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Autoimmune Thyroid Disorders in Patients With Vitiligo

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Background: Vitiligo is a common skin pigmentation disorder affecting 0.5-2% of the general population. The pathogenesis of vitiligo is not well-known; however, some evidences have shown the role of autoimmune processes. Increased prevalence of thyroid autoimmune disorders in patients with vitiligo has been reported.

Objectives: We aimed to assess the prevalence of autoimmune thyroid disorders among patients with vitiligo who referred to Sina Hospital of Hamadan in west of Iran in 2008.

Patients and Methods: This case-control study comprised 45 patients with vitiligo and 45 healthy individuals (control group). Data on age, gender, family history of vitiligo, distribution pattern and duration of the disease were collected through a questionnaire. Fasting blood samples of the patients were tested to measure blood thyroid stimulating hormone (TSH), thyroxin (T4), and anti-thyroid peroxidase (anti-TPO) levels.

Results: The mean ages of cases and controls were 30.71 ± 4.8 and 30.31 ± 3.7 years old, respectively. Totally, 86.7% of cases had generalized lesions. In 32.2% of cases, trunk was the first involved region. Average duration of the disease was 7.76 years. The mean T4 level was 1.55 ± 0.27 pmol/L in case and 1.48 ± 0.22 pmol/L in control groups. The mean blood TSH levels were 1.94 ± 1.42 mIU/L in case and 2.8 ± 6.51 mIU/L in control groups and the mean anti-TPO levels were 136.82 ± 45.54 and 86.87 ± 23.05 IU/mL in case and control groups, respectively. None of the aforementioned differences were statistically significant.

Conclusions: Our findings showed that the small difference in thyroid test results between the two groups was not statistically significant. According to our findings, patients with vitiligo were not at a higher risk for either autoimmune or functional thyroid disorders in comparison with the healthy ones.

Keywords: Vitiligo; Thyroid Gland; Thyrotrophic; Thyroxin

1. Background

Vitiligo is an acquired idiopathic disorder, presenting with round depigmented macules and patches. Functional melanocytes disappear from the affected skin without any clear etiology and pathogenesis (1). Vitiligo mainly affects children and young adults. This disease is mainly developed in patients under 20 years of age and occurred in 0.5-2% of the general population (2). In a study by Zamanian et al. in 2006, the prevalence of vitiligo was 0.8% in rural areas of Hamadan city, Iran (3). Vitiligo is commonly characterized by usually white or chalk-white depigmented or amelanotic circumscribed macules or patches surrounded by normal skin. Patches of vitiligo have clear margins with a round/oval, or linear shape. Lesions of vitiligo gradually enlarge centrifugally. Normally, hyperpigmented regions of the body such as nipple, axilla, umbilicus, sacrum, and inguinal areas are the most common involved regions. According to the lesions, vitiligo can be classified into four groups: generalized vitiligo, including depigmented lesions of face, especially in the perioral area, neck, trunk region, extensor surfaces, and bony processes of limbs; acrofacial type, including depigmented areas in distal fingers as well as in periorificial regions; focal type, which includes focally extended lesions in any region without dermatomal distribution; and segmental type, which includes focally extended lesions with dermatomal distribution (1). Because of the important role of skin in people's appearance as well as their social behavior and interpersonal relations, vitiligo should be assumed as an important skin disorder which may affect the socio-psychological aspects of patient's lives. Vitiligo can cause negative feelings such as shame, anxiety, guilt accompanied with self-esteem problems, and psychological disorders such as depression, which can impose costs on both patients and the society (4-7). Vitiligo is a multifactorial disorder caused by both genetic and environmental factors. Vitiligo is characterized by lack of functional melanocytes in involved areas. The probable mechanism and pathogenesis include au-

toimmune process, neurohormonal factors, increased sensitivity to oxidative stress, and melanocytorrhagy (death of melanocytes) (8). Although none of the mentioned mechanisms have been proven yet, it seems that autoimmune hypothesis is the most prevalent cause (9). In patients with vitiligo, the level of specific autoantibodies against specific cells such as thyroid cells and gastric parietal cells or adrenal cells can be higher in comparison with the general population. Although most of the patients with vitiligo have good general health conditions, some of the autoimmune endocrinopathies have shown stronger association with vitiligo. The most frequent autoimmune endocrinopathies are insulin-dependent diabetes mellitus, pernicious anemia, autoimmune thyroiditis, Grave's disease, Adison, and alopecia areata (1). With reference to the literature, vitiligo has the strongest association with thyroid dysfunction including hyperthyroidism or hypothyroidism (Grave's disease or Hashimoto thyroiditis). The association between vitiligo and autoimmune thyroid diseases has been reported by Iacovelli et al. (10), Dave et al. (11), Daneshpazhooh et al. (12), Manighalam et al. (13), and Vanderpump et al. (14); however, there are other studies that have not confirmed this association or have even found unknown patterns of thyroid involvements in patients with vitiligo.

2. Objectives

We aimed to compare patients with vitiligo and healthy ones with respect to thyroid autoimmune and functional factors to understand the association between vitiligo and thyroid diseases.

3. Patients and Methods

This case-control study was conducted at Farshchian Hospital, Hamadan city, Iran, from February 2007 to March 2009. The case group comprised 45 patients diagnosed with vitiligo and the control group comprised 45 healthy individuals without vitiligo or family history of vitiligo. The control and case groups were age-and gender-matched. The exclusion criteria for both groups were patients with history of thyroid surgery, hyperthyroidism or hypothyroidism, chronic kidney disease, liver or cardiac diseases, infectious diseases, any kind of immune deficiency and history of radioactive iodine therapy. All the participants signed a written informed consent in accordance with the ethical standards of the Institutional Ethics Committee. Gender, age, duration of the disease, the first involved body region and the presence of symptoms and signs of thyroid disorders were asked through a specific questionnaire. Afterwards, venipuncture was performed and 3 mL fasting blood sample was taken to measure the blood thyroid stimulating hormone (TSH), thyroxin (T4), and antithyroid peroxidase (anti-TPO) levels. Moreover, T4 and anti-TPO levels were measured by microplate enzyme assay. The normal range of these laboratory tests were as follows: T4, 0.8-2 pmol/L; TSH, 0.39-5.95 mIU/L; anti-TPO, < 40 IU/mL. Finally, data were analyzed by predictive analytic software (PASW) statistics (version 17.0.3, IBM Corporation, Armonk, NY, USA), using student t-test, chi-square and Fisher exact tests. We considered P value < 0.05 statistically significant. In this study, the case group comprised 19 (42%) male and 26 (58%) female patients with vitiligo, while the control group comprised 18 (40%) male and 27 (60%) female healthy individuals. Gender distribution was similar in both groups.

4. Results

Totally, 39 (60%) of 45 cases had the generalized type of vitiligo, 5 (11.1%) had the localized type and 1 (2.2%) had the acrofacial type. The mean duration of the disease was 7.76 ± 6.54 years (8.77 ± 7.4 years in females and 6.37 ± 4.87 years in males [P = 0.228]). The mean age in case and control groups was 30.71 ± 14.83 and 30.31 ± 13.97 years old, respectively (P = 1.00). None of the controls and three of the patients with vitiligo had clinical symptoms of thyroid disorders. The mean duration of vitiligo was 2.67 ± 1.52 years in these three cases, while the duration was 8.12 ± 6.61 years in other 42 patients (P = 0.166). All of these three cases had abnormal anti-TPO levels, two had abnormal TSH levels, and one had an abnormal T4 level. Two of the patients and one of the participants in the control group had abnormal T4 level (P = 1.00). Three cases in each group had abnormal TSH levels. Five cases in each group had abnormal anti-TPO levels (P = 1.00). The correlation between the duration of the disease and the quantitative levels of TSH, T4 and anti-TPO was analyzed by bivariate Pearson coefficient. In the case group, T4 showed some correlations with duration of the disease (r = 1.3; P = 0.65). Pearson's correlation coefficient for the association of TSH and anti-TPO values with disease duration were respectively as follows: r = 0.19 and P = 0.22; r = 0.29 and P = 0.06.

5. Discussion

In our study, 86.7% of patients had generalized vitiligo and 11.1% had the localized type. In Arycans' study on 113 patients in Turkey, 51.3% of participants had generalized and 41.6% had localized types of the disease (15). In a study in Romania by Birlea et al. in 2008, 82% of patients had generalized vitiligo (16). In another study, Fernandes et al. evaluated 50 patients with vitiligo, from whom 48% had the generalized type while only 10% had acrofacial vitiligo (17). In general, more than 90% of patients with vitiligo had the generalized type (1). According to the distribution pattern of the lesions, our findings were similar to the aforementioned studies. In our study, the mean age of patients in case and control groups was 30.71 ± 14.83 and 30.31 ± 13.79 years old, respectively. The mean age of female participants was 27 ± 5 and the mean age of male participants was 34 years old. In the study by Stanca et al. the mean age of patients was 36 ± 15 years old, while the

mean age of control group was 34 ± 4 years old. In a study by Moradi et al. (18), this amount was 29 ± 12 for males and 33 ± 4 for females by Arycan et al. (15). In our study, there was no significant difference between ages of case and control groups. In our study, the mean disease duration was 7.76 ± 6.54 years. This time was 8.7 ± 7.4 years for females and 6.37 ± 4.8 years for males. Males and females showed no difference in duration of the disease. In this study, the average age of vitiligo onset was 28 years old in males and 20 years old in females. These findings were similar to many other previous studies which showed that more than half of the first vitiligo onsets occurred at the third decade of life. For example, in studies by Behl et al. (19), Herane et al. (20), Jaigirdar et al. (21), Engel et al. (22), Lerner et al. (23), and Nordlund et al. (24), the age of first presentation in half of the patients with vitiligo was before 30 and 70% to 80% of the first disease onsets were before the age of 40. The mean level of T4 in the case group was slightly more than that of the control group and the number of participants with abnormal T4 levels in the case group was more than that of the control group. However, this amount was not significant. For TSH and anti-TPO levels, the mean blood level in the case group was slightly higher than the control group and the number of participants with abnormal blood TSH and anti-TPO levels were equal in both groups; however, the differences in blood TSH and anti-TPO levels were not significant between the two groups. Finally, based on the results of these three variables (blood TSH, T4 and anti-TPO levels), there was no statistically significant increase in thyroid parameters in patients with vitiligo in comparison to the healthy ones. The association between thyroid disorders and vitiligo has been studied by numerous researchers in recent years. Iacovelli et al. has reported the association between vitiligo and autoimmune thyroid disorders in 30% of patients with vitiligo; this association was most commonly seen in patients with positive serum anti-TPO (10). Dave et al. reported abnormal thyroid test results in 57.1% of patients with vitiligo, while only 10% of the individuals in control group showed abnormal results (11). Vanderpump et al. studied 40 patients with vitiligo and showed that 34% of those had abnormal anti-TPO levels (14). Daneshpazhooh et al. measured blood T4, TSH, and anti-TPO levels in 96 patients with vitiligo and 96 controls. They found that blood T4 levels in 94.7% of patients and 96.9% of controls were in normal range without any significant difference between the two groups. In that study, the mean level of TSH was 1.59 mIU/L in patients and 1.14-1.59 mIU/L in controls with a P value less than 0.05. Their findings showed that blood TSH level was significantly higher in patients; however, the number of patients with abnormal TSH levels in the two groups did not show any significant differences. In that study, 13.1% of patients and 70.3% of controls showed abnormal anti-TPO results and significant difference in 18-25-year-old- females was observed (12). Moradi and Ghafarpoor evaluated the results of thyroid tests in 119 patients with vitiligo. In their study, 17.4% of patients showed abnormal TSH test results, 36.7% of whom had positive anti-TPO. Hypothyroidism was the most common form of thyroid disorders in patients with vitiligo (18). Kumar et al. stated that vitiligo had a weak association with hyperthyroidism, but not with hypothyroidism (25). Based on the study by Hegedus et al. clinical and subclinical thyroid disorders in patients with vitiligo were significantly more prevalent in the case group in comparison with the control group (26). Zetting et al. compared 106 patients with vitiligo with a control group. In their study, all the participants in both groups had normal blood T3 and T4 levels, while 21% of patients had abnormal anti-TPO values, significantly higher than the control group (27). Acyran et al. reported the association between vitiligo and thyroid autoimmune disorders in 4.4% of patients with vitiligo. On the other hand, Manighalam et al. compared T3, T4, and TSH blood levels in 30 patients with vitiligo and 30 healthy individual as the control group. The mean serum level of T3 was 150 ± 45 pmol/L in patients and 149 ± 47 pmol/L in controls. The mean serum level of T4 was 8.8 ± 2.8 pmol/L and 7.5 ± 3.2 pmol/L in cases and controls, respectively; the mean serum TSH level was 0.75 ± 0.5 mIU/L in cases and 0.81 ± 0.5 mIU/L in controls. In this study, differences between the two groups were not statistically significant (13). Fernandes et al. compared the thyroid profile of 40 patients with vitiligo with a control group. They showed that there was not a significant difference between the clinical signs, TSH, and anti-TPO levels in the two groups. The results of patients with vitiligo did not show a higher risk for thyroid diseases or antithyroid antibodies. With this knowledge, no changes regarding vitiligo were observed even if a gland dysfunction was detected and treated (17). In another study, Majumder et al. did not find any association between thyroid disorders and vitiligo (28). Reviewing the literature showed that the association between vitiligo and thyroid disorders is still controversial. Many studies have evaluated this association, but none of those could exactly specify the pattern of this association. In our study, there was no significant difference between patients with vitiligo and the control group regarding thyroid conditions. Therefore, based on our findings, patients with vitiligo are not at higher risk for thyroid disorders (functional or autoimmune) compared to healthy individuals. With regard to previous studies, our study could neither confirm nor reject all of their findings. This controversy may be due to the unknown nature of thyroid involvement pattern in vitiligo or even incomprehensive laboratory profiles of detecting thyroid disorders.

Authors' Contributions

Abbas Zamanian: study concept and design, study supervision. Pezhman, Mobasher: acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for im-

portant intellectual content, statistical analysis. Akram Ansar: critical revision of the manuscript for important Intellectual content. Shaghayegh Manuchehri: study administrative, technical and material support. Ghazaleh Ahmadi Jazi: analysis and interpretation of data, statistical analysis.

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