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Frequency of Autoimmune Diseases in Those Suffering from Vitiligo in Comparison with Normal Population

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Abstract: Vitiligo is more common in people with certain autoimmune diseases. Here we studied the association between vitiligo and autoimmune diseases. In this case control study, 86 patients with vitiligo were questioned about the location of vitiligo, family history, treatment and therapeutic response. All patients were examined both clinically and with laboratory tests to detect the presence of autoimmune disorders including autoimmune thyroid disease, pernicious anemia, insulin dependent diabetes, and Systemic Lupus Erythematic (SLE) and Addison disease. We compared the prevalence of autoimmune disorder in vitiligo patients with that in a group of age-and gender-matched normal population. Average age of disease onset was 21.8±11 years; 61% of patients were female and 39% were male. The most common locations of vitiligo were hands (33.7%) and face (32.1%). The most common pattern of onset was vulgaris type (40%). Nearly one-fourth of patients had a positive family history of vitiligo. Prevalence of thyroid disorders in vitiligo patients and control group was 21.1 and 7%, respectively. The difference was statistically significant ($p = 0.008$). The most common autoimmune disorder in patient with vitiligo was hypothyroidism. Family history had a poor prognostic effect on response to therapy.

Key words: Vitiligo, autoimmunity, thyroid

INTRODUCTION

Vitiligo is a pigmentation disorder in which melanocytes (the cells that make pigment) in the skin are destroyed. It is the most prevalent acquired disease of pigmentation disorder appearing as skin and rarely mucous pigmented patches (Prindaville and Rivkees, 2011). It affects all races, but may be more noticeable in people with darker skin (Silva de Castro *et al.*, 2012). It usually starts as small areas of pigment loss that spread with time. Clinically, half of the cases begin before 20 years old (Gonul *et al.*, 2011). Hypomelanotic macules are initially considered in areas exposed to sun light. The disease progresses gradually and the lesions become amelanotic after some times (Oiso *et al.*, 2011). About 30-40% of patients state vitiligo family records. Previous studies suggest that vitiligo is an autoimmune disease resulting from complex reactions between several congenital risk factors and environmental susceptible factors (Narita *et al.*, 2011). In a study conducted on 2624 cases of vitiligo, it was made clear that disease outbreak age is lower in family cases. Prevalence of concurrent thyroid diseases was 19.4% which is about ten times more than its

prevalence in normal population. Also, pernicious anemia, Addison and lupus had more prevalence than healthy population (Alkhateeb *et al.*, 2003). In other studies, prevalence of thyroid diseases has been reported as 34% in those suffering from vitiligo (Yaghoobi *et al.*, 2011). Considering objectives of the study, i.e. evaluating frequency of autoimmune diseases especially thyroid in vitiligo and probability of intensifying or starting of this cutaneous disease in those suffering from autoimmune diseases, the obtained evidences indicate higher prevalence of autoimmune diseases in vitiligo patients (Nunes and Esser, 2011; Poojary 2011). At present, vitiligo patients are screened just in some centers considering other autoimmune diseases. Therefore, the hypothesis of autoimmune nature of vitiligo will be reinforced if this association is approved. Additionally, use of treatments playing a controller role in immune system will be more appropriate and may be more effective in treating vitiligo diseases (Boissy and Nordlund, 2011; Sandoval-Cruz *et al.*, 2011). The aim of this study was to evaluate the frequency of autoimmune diseases in those suffering from Vitiligo in comparison with normal population.

MATERIALS AND METHODS

In this case-control study, patients referring with pigmented patches manifestations to skin clinic of Tabriz Sina Training and Therapeutic Center were evaluated and examined regarding vitiligo. The disease was diagnosed based on clinical examinations. If suspected, skin biopsy was conducted. The required information including patient's age, disease outbreak age, gender, existence of records of similar disease in 1st and 2nd class relatives, location of the initial lesions, previous treatments and treatment response (at the opinion of the patient) were asked from the patients and inserted in case group checklist. Cases were excluded from the study whose job posed probability of depigmentation due to contact with substances. The patients were examined considering developing of lesions and determining disease type. Autoimmune disease symptoms were asked from the patients. Symptoms such as light sensitivity, malar rash, lymphadenopathy, arthritis, mouth sore, skin telangiectasia, possible paleness, and existence of erythemato lupus discoid were evaluated. The patients were asked about records of thyroid diseases, lupus, Addison, pernicious anemia, spasm or psychosis, diarrhea or constipation. Other autoimmune diseases such as hypoparathyroidism, hypogonadism and etc., were not evaluated due to less prevalence and lack of evidences in the previous studies. Positive points were registered in the checklist. Required tests including ESR, FBS, ANA, T3, T4, TSH, Na, K, and Hb were conducted after describing them to the patients and acquiring their satisfaction. In this study, Anti-TPO and Anti-TG were not asked from the patients because of its high expensed. Patients with laboratory changes based on autoimmune disease were only referred to oncologist. According to the oncologists, the above-mentioned tests were not necessary in most patients. Also, reportable obvious changes were not observed in those patients underwent these tests. The patients returned after conducting the tests and the obtained results were inserted in the checklist. The control group was selected from patients referring to the skin clinic with melasma, wart, molosecum and eczema diagnoses. Similar to the case group, this group was also examined considering autoimmune diseases and underwent paraclinical tests willingly. The case and control groups were matched considering background variables (age and gender). The results were analyzed using SPSS-15 statistical software and compared applying Chi-Square and t-tests. Tests significant level (p-value) was considered less than 0.05 ($p < 0.05$).

RESULTS

Following results were obtained through evaluating frequency of autoimmune diseases in 86 patients suffering from vitiligo and their comparison with normal population: mean age of those suffered from vitiligo was 28.11 ± 12.5 years. They were constituted of 52 females (61.2%) and 33 males (38.8%). Mean age of disease outbreak was 21.86 ± 11.7 years. Half of the patients had disease outbreak age less than 20 years. Mean of diseases duration was calculated as 6 years. Hands (33.7%) and then face (32.1%) were the most common areas affected by the disease. At referring, vulgaris was the most prevalent development type of the lesion (40%). In this study, 21 patients (24.7%) stated records of vitiligo in their family (1st and 2nd class relatives). Thirty nine patients referred to treat the problem for the first time. In 47 patients were under treatment, topical steroid was the most commonly used treatment (51%). Some patients used topical methoxsalen to treat the problem. Twenty patients (42.5%) did not mention the treatments, 16 patients (34%) had partial response and 12 (25.5%) complete or near to complete recovery. Out of 86 patients with vitiligo, 18 ones suffered from thyroid disease (21.1%), 6 (7%) from under clinical hypothyroidism (normal T3 and T4 and high TSH), 6 (7%) from hypothyroidism (low T3 and T4, and high TSH), 6 (7%) from hyperthyroidism (low T3, T4 and TSH). In this group, disease outbreak age was compared with other patients and it was made clear that the difference was not statistically meaningful ($p = 0.5$). There were no cases of pernicious anemia, SLE, Addison, ulcerative colitis. Of course, none of the patients had any clinical symptom susceptible to these diseases. There was high FBS in 4 patients (4.7%). Out of them, 3 were Type II and one patient was Type I diabetes. ANA was positive in 3 patients (3.5%). According to treatment results, the patients were divided into two general class of without response and clinical response (including partial and complete). Treatment results were evaluated based on vitiligo family records and using Fischer Exact Test. The difference was statistically meaningful ($p = 0.013$) (Table 1). Mean age of the control group was 32.6 ± 13.8 years. It was compared with mean age of the case group and no significant difference was observed ($p = 0.2$). The control group was constituted of 35 males (41.2%) and 50 females (58.8%). Gender difference between case and control groups was compared using Chi-Square test. There was no statistically difference ($p = 0.1$). There was thyroid disease in 6 patients (7%) of the control group (4 cases with hypothyroidism, 1 case with subclinical

Table 1: Response to treatment according to family history

	Without response		Partial or complete response		p-value
	No.	%	No.	%	
Negative family history	19	39.6	18	37.5	0.013
Positive family history	1	2	10	20.9	

Table 2: Autoimmune disorders in study population

	Vitiligo		Normal population		p-value
	N	%	N	%	
Addison	0	0	0	0	0
Diabetes Mellitus	4	4.7	3	3.9	0.68
ANA +	0	0	0	0	0
High ESR	0	0	0	0	0
Pernicious Anemia	0	0	0	0	0
Thyroid Diseases	18	21.1	6	7	0.024

hypothyroidism and 1 patient with hyperthyroidism). Frequency ratio of thyroid disease in control and case groups was compared using Chi-Square test. The difference was statistically meaningful ($p = 0.008$). Prevalence of other laboratory disorders in case and control group has been stated in Table 2. Prevalence of diabetes, positive ANA, high ESR and anemia was compared in the case and control groups and no statistically significant difference was observed ($p > 0.05$).

DISCUSSION

In this study, mean age of the disease outbreak and its average were respectively 21.86 and 20 years. In other studies, it has been stated that half of the patients are affected by the disease before 20 years old Viles *et al.* (2010). Outbreak age was 22.4 years in Caucasian race which was very close to our study. Schallreuter and Salem (2010) The patients were constituted of 61% female and 39% male. Similar to other studies, women constitute more part of the patients which may be attributed to their more reference to treat their problem. Other studies based on voluntary participation of the patients, report high ratio of women to men (Pajvani *et al.*, 2006). According to previous studies the lesions are started at darker parts of the skin (Akay *et al.*, 2010). In our study, most patients have stated hands (32.7%) and face (32%) involvement as the first locations of the disease. Considering that these areas are exposed to sun light, it can be assumed as disease starting factor (Abu Tahir *et al.*, 2010) Considering mental issues, anatomic distribution of the disease is very effective because it is exposed to sight. Feeling of stress and being ashamed of the problem in encountering with strangers, feeling of sin and decrease of self-confidence especially regarding areas which are exposed to sight may be considered (Hartmann, 2009). Family records of vitiligo have been mentioned as 18-40% in other studies. In this study, family records was positive in 24.7% which is in correspondence with the previous studies (Laberge *et al.*, 2005). Treatment response in

family and sporadic cases were respectively 20% and 37.5%. The difference was statistically meaningful ($p = 0.013$). Therefore, more strong treatments will be needed if the patient has experienced vitiligo family records. Also, it is better that the patient is provided with required information regarding probability of no recovery. Other studies have not referred to this finding (Bordere *et al.*, 2009). In this study, 42% of patients (about half of them) had no treatment response. Complete or near to complete recovery as seen just in 25% of cases. The ratios state disease weak prognosis even with appropriate treatments. In previous studies, association of thyroid diseases with vitiligo has been introduced as the most common association from among autoimmune diseases and its prevalence has been mentioned as 21, 34, 19.4% (Hari Kumar *et al.*, 2012; Kroon *et al.*, 2012). In the present study, prevalence of thyroid diseases was 21.1% which corresponds with the previous studies. In comparison with the control group (7%), association of vitiligo and thyroid diseases was statistically more prevalent than its prevalence in the normal population. In other studies, prevalence of thyroid autoimmune diseases in the normal population has been mentioned as 2% (Nunes and Esser, 2011). Therefore, high prevalence of the disease in our country is considerable. In the previous studies, thyroid diseases prevalence in vitiligo was 8 times more than normal population (Fernandes and Campos, 2009). In our study, although the difference is statistically meaningful, it is attributed to higher prevalence of thyroid disorders in normal population of the country. Hypothyroidism was the most prevalent thyroid disease (60%). The same results have been obtained in other studies. Sedighe and Gholamhossein (2008) In this study, there was no difference considering prevalence of autoimmune diseases except to thyroid in the case and control groups. There were not clinical symptoms susceptible to other autoimmune diseases in patients of both groups. Meanwhile, records of doubtful symptoms of the diseases were not observed in files of patients and the control group. Therefore, expensive

and unnecessary tests were excluded and susceptible cases were referred to the related specialist and no disease was reported. Also, routine tests helpful in primary diagnosis of the diseases were asked. Results of both groups were not different considering other autoimmune diseases. In our study, response to treatment was 20% in family cases while it was equal to 37.5% in sporadic cases. The difference was statistically meaningful. Therefore, positive family records are regarded as the negative prognosis factor in response to treatment. High expenses of some tests required to exactly diagnose the autoimmune diseases was regarded as limitations of the research. It is hoped that the problem will be solved in future through exact studies as research plan.

CONCLUSION

According to this study and previous ones and considering that the disease is often seen in youths and it is started before twenty years old in half of the cases, apparent lesions may play a significant role in developing mental problems and decreasing patients' self-confidence. Lesions seen in areas such as hands and face which are exposed to sun light, introduce it as one of the etiological factors. In spite of providing different treatments, complete or near complete treatment response is seen in 25% of cases. Thyroid diseases are the most prevalent autoimmune disease associated with vitiligo and is seen in 20% of cases. Its prevalence is at least three times more than that of the normal population. Treatment response in the group with positive family records was less than other patients such that family records is effective in treatment response.

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