]

Overt hypothyroid patients with HT had a significantly higher prevalence of vitamin D insufficiency and lower 25(OH)D levels than euthyroid or subclinical hypothyroid patients with HT or those with non-AITD. This in agreement with tamer et al 2011 who find Among HT cases, the prevalence rate of vitamin D insufficiency showed a trend to be higher in patients with overt hypothyroidism (47 of 50, 94%) or subclinical hypothyroidism (44 of 45, 98%) than in those with euthyroidism (57 of 66, 86%).[10]

In the present study, the vitamin D defficiency group had a significantly higher TSH level and prevalence of thyroid autoantibody positivity than the vitamin D sufficiency group, and inversely correlated with serum anti-TPO thyroid antibodies, this is in agreement of Barchetta et al 2015 and Mazokopakis et al 2015 who find After 4 months of vit D supplementation in HT patients with vitamin D deficiency, a significant decrease (20.3%) of serum anti-TPO levels was found.[20,23] These findings suggest that vitamin D deficiency may be related to pathogenesis of HT and that its supplementation could contribute to the treatment of patients withHT.

However, This not agree with Tayyibe et al 2014 who found that the frequency of Hashimoto's thyroiditis was similar in subjects with or without vitamin D deficiency and no correlation was found between vitamin D and thyroid auto antibodies.[24]

Other studies showed no association between low vitamin D status and thyroid autoimmunity.[22,25] It is unclear whether the low 25(OH)D levels observed in AITD or HT are the result of the autoimmune disease process or part of its cause.[6,19,25]

In this study vitamin D defficiency was found in 8.84 % of males and 34.07 %of females this in agreement of One of the Korean studies Choi et al 2011 and Korea National Health and Nutrition Examination Surveys in the Korean popu-lation in 2008, they find vitamin D insufficiency in 47.3% of males and 93.3% of females.[26] Also other studies found that Hashimoto's thyroiditis and vitamin D deficiency are more common disorders in women population.[3,27,28] But this is not agree with Yasmeh J1 2016.[29] Our results revealed decreased serum 25 (OH) vit D levels in females than those of male, otherwise this decrease was non-significant but we can refer this non siignificant decrease to the small sample size of our study, In concordance to our results, previous studies have observed that serum 25(OH)D levels did not differ significantly between males and females.[13]

In contrast to our results, Naeem et al, 2011 stated that vit D serum levels are significantly more decreased in females than males.[30]

Pathogenesis of AITD is multifactorial, combining genetic, immune, environmental, and hormonal influences like vitamin D.[19] In genetically predisposed individuals, the disruption of these neuroendocrine-immune interactions by environmental factors results in thyroid autoimmune dysfunction , These interactions are able to shift the balance between type 1 T helper (Th1)-Th2 immune response, resulting in a Th1-cell-mediated autoimmune reaction with thyrocyte destruction and hypothyroidism in HT.[31]

The mechanism underlying the link between vitamin D and autoimmunity is not completely understood but is probably associated with its anti-inflammatory and immunomodulatory functions.[20,26] The expression of the nuclear vitamin D receptor (VDR) and the vitamin-D-activating enzyme 1α-hydroxylase (CYP27B1) in most immune cells, including T cells, B cells, and antigen-presenting cells (APCs) including macrophages and dendritic cells (DCs), highlighted the potential involvement of vitamin D in the immune system and in the pathogenesis of autoimmune diseases.[32,33]

One of two mechanisms may explain the low levels of vitamin D in patients with hypothyroidism. First, the low levels of vitamin D may be due to poor absorption of vitamin D from the intestine. Second, the body may not activate vitamin D properly. Importantly, both vitamin D and thyroid hormone bind to similar receptors called steroid hormone receptors. A different gene in the Vitamin D receptor was shown to predispose people to autoimmune thyroid disease including Graves' disease and Hashimoto's thyroiditis.[13]

The discordance of findings between current study and other studies may depend on patient selections (gender, age, BMIs, exclusion criteria, etc), group creations (properties of groups, level of vitamin D deficiency), society differences (genetic properties, peoples).

In conclusion, vitamin D defficiency is common in women and was associated with AITD and HT as well as with progress of thyrocyte damage in HT.

There was a negative correlation between vitamin D and TSH levels.

Further studies are needed to investigate whether vitamin D defficiency is a causal factor in the pathogenesis of AITD (HT) to investigate the mechanisms by which vitamin D affects autoimmunity and whether vitamin D supplementation would be helpful in patients with these diseases and also to evaluate the cost-effectiveness of vitamin D supplementation and to suggest the possible optimal dose treatment.

Considering current evidence, presented in this study, screening for vitamin D deficiency and careful vitamin D supplementation, when required, may be recommended for patients with HT.

REFERENCES

1. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. Autoimmun Rev 2014; 13: 391-7.
2. Hell J Nucl Med 2017; 20(1): 51-56 Epub ahead of print: 20 March 2017.
3. Kirim S, Keskek SO, Köksal F, Haydardedeoglu FE, Bozkirli E, Toledano Y. Depression in patients with euthyroid chronic autoimmune thyroiditis. Endocr J. 2012; 59(8): 705-708.
4. Makariou S, Liberopoulos EN, Elisaf M, Challa A, 2011 Novel roles of vitamin D in disease: What is new in 2011? Eur J Intern Med 22: 355-362.
5. Wang J, Lv S, Chen G et al. Meta-analysis of the association between vitamin D and autoimmune thyroid disease. Nutrients 2015; 7: 2485-98.
6. Mazokopakis EE, Kotsiris DA. Hashimoto's autoimmune thyroiditis and vitamin D deciency. Current aspects. Hell J Nucl Med 2014; 17: 37-40. 2.
7. Caprio M, Infante M, Calanchini M et al. Vitamin D: not just the bone. Evidence for bene cial pleiotropic extraskeletal e_ects. Eat Weight Disord 2016.
8. Yasuda T, Okamoto Y, Hamada N, 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.
9. Shin DY, Kim KJ, Kim D, Hwang S, Lee EJ, 2014 Low serum vitamin D is associated with anti-thyroid peroxidase antibody in autoimmune thyroiditis. Yonsei Med J 55: 476-481.
10. Tamer G, Arik S, Tamer I, Coksert D, 2011 Relative vitamin D insufficiency in Hashimoto's thyroiditis. Thyroid 21: 891-896.
11. Snijder M, van Dam R, Visser M, Deeg D, Seidell J, Lips P To, et al. Vitamin D and diabetes. Diabetologia 48:1247-1257. Diabetologia. 2006; 49(1): 217-218. Epub 2005 Dec 13.
12. Deluca HF, Cantorna MT. Vitamin D: its role and uses in immunology. FASEB J. 2001; 15(14): 2579-2585.
13. Dr. Amal Mohammed Husein Mackawy,(1) Bushra Mohammed Al-ayed,(2) and Bashayer Mater Al-rashidi . Int J Health Sci (Qassim). 2013 Nov; 7(3): 267–275.
14. Munger KL, Levin LI, Massa J, Horst R, Orban T, Ascherio A. Preclinical serum 25-hydroxyVd levels and risk of type 1 diabetes in a cohort of US military personnel. Am J Epidemio 2013; 177: 411-419.
15. 15. Erkal MZ, Wilde J, Bilgin Y, Akinci A, Demir E, Bödeker RH, et al. High prevalence of vitamin D deficiency, secondary hyperparathyroidism and generalized bone pain in Turkish immigrants in Germany: identification of risk factors. Osteoporos Int. 2006; 17(8): 1133-1140.
16. Ergür AT, Berberoğlu M, Atasay B, Şıklar Z, Bilir P, Arsan S, et al. Vitamin d deficiency in Turkish mothers and their neonates and in women of reproductive age. J Clin Res Pediatr Endocrinol. 2009; 1(6): 266-269.
17. Bozkurt NC, Karbek B, Ucan B et al. The association between seve-rity of vitamin D de ciency and Hashimoto's thyroiditis. Endocr Pract. 2013; 19: 479-84.
18. Swati Sonawane, Sahil Bansal. Vitamin D deficiency and its association with thyroid diseases. International Journal of Contemporary Medical Research 2017;4(8):1765-1767.
19. Kivity S, Agmon-Levin N, Zisappl M, et al, 2011 Vi-tamin D and autoimmune thyroid diseases. Cell Mol Immunol 8: 243-247.
20. Mazokopakis EE, Papadomanolaki MG, Tsekouras KC, Evangelopoulos AD, Kotsiris DA, Tzortzinis AA, 2015 Is vitamin D related to pathogenesis and treatment of Hashimoto's thyroiditis? Hell J Nucl Med 18: 222-227.
21. Choi YM, Kim WG, Kim TY, et al, 2014 Low levels of serum vitamin D3 are associated with autoimmune thyroid disease in pre-menopausal women. Thyroid. 2014 Apr;24(4):655-61.
22. Goswami R, Marwaha RK, Gupta N, et al, 2009 Preva-lence of vitamin D deficiency and its relationship with thyroid autoimmunity in Asian Indians: a community-based survey. Br J Nutr 102: 382-386.
23. Barchetta I, Baroni MG, Leonetti F, et al, 2015 TSH levels are associated with vitamin D status and seasonal-ity in an adult population of euthyroid adults Clin Exp Med 15: 389-396.
24. Tayyibe Saler1, Şakir Ozgur Keşkek2, *, Suleyman Ahbab3, Sedat Cakir1, Gulay Ortoğlu2,Mehmet Bankir2, Omer Arif Pamuk2: Frequency of Hashimoto's thyroiditis in women with vitamin D deficiency: A cross sectional study American Journal of Internal Medicine 2014; 2(3): 44-48 .
25. D'Aurizio F, Villalta D, Metus P, Doretto P, Tozzoli R, 2015 Is vitamin D a player or not in the pathophysiology of autoimmune thyroid diseases? Autoimmun Rev14: 363-369.
26. Choi HS, Oh HJ, Choi H, et al, 2011 Vitamin D insuf-ficiency in Korea-a greater threat to younger generation: the Korea National Health and Nutrition Examination Survey (KNHANES) 2008. J Clin Endocrinol Metab 643-651.
27. Mocanu V. Vitamin D deficiency and metabolic syndrome among nursing home residents. Acta Endocrinol (Buc).2013; 9(1): 53-62.
28. Alagöl F, Shihadeh Y, Boztepe H, Tanakol R, Yarman S, Azizlerli H, et al. Sunlight exposure and vitamin D deficiency in Turkish women. J Endocrinol Invest. 2000; 23(3):173-177.
29. Yasmeh J1, Farpour F1, Rizzo V1, Kheradnam S1, Sachmechi I1. 1From: Department of Medicine, Queens Hospital Center, Icahn School of Medicine at Mount Sinai . Endocr Pract. 2016 Mar 28.
30. Naeem Z, AlMohaimeed AbdulRahman, Khalil FS, Ismail, Faiza Sh, Inam SN. Vitamin D status among population of Qassim Region, Saudi Arabia. International Journal of Health Sciences, Qassim University. 2011;(5):2.
31. Klecha AJ, Barreiro Arcos ML, Frick L, Genaro AM, Cremaschi G, 2008 Immune-endocrine interactions in autoimmune thyroid diseases. Neuroimmunomodula-tion 15: 68-75.
32. Baeke F, Takiishi T, Korf H, Gysemans C, Mathieu C, 2010 Vitamin D: modulator of the immune system. Curr Opin Pharmacol 10: 482-496.
33. Mathieu C, Adorini L, 2002 The coming of age of 1,25-dihydroxyvitamin D3 analogs as immunomodula-tory agents. Trends Mol Med 8: 174-179.

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