Clinical Findings of Vitiligo Patients Attending a University Hospital Dermatology Clinic in Turkey

Türkiye'de Bir Üniversite Hastanesi Dermatoloji Kliniğine Başvuran Vitiligo Hastalarının Klinik Bulguları

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Abstract

Vitiligo is a common disorder which affects about 1% of the world population. The aim of this study was to evaluate the epidemiological data, comorbid diseases, and several blood parameters of the vitiligo patients. This study was performed as a retrospective chart review. Patient records were screened from the electronic database of the hospital. Descriptive statistics were given as mean ± standard deviation or median and interquartile ranges according to the distribution of the data. Categorical variables were summarized as number and percentage. Statistical analyses were performed with Jamovi program and $p<0.05$ was accepted as significance level (p value) in statistical analyses. This study included 68 individuals, 30 (44.1%) of whom were males, and 38 (55.9%) of whom were females. Comorbid diseases were detected in 22 (32.4%) patients. Thyroid diseases were present in 15 (22.1%) patients, and thyroid autoantibodies were positive in 12 (17.6%) patients. Exacerbations of disease were more frequent in females ($p=0.025$), and history of stress was also more frequent in females ($p=0.011$). History of stress related exacerbations were more frequent in females and patients older than 18 years of age. Therefore, it is important to evaluate psychological factors especially in women with vitiligo and to consult to a psychiatrist when necessary.

Keywords: Stress, Thyroid autoantibodies, Vitiligo

Öz

Vitiligo, dünya nüfusunun yaklaşık %1'ini etkileyen yaygın bir hastalıktır. Bu çalışmanın amacı vitiligo hastalarının epidemiyolojik verilerini, komorbid hastalıkları ve çeşitli kan parametrelerini değerlendirmektir. Bu çalışma retrospektif olarak yapıldı. Hasta kayıtları hastanenin elektronik veri tabanından tarandı. Verilerin dağılımına göre tanımlayıcı istatistikler ortalama ± standart sapma veya ortanca ve çeyrekler arası değerler olarak verildi. Kategorik değişkenler sayı ve yüzde olarak özetlendi. İstatistiksel analizler Jamovi programı ile yapıldı ve istatistiksel analizlerde anlamlılık düzeyi (p değeri) olarak $p<0.05$ kabul edildi. Çalışmaya 30'u (%44.1) erkek, 38'i (%55.9) kadın olan 68 kişi katıldı. Komorbid hastalıklar 22 (%32,4) hastada tespit edildi. 15 (%22.1) hastada tiroid hastalığı, 12 (%17.6) hastada tiroid otoantikorları pozitif bulundu. Hastalık alevlenmeleri ($p=0.025$) ve stres öyküsü kadınlarda daha sıktı ($p=0.011$). Strese bağlı alevlenme öyküsü kadınlarda ve 18 yaşından büyük hastalarda daha sık görüldü. Bu nedenle, özellikle vitiligolu kadınlarda psikolojik faktörlerin değerlendirilmesi ve gerektiğinde psikiyatriste danışılması önemlidir.

Anahtar Kelimeler: Stres, Tiroid otoantikorları, Vitiligo

Introduction

Vitiligo is a common disorder which is characterized pathologically by the loss of melanocytes in the epidermis and clinically by depigmented macules (1). Although the prevalence rates as high as 8.8% have been reported from India, about 1% of the world population have been reported to have vitiligo (2,3). The second and third decades of life have the greatest incidence although the disease onset may be at any age (4). Vitiligo prevalences are similar in both sexes although females may be represented more in dermatology clinics due to cosmetic reasons (5).

Classification of vitiligo can be made according to the pattern of distribution as focal, segmental, acrofacial, generalized, universal, and mucosal type (6). It is not easy to predict the disease course; and the enlargement of existing lesions or the development of new lesions suggest active vitiligo (7). Vitiligo etiology is not clear. In the pathogenesis of the disease, genetic predisposition, autoimmunity, neural mechanisms, and toxic metabolites are thought to be responsible (8). Despite varying hypotheses, the absence of functional melanocytes is a common finding agreed by researchers (3).

Supporting the autoimmune hypothesis, many autoimmune disorders including type I diabetes, Addison's disease, diabetes mellitus, myasthenia gravis, scleroderma, rheumatoid arthritis, alopecia areata, and autoimmune thyroid diseases commonly accompany vitiligo (9). A very high rate of autoimmune disorders was also reported in a Turkish study (10).

The aim of our study was to evaluate epidemiological data, comorbid diseases, and several blood parameters of the vitiligo patients admitted to the dermatology clinic of Ministry of Health Çorum Erol Olçok Research and Education Hospital between December 2016 and October 2018 retrospectively.

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Material and Method

This study was performed as a retrospective chart review. Ethics committee approval; Hitit University Medical Faculty Clinical Research Ethics Committee permission was obtained with the

letter dated 04.01.2019 and numbered 16. Patient records were screened from the electronic database of the hospital. All patients diagnosed as vitiligo between December 2016 and October 2018 were included. Patients whose records had serious missing variables were excluded. The study was approved and the consent was obtained from the local ethics committee (2019-16). The diagnosis of vitiligo was made clinically by dermatologists and for patients with uncertain diagnoses, investigations such as wood's lamb examination and fungal skin scrapings were done to rule out common differentials.

Age, sex, age of onset of vitiligo disease, family history of vitiligo, reason for the first attack and exacerbation, presence of hair and nail involvement, comorbid diseases, serum iron, ferritin, vitamin B12, folate, and thyroid autoantibody levels were obtained from the records. Vitiligo was classified segmental, focal, vulgaris, acrofacial and mixed type (3,6).

To summarize the data obtained from the study, descriptive statistics were given as mean ± standard deviation or median and interquartile range according to the distribution of the data. Categorical variables were summarized as number and percentage. Numerical variables were controlled with the Kolmogorov-Smirnov test. To compare two independent groups, Independent Samples t test was used when numerical variables had a normal distribution and Mann-Whitney U test was used when they didn't have. To make comparisons in categorical variables, the Pearson Chi-Square test was used in 2x2 tables and Fisher's Exact Test was used in RXC tables. Statistical analyses were performed with Jamovi program and $p<0.05$ was accepted as significance level (p value) in statistical analyses.

Results

This study included 68 individuals, 30 (44.1%) of whom were males, and 38 (55.9%) of whom were females. The mean age of the patients was 35 (±16.66), and 16 (23.5%) individuals were at the range of 11-20 years of age. The age of the onset of the disease was below 18 years in 21 (30.9%) patients. A family history of vitiligo was found in 15 (22.1%) individuals. Hair involvement was present in 11 (16.2%), and nail involvement was present in 8 (11.8%) individuals. The reason for the exacerbation of the disease was history of stress in 42 (61.8%) patients, exercise in 1 patient (1.5%), and sunburn in 3 (4.4%) patients. The reason for the first attack was spontaneous in 28 (41.2%) individuals and history of stress in 40 (58.8%) individuals (Table 1).

Comorbid diseases were detected in 22 (32.4%) patients. The most common co-morbidity was thyroid disease (Table 2).

We compared sociodemographic and clinical variables in terms of sex. Acrofacial involvement was more prevalent in males (p=0.048). Exacerbations of disease were more frequent in females (p=0.025), and stress was also more frequent in females (p=0.011). Plasma iron and ferritin levels were lower in females (Table 3).

Table 1. Demographic and clinical data of the patients

	n (%)
Age (mean ± SD)	35 ± 16.66
Age (%)	
11-20 years	16 (23.5)
21-30 years	13 (19.1)
31-40 years	13 (19.1)
41-50 years	15 (22.1)
51-64 years	11 (16.2)
Age (%)	
Below 18 years	12 (17.6)
18 years and above	56 (82.4)
Gender (%)	
Male	30 (44.1)
Female	38 (55.9)
Family History of Vitiligo (%)	15 (22.1)
Age of onset of vitiligo (%)	
Below 18 years	21 (30.9)
18 years and above	47 (69.1)
Vitiligo Types (%)	
Segmental	1 (1.5)
Focal	16 (23.5)
Vitiligo vulgaris	23 (33.8)
Acrofacial	22 (32.4)
Mixed	6 (8.8)
Hair involvement (%)	11 (16.2)
Nail involvement (%)	8 (11.8)
Reason for exacerbation (%)	45 (66.2)
History of stress (%)	42 (61.8)
Exercise (%)	1 (1.5)
History of Sunburn (%)	3 (4.4)
Reason for the first attack (%)	
Spontaneous	28 (41.2)
History of stress	40 (58.8)

SD, Standard deviation. Descriptive statistics were given as ± standard deviation and number (%).

We also compared sociodemographic and clinical variables in terms of the age of disease onset being before or after 18 years of age. Patients with earlier disease onset were less likely to have history of stress as a cause of disease exacerbation (p=0.016), and their first attack was more likely spontaneous (Table 4).

Discussion

In this retrospective chart review, we investigated sociodemographic and laboratory findings of the vitiligo patients admitted to a university hospital dermatology clinic. In our study, there were more female patients than male patients. At least two previous studies also reported female predominance in their sample (11,12) but many other studies, including two studies from Turkey,

reported equal rates in males and females (10,13,14). We think female predominance in our sample doesn't reflect a true prevalence in females. Instead, it may be attributed to higher cosmetic worries of women causing more frequent hospital visits.

Table 2. Comorbid diseases and laboratory findings

	n (%)
Presence of comorbidity (%)	22 (32.4)
Allergic rhinitis (%)	1 (1.5)
Depression (%)	1 (1.5)
Thyroid disease (%)	15 (22.1)
Type 1 DM (%)	1 (1.5)
DM (%)	4 (5.9)
HT (%)	5 (7.4)
Cardiac disease (%)	2 (2.9)
Migraine (%)	1 (1.5)
Polycystic kidney disease (%)	1 (1.5)
Asthma (%)	1 (1.5)
Psoriasis (%)	1 (1.5)
History of atopia (%)	5 (7.4)
Elevated glucose (%)	6 (8.8)
Iron level (%)	
Low	23 (33.8)
Normal	43 (63.2)
High	2 (2.9)
Ferritin level (%)	
Low	15 (22.1)
Normal	53 (77.9)
Vit B12 deficiency (%)	9 (13.2)
Folate deficiency (%)	6 (8.8)
Elevated Anti TPO (%)	10 (14.7)
Elevated Anti TG (%)	9 (13.2)
Thyroid Autoantibodies (%)	
Negative	56 (82.4)
Positive	12 (17.6)

DM, diabetes mellitus; HT, hypertension; n, number; TG, thyroglobulin; TPO, thyroid peroxidase. Descriptive statistics were given as number (%).

The onset of vitiligo was below 18 years of age in 30.9% of our patients. Similar findings were reported in the literature in previous studies. In Pradhan et al.'s study, the age of disease onset was below 25 years in the majority of the patients (4). Topal et al. found that 20% of their patients had disease onset before 20 years of age (15). The mean age of our sample was 35, which was very similar to the mean age of 34.9 in Topal et al.'s study (15) and 37.4 in Gonul et al.'s study (5).

Vitiligo is known to have a genetic predisposition and multiple studies have reported about the rate of family history of vitiligo in vitiligo patients. Zhang et al. reported that 30% of their vitiligo cases were known to have an affected relative (16). Topal et al. found the familial history of vitiligo in 27% of their cases (15). The rate in our study was 22.1% which was similar to previous studies in Turkey but higher than a Japanese study which reported a 3.4% rate of family history in vitiligo patients which may be related to a high rate of consanguineous marriages in Turkey (17).

Table 3. Comparison of comorbid diseases and several laboratory parameters according to the sex of the patients

	Sex		**p**
	Male (n=30)	**Female (n=38)**	
Age (mean ± SD)	35.4 ± 18.5	34.7 ± 15.3	0.865
Age (%)			
Below 18 years	7 (23.3)	5 (13.2)	0.440
18 years and above	23 (76.7)	33 (86.8)	
Family history of vitiligo (%)	5 (16.7)	10 (26.3)	0.510
Vitiligo age of onset	31.6 ± 18.2	27.8 ± 16.3	0.381
Vitiligo age of onset (%)			
Below 18 years	10 (33.3)	11 (28.9)	0.901
18 years and above	20 (66.7)	27 (71.1)	
Vitiligo Types (%)			
Segmental	0 (0.0)	1 (2.6)	0.999
Focal	4 (13.3)	12 (31.6)	0.141
Vitiligo vulgaris	9 (30.0)	14 (36.8)	0.738
Acrofacial	14 (46.7)	8 (21.1)	**0.048***
Mixed	3 (10.0)	3 (7.9)	0.999
Comorbidity (%)	8 (26.7)	14 (36.8)	0.529
Allergic rhinitis (%)	1 (3.3)	0 (0.0)	0.441
Depression (%)	0 (0.0)	1 (2.6)	0.999
Thyroid disease (%)	3 (10.0)	12 (31.6)	0.066
Thyroid Autoantibody (%)			
Negative	27 (90.0)	29 (76.3)	0.250
Positive	3 (10.0)	9 (23.7)	
Type 1 DM (%)	1 (3.3)	0 (0.0)	0.441
DM (%)	3 (10.0)	1 (2.6)	0.314
HT (%)	0 (0.0)	5 (13.2)	0.062
Cardiac disease (%)	1 (3.3)	1 (2.6)	0.999
Migraine (%)	0 (0.0)	1 (2.6)	0.999
Policystic Kidney Disease (%)	0 (0.0)	1 (2.6)	0.999
Asthma (%)	0 (0.0)	1 (2.6)	0.999
Psoriasis (%)	1 (3.3)	0 (0.0)	0.441
History of atopia (%)	1 (3.3)	4 (10.5)	0.374
Hair involvement (%)	5 (16.7)	6 (15.8)	0.999
Nail involvement (%)	3 (10.0)	5 (13.2)	0.999
Exacerbation (%)	15 (50.0)	30 (78.9)	**0.025**
History of stress (%)	13 (43.3)	29 (76.3)	**0.011**
Exercise (%)	0 (0.0)	1 (2.6)	0.999
History of Sunburn (%)	2 (6.7)	1 (2.6)	0.579
Reason for the first attack (%)			
Spontaneos	14 (46.7)	14 (36.8)	0.569
History of stress	16 (53.3)	24 (63.2)	
Iron	107.7 ± 40.0	62.3 ± 38.0	**<0.001**
Ferritin (median [IQR])	56.4 [36.0 – 85.8]	13.3 [6.8 – 26.8]	**<0.001**
Elevated Glucose (%)	3 (10.0)	3 (7.9)	0.999
Iron level (%)			
Low	1 (3.3)	22 (57.9)	**<0.001**
Normal	27 (90.0)	16 (42.1)	
High	2 (6.7)	0 (0.0)	
Ferritin level (%)			
Low	0 (0.0)	15 (39.5)	**<0.001**
Normal	30 (100.0)	23 (60.5)	
Vit B12 deficiency (%)	6 (20.0)	3 (7.9)	0.169
Folate deficiency (%)	3 (10.0)	3 (7.9)	0.999
Elevated Anti-TPO (%)	2 (6.7)	8 (21.1)	0.167
Elevated Anti-TG (%)	3 (10.0)	6 (15.8)	0.721

DM, diabetes mellitus; HT, hypertension; IQR, interquartile range; n, number; SD, Standard deviation; TG, thyroglobulin; TPO, thyroid peroxidase. Descriptive statistics for normally distributed variables were given as mean ± SD and Independent Samples t test was used for comparison. Descriptive statistics for variables that didn't have normal distribution were given as median [IQR] and Mann Whitney U test was used for comparison. Descriptive statistics for categorical variables were given as number (%) and Pearson Qhi-Square test or Fisher Exact test was used for comparison. P values in bold were accepted to be statistically significant ($p<0.05$).

Table 4. Comparison of comorbid diseases and laboratory findings according to the age of onset of vitiligo

	Vitiligo age of onset		
	Below 18 years (n=21)	**18 years and above** (n=47)	**p**
Vitiligo family history (%)	5 (23.8)	10 (21.3)	0.999
Vitiligo Types (%)			
Segmental	1 (4.8)	0 (0.0)	0.309
Focal	8 (38.1)	8 (17.0)	0.071
Vitiligo vulgaris	7 (33.3)	16 (34.0)	0.999
Acrofacial	3 (14.3)	19 (40.4)	0.065
Mixed	2 (9.5)	4 (8.5)	0.999
Presence of Comorbidity (%)	3 (14.3)	19 (40.4)	0.065
Allergic rhinitis (%)	0 (0.0)	1 (2.1)	0.999
Depression (%)	0 (0.0)	1 (2.1)	0.999
Thyroid disease (%)	2 (9.5)	13 (27.7)	0.122
Thyroid Autoantibodies (%)			
Negative	19 (90.5)	37 (78.7)	0.317
Positive	2 (9.5)	10 (21.3)	
Type 1 DM (%)	0 (0.0)	1 (2.1)	0.999
DM (%)	0 (0.0)	4 (8.5)	0.303
HT (%)	0 (0.0)	5 (10.6)	0.314
Cardiac Disease (%)	1 (4.8)	1 (2.1)	0.525
Migraine (%)	0 (0.0)	1 (2.1)	0.999
Policystic Kidney Disease (%)	0 (0.0)	1 (2.1)	0.999
Asthma (%)	1 (4.8)	0 (0.0)	0.309
Psoriasis (%)	0 (0.0)	1 (2.1)	0.999
History of atopia (%)	3 (14.3)	2 (4.3)	0.167
Hair involvement (%)	5 (23.8)	6 (12.8)	0.295
Nail involvement (%)	3 (14.3)	5 (10.6)	0.695
Reason for exacerbation (%)	10 (47.6)	35 (74.5)	0.059
History of stress (%)	8 (38.1)	34 (72.3)	**0.016***
Exercise (%)	0 (0.0)	1 (2.1)	0.999
History of Sunburn (%)	2 (9.5)	1 (2.1)	0.223
Reason for the first attack (%)			
Spontaneous	13 (61.9)	15 (31.9)	**0.020***
History of stress	8 (38.1)	32 (68.1)	

DM, diabetes mellitus; HT, hypertension; n, number. Descriptive statistics for categorical variables were given as number (%) and Pearson Chi-Square test or Fisher's Exact test was used for comparison. p values in bold were accepted to be statistically significant ($p<0.05$).

In previous studies, the most common form was generally vitiligo vulgaris, which is associated with bilateral, symmetric lesions at limbs and also through whole body (5,18). This was also true for our study. This common presentation of vitiligo vulgaris may be due to a real higher incidence or it may be a consequence of higher cosmetic disfigurement caused by such lesions.

The association between vitiligo and autoimmune disorders has been frequently investigated. Zheng et al. found that vitiligo was commonly associated with autoimmune disorders such as rheumatoid arthritis, hyper and hypothyroidism, alopecia areata, and chronic urticaria (16). Topal et al. found higher rates of thyroid disorders, essential hypertension, and alopecia areata (15). In Gonul et al.'s study, autoimmune thyroid disease, diabetes mellitus and hypertension were the most common accompanying disorders (5). In our study, thyroid diseases, hypertension and diabetes mellitus were common in patients with vitiligo. Thyroid autoantibody positivity was found in different rates in studies from Turkey (10,15,19). We found thyroid autoantibodies in 17.6% of our patients. This rate is higher than the rate of anti-TPO positivity of 7-8% reported in Onarslan et al.'s study (19). When other Turkish studies are reviewed, it is seen that anti-TPO positivity values were found to be 31% in Akay et al.'s study (10), and 36% in Topal et al.'s study (15). In our study, thyroid autoantibody positivity was lower than that of these studies (10,15). Topal et al. reported that thyroid autoantibodies were more common in patients with focal vitiligo (15). The low rate of focal vitiligo in our study may be the reason of lower thyroid autoantibodies in our study.

In our study, disease exacerbations were more frequent in females and history of stress was a more frequent cause of exacerbations in females. This difference may reflect both a higher prevalence of psychiatric disorders like anxiety and depression in females in this age group and also a higher effect of vitiligo on females. We also found lower ferritin, and iron levels in females. Iron deficiency is also common in females without vitiligo who were at childbearing age. So these findings in our study probably don't reflect a difference due to the effects of vitiligo but instead reflect the differences found between genders in normal population. Another difference between males and females in our study was the higher frequency of acrofacial involvement in males. This is consistent with Singh et al.'s (20) and Gonul et al.'s studies which found higher incidence of vitiligo on the trunk in females (5). They have explained this by Koebnerization phenomenon due to the fact that women wear tighter clothes and brasseries. Also, sun exposure of men during going outside and working conditions may be the reason for increased acrofacial involvement in males due to Koebnerization.

In our study, the major differences between patients with disease onset below or above 18 years of age were the lower rate of stress as a cause of exacerbation of stress and more common spontaneous attacks in young patients. Psychiatric disorders related to stress generally increase in prevalence with increasing age (21). Therefore, young vitiligo patients don't have as many psychiatric disorders as older patients and stress plays a less significant role in their lives.

In vitiligo, many factors including genetics and environment play role in the etiology of the disease. Association with autoimmunity has been well established. Stress related exacerbations are more frequent in females and patients older than 18 years of age. Therefore, it is important to evaluate

psychological factors especially in women with vitiligo and to consult a psychiatrist when necessary.

Ethics Committee Approval: Hitit University Medical Faculty Clinical Research Ethics Committee permission was obtained with the letter dated 04.01.2019 and numbered 16.

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