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Zinc, Vitamin D, and TSH Levels in Patients with Vitiligo

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ABSTRACT

Objective: Vitiligo is an acquired depigmenting autoimmune disorder of the skin. The disease association with autoimmune diseases, such as thyroid diseases, has been reported. Previous studies among patients with vitiligo have suggested possible correlation between zinc and vitamin D levels with conflicting results. Here we compared the thyroid hormones, zinc, and vitamin D levels in patients with vitiligo with normal healthy subjects.

Materials and Methods: We recruited 98 patients with vitiligo and 98 age- and sex-matched healthy subjects visiting dermatology clinics during spring and summer 2017. Serum zinc and vitamin D levels as well as thyroid stimulating hormone (TSH) and thyroid peroxidase antibody (anti-TPO) were measured and compared between groups.

Results: Patients with vitiligo had significantly lower zinc (p=0.01) and higher anti-TPO levels (p=0.02) with no difference in vitamin D (p=0.73) and TSH levels (p=0.31). Patients with vitiligo had also significantly higher rate of increased TSH (p=0.02) and positive anti-TPO (p=0.01). We observed no significant correlation between serum levels of vitamin D, zinc, and TSH with age, gender, and disease duration in patients with vitiligo.

Conclusion: Patients with vitiligo, compared to healthy subjects, had lower serum zinc levels, but not vitamin D levels. Increased TSH levels were higher in patients with vitiligo with non-significantly higher anti-TPO AB as suggested to be related to autoimmune disease.

Keywords: Vitiligo, zinc, vitamin D, thyroid function

INTRODUCTION

Vitiligo is an acquired depigmenting autoimmune disorder of the skin due to the destruction of functional melanocytes in the involved epidermis (1–3). Vitiligo can occur in both sexes with no racial differences and no preference in skin type and affects up to 2% of the general population (4). It can occur in any age with most common period of 10–30 years (5).

The disease etiology is complex and multifactorial, including autoimmune, neural, and self-destructive mechanisms as well as genetics, environment, inflammatory, and oxidative stress origin (6–9). The disease association with other autoimmune diseases, such as systemic lupus erythematosus, scleroderma, alopecia areata, and autoimmune thyroid diseases, has been demonstrated before (1, 4, 7–10). Even recent studies have suggested that thyroid autoimmunity would trigger and affect the depigmentation process of vitiligo (8).

Vitiligo can involve every part of the skin but usually it appears in the exposed areas, and many patients cover their vitiligo. Some studies have reported the low levels of some elements such as zinc and vitamin D levels and their possible role in the disease pathogenesis (3, 4, 11).

Vitamin D is a steroid hormone that regulates bone metabolism, calcium homeostasis, controls cell proliferation and differentiation, and may exert several immunomodulatory activities. Vitamin D plays its role through vitamin D receptor, which is expressed by melanocytes indicative of vitamin D role in the melanogenesis (3).

In the human body, zinc has antioxidant effects and is involved in the melanogenesis (5, 12). It is plausible that the deficiency of both vitamin D and zinc levels due to their role in monogenesis, can affect disease progression and severity. However, different studies have reported conflicting results regarding the vitamin D and zinc levels in these patients (4–6, 13–15). Also, the association between vitiligo and thyroid disease is not well understood. We conducted this study to evaluate and compare the thyroid hormones, zinc, and vitamin D levels between patients with vitiligo and normal healthy subjects.

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Table 1. Demographic findings between patients with vitiligo and control subjects

	Patients with vitiligo		Control subjects		p
	n	%	n	%	
Age (years) Mean±SD	30.06±16.18		29.45±13.16		0.77
Gender					
Male	50	51	53	54.1	0.66
Female	48	49	45	45.9	
Skin type					
III	80	81.6	87	88.8	0.15
IV	18	18.4	11	11.2	
Familial history of thyroid disease	29	29.6	24	24.5	0.42
Familial history of vitiligo	17	17.3	3	3.1	<0.001

SD: Standard deviation

MATERIALS and METHODS

This is a case control study including 98 patients with vitiligo and 98 age- and sex-matched healthy subjects randomly recruited from outpatient dermatology clinics, Sina Hospital, Tabriz, Iran, during spring and summer 2017. Control group were completely healthy individuals with no known systemic or autoimmune diseases. Patients consuming any immunosuppressive medication or with any chronic systematic diseases, using zinc or vitamin D supplements or steroids, magnesium-based laxatives, anticonvulsant drugs, diuretics, or alcohol use were also excluded in both groups. The Ethics Committee of Tabriz University of Medical Sciences approved the study (♯58197), and informed written consents were obtained from all participants.

Fasting blood samples were taken from all participants. the concentration of zinc levels was determined using flame atomic absorption spectrometry method using commercially available kits (Biorexfars Co. LTD, Tehran, Iran). Serum 25(OH)D was measured using a DIAsource immunoassay kit (Belgium). Vitamin D deficiency was defined as plasma levels of 25-OH vitamin D <10 ng/ml and insufficiency as 10–30 ng/ml. Thyroid stimulating hormone (TSH) was recorded using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Diaplus Inc., Canada) and anti-thyroid peroxidase (anti-TPO) levels were assayed by available ELISA kits (Monobind Inc., USA). The cutoff values of positivity for anti-TPO were 40 IU/ml. The normal range for TSH was 0.5–5.5 mIU/L.

Statistical Analysis

All data were analyzed using SPSS22 (version 22; SPSS Inc., Chicago, IL). The results are expressed as mean±standard deviation or percentage. Levene test was applied to test the homogeneity of variance. Kolmogorov–Smirnov test was used to assess normality of data distribution. Pearson chi-square analysis and Fisher exact test and independent T-test were used to compare data between groups. Pearson's correlation was used to evaluate possible correlations between zinc, vitamin D, and TSH levels with age, and disease duration. p-values <0.05 were considered significant.

RESULTS

Both groups were similar regarding baseline findings (Table 1). Patients with vitiligo had significantly higher positive familial history of vitiligo.

Laboratory findings between groups are demonstrated in Table 2. Patients with vitiligo had significantly lower zinc levels and higher anti-TPO levels. Patients with vitiligo had significantly higher rate of increased TSH and positive anti-TPO. However, there was no significant difference between groups regarding TSH, vitamin D levels, and abnormal vitamin D levels.

The disease duration in case group was 34.65±3.35 months including 84 cases (85.7%) <5 years and 14 (14.3%) >5 years. We found no correlation between age and disease duration and zinc levels, TSH, and vitamin D (Table 3). Also, there was no difference in laboratory findings between males and females (Table 4) and between cases with less or above 5 years of duration among patients with vitiligo (Table 5).

DISCUSSION

Vitiligo is a depigmenting disorder with unknown etiology with autoimmunity as the major etiological factor. Its association with different autoimmune diseases has been shown previously. The correlation between vitiligo and thyroid disorders has also been suggested (1, 4).

In our study, we observed no significant differences between patients with vitiligo and healthy subjects in TSH and anti-TPO levels or with positive anti-TPO rate. However, increased TSH levels were significantly higher in patients with vitiligo (17.3% vs. 7.1%). Gender, age, or disease duration had no significant difference in TSH levels in patients with vitiligo.

Previous studies have reported presence of hypothyroidism in 15–40% of patients with vitiligo in different regions (1, 7, 10, 16, 17). Similar to our findings, Sedighe and Gholamhossein (16) reported 15.7% hypothyroidism among Iranian patients with vitiligo, while Nejad et al. (18) reported 21.1% autoimmune thyroid disease in patients with vitiligo.

Table 2. Laboratory findings between patients with vitiligo and control subjects

	Patients with vitiligo		Control subjects		p
	n	%	n	%	
Zinc levels (µg/dL) Mean±SD	87.87±21.11		97.40±29.79		0.01*
TSH levels (mIU/L) Mean±SD	3.95±0.47		3.28±0.47		0.1
Increased TSH	17	17.3	7	7.1	0.02*
Anti-TPO (IU/mL) Mean±SD	129.43±33.38		83.89±25.73		0.02*
Increased anti-TPO	34	34.7	18	18.4	0.01*
Vitamin D (ng/ml) Mean±SD	24.23±14.29		24.86±11.75		0.73
Vitamin D					
Sufficient	28	28.6	35	35.8	
Insufficient	53	54.1	46	46.9	0.52
Deficient	17	17.3	17	17.3	

SD: Standard deviation; TSH: Thyroid stimulating hormone; Anti-TPO: Thyroid peroxidase antibody. *Two sided significant

Studies have also reported an increased risk of thyroid disease development with age and doubling risk in every 5 years (9). Although we found no increase in abnormal TSH levels regarding age or duration of the disease, Gopal and colleagues (7) also reported no correlation between prevalence of hypothyroidism and sex, age, and duration of the disease.

Studies have suggested screening for thyroid abnormalities in these patients with no united guidelines; most of the guidelines have recommend screening in those with familial history of thyroid disease, female gender, longer duration and stressful events (9). It seems that due to the increased rate of abnormal TSH levels in these patients, it would be better to have annual physical examination and ask patients about thyroid symptoms and maybe check thyroid function tests at least every 2 years.

Previous studies have reported conflicting results regarding vitamin D levels in patients with vitiligo (19, 20). A recent systematic review found lower vitamin D levels in patients with vitiligo compared to healthy subjects (4). We observed no significant difference in vitamin D levels between patients with vitiligo and normal subjects. Karagun and colleagues (15), Ustun and colleagues (19) and Khurrum and al-Ghandi (21) found similar results. However, the last study observed significantly lower levels of vitamin D in younger

Table 3. Correlation between age and disease duration with laboratory findings

	With age		With disease duration	
	Pearson correlation	p	Pearson correlation	p
Zinc	-0.092	0.370	0.027	0.79
TSH	0.126	0.21	0.006	0.95
Vitamin D	0.192	0.058	0.031	0.76

TSH: Thyroid stimulating hormone

Table 4. Laboratory findings between male and female patients with vitiligo

	Males		Females		p
	n	%	n	%	
Zinc levels (µg/dL) Mean±SD	90.94±20.88		84.68±21.08		0.14
TSH levels (mIU/L) Mean±SD	3.89±0.74		4.01±0.57		0.9
Increased TSH	8	16	9	18.8	0.71
Anti-TPO (IU/mL) Mean±SD	118.71±45.23		140.59±49.69		0.74
Increased anti-TPO	9	18	14	29.2	0.19
Vitamin D (ng/ml) Mean±SD	22.37±10.78		26.16±17.11		0.19
Vitamin D					
Sufficient	10	20	18	37.4	0.10
Insufficient	32	64	21	43.8	
Deficient	8	16	9	18.8	

SD: Standard deviation; TSH: Thyroid stimulating hormone; Anti-TPO: Thyroid peroxidase antibody

Table 5. Laboratory findings in patients with vitiligo according to the disease duration

	<5 years		>5 years		p
	n	%	n	%	
Zinc levels (µg/dL), Mean±SD	87.55±20.29		89.79±26.30		0.71
TSH levels (mIU/L), Mean±SD	4.01±0.54		3.60±0.65		0.18
Increased TSH	14	16.9	3	20	0.7
Anti-TPO (IU/mL), Mean±SD	111.33±32.96		238.03±124.68		0.76
Increased anti-TPO	17	20.5	6	40	0.08
Vitamin D (ng/ml), Mean±SD	24.17±14.50		24.57±13.46		0.92
Vitamin D					
Sufficient	24	28.9	4	26.7	0.86
Insufficient	44	53	9	60	
Deficient	15	18.1	2	13.3	

SD: Standard deviation; TSH: Thyroid stimulating hormone; Anti-TPO: Thyroid peroxidase antibody

age, male gender, and longer duration of the disease in vitiligo group (21), while in our study there were no significant differences.

A possible explanation for the difference in vitamin D levels in different studies can be related to seasonal variations and geographical area that the study was conducted in. As in cold areas like the area in our study or in cold seasons, it is possible to observe lower vitamin D levels for all subjects.

It is reported that vitamin D has antiapoptotic effects and can increase melanogenesis and tyrosinase content (4, 22). So, some studies have recommended using oral vitamin D or its analogs alone or along with other therapies, which have shown promising results (4).

Another finding in our study was lower levels of zinc in patients with vitiligo. However, there were no significant differences in zinc levels regarding age, gender, and disease duration among patients with vitiligo.

Rostami Moghaddam and colleagues (13) reported lower zinc levels in patients with vitiligo. Mirnezami and Rahimi (5) also reported low serum zinc levels in generalized patients with vitiligo. Unlike our findings, they also reported significant decrease in zinc levels with increase in the duration of the disease. A meta-analysis by Zeng et al. (23) also demonstrated lower serum zinc levels among Chinese patients with vitiligo. However, some other studies have reported conflicting results; Arora et al. (24) found that zinc levels were not significantly different between patients with vitiligo and healthy subjects. Helmy et al. (25) on the other side have reported higher serum zinc levels in patients with vitiligo.

Zinc is known for its antiapoptotic and antioxidant effects and for its role in melanogenesis (14). Apoptosis of melanocytes is considered to be involved in the pathogenesis of vitiligo. It is plausible to consider that vitamin D and zinc supplementation would have considerable effects on vitiligo due to their role in prevention of apoptosis.

This study had some limitations. First, this was an observational and cross-sectional study. As a single-center study from a tertiary educational hospital, we could not generalize our findings to all patients with vitiligo in the general population.

CONCLUSION

Our results showed that patients with vitiligo compared to healthy subjects had lower serum zinc levels, but not vitamin D levels. Increased TSH levels are higher in patients with vitiligo with non-significantly higher anti-TPO AB is suggested to be related to autoimmune disease.

Ethics Committee Approval: The Ethics Committee of Tabriz University of Medical Sciences approved the study (♯58197).

Informed Consent: Informed written consents were obtained from all participants.

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Author Contributions: Conceived and designed the experiments or case: SS, AGZ. Performed the experiments or case: SS, AGZ, AR. Analyzed the data: SS, AR. Wrote the paper: AGZ, AR. All authors have read and approved the final manuscript.

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