Frequency of autoimmune diseases in first degree relatives of psoriatic patients compared with controls: A cross-sectional study

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Background: Psoriasis is a chronic autoimmune skin disorder with relapsing erythematous scaling plaques and joint or nail involvement. A greater occurrence of other autoimmune diseases has been reported in these patients. Additionally, their family members are more likely to be diagnosed with psoriasis. The aim of this study is to assess the prevalence of certain autoimmune diseases in first degree relatives of patients with psoriasis compared with a control group.

Methods: In this cross-sectional study we used a questionnaire to compare the frequency of type 1 diabetes, autoimmune thyroid disease, vitiligo, lupus erythematosus, multiple sclerosis, ulcerative colitis, Crohn's disease, and rheumatoid arthritis in first degree relatives of 109 pathologically confirmed psoriasis cases with the first degree relatives of 109 age-sex matched controls. R programming language (version 3.3.1 for Windows) and the rattle graphical user interface (GUI) package were applied for statistical analysis. A P-value ≤ 0.05 was considered to be statistically significant.

Results: We compared 955 first degree relatives of psoriatic patients with 934 family members of the controls. There was significantly greater total autoimmune diseases [odds ratio (OR): 2.74, 95% confidence interval (CI): 1.95-3.87, $P<0.001$), particularly psoriasis (OR: 38.66, 95% CI: 5.3-282.19, $P<.0001$), in first degree relatives of psoriatic patients compared to family members of the control group. Regardless of gender, autoimmune thyroid disease was more prevalent among first degree relatives of psoriatic patients (OR: 2.81, 95% CI: 1.36-5.83, P=.0066). No statistically significant difference was found regarding type 1 diabetes, rheumatoid arthritis, multiple sclerosis, vitiligo, Crohn's disease, and ulcerative colitis.

Conclusion: First degree relatives of patients with psoriasis had significantly higher autoimmune diseases. This finding was particularly noticed for psoriasis and autoimmune thyroid disease.

Keywords: frequency, autoimmunity, familial, psoriasis, epidemiology

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INTRODUCTION

Psoriasis is a genetic skin disorder characterized by chronic inflammation and intermittent exacerbations and remissions that have tremendous impact on a patient's quality of life. The most common form, psoriasis vulgaris (85%-90% of patients), presents with localized or widespread erythematous plaques

with sharp borders and silvery scales [1,2]. Other less prevalent types include guttate psoriasis, erythrodermic psoriasis, and pustular psoriasis [3]. The worldwide prevalence rate is 0.6% to 4.8%, with an equal distribution among men and women. Although psoriasis can be diagnosed at any age, it is most likely to affect patients in two age groups: early onset, which usually occurs at the age of 16 in females and 22 in males and late onset, which occurs at the age of 57 in men and 60 in women [4].

Multiple exogenic factors are proposed to be intertwined with the genetic background of the disease [5,6]. Several trigger factors such as infection, psychological distress, medications, and trauma (leading to Koebner phenomenon) are known causes for psoriasis flare-ups [5,6]. A positive family history in patients with psoriasis is well-established, in which involvement of both parents, a single parent, or a sibling are the most reported patterns [7,8]. Genetic studies confirm a crucial role of T-helper (Th) 1 and Th 17 overactivation in pathogenesis of psoriasis, which results in keratinocyte proliferation, infiltration of inflammatory cells, and dendritic cell-induced inflammation coupled with identification of susceptibility loci that comprise polymorphism of interleukin and nuclear factor κB (NF-κB)-dependent signaling pathways [9-11]. Although various immunologic biomarkers have been sought, the diagnosis is clinical with the help of histopathology, which has low sensitivity during the early disease stages [3].

Previous studies suggest that there is a greater frequency of other autoimmune diseases among patients with psoriasis compared to the general population [12-15]. First-degree relatives of individuals with psoriasis are at increased risk for this disorder, but little is known about their risk for other diseases that have an immunologic-based pathogenesis, specifically autoimmune diseases.

Considering these facts, along with the heritable nature of autoimmune diseases, we have designed this study to evaluate the prevalence of several autoimmune diseases as well as psoriasis in first degree relatives of psoriatic patients. To the best our knowledge, there is no such a study in the current literature.

MATERIALS AND METHODS

A total of 109 patients with pathologically confirmed psoriasis and negative history of other autoimmune diseases enrolled in this cross-sectional study. Patients had consecutively referred to the Dermatology Teaching Clinic of Faghihi Hospital,

Table 1. Questionnaire Form

Name: Gender: Age: Tel:						
Chief complaint at the time of diagnosis:						
Number of sisters: Number of sons:						
Number of brothers: Number of daughters:						
Positive history of autoimmune disease in first degree relatives:						
Brother ☐ Sister ☐ Daughter ☐ Son ☐ Father ☐ Mother ☐						
If more than one first degree relatives please insert the number besides each box.						
	Brother	Sister	Daughter	Son	Father	Mother
Type 1 diabetes						
Lupus erythematosus						
Autoimmune thyroid disease						
Rheumatoid arthritis						
Multiple sclerosis						
Psoriasis						
Crohn's disease						
Ulcerative colitis						
Vitiligo						

Shiraz University of Medical Sciences, Shiraz, Iran, during November 2013 to October 2014. The control group consisted of 109 age-sex matched subjects who had negative histories of autoimmune diseases, including psoriasis, and referred to the same dermatology clinic. All participants completed an informed consent form. The Ethics Committee, Deputy of Research, Shiraz University of Medical Sciences approved this study.

We presented a questionnaire (Table 1) to each patient to obtain demographic data, information on number of first degree relatives, as well as positive history of type 1 diabetes, autoimmune thyroid disease, vitiligo, lupus erythematosus, multiple sclerosis, ulcerative colitis, rheumatoid arthritis, and psoriasis in first degree relatives. Questionnaires were completed for both case and control groups through personal interview or phone call. Any suspicious history of autoimmune diseases in first degree relatives was confirmed by direct contact with that relative and an internist or a neurologist consultation, if necessary. We excluded non-responders (n=3) from the study.

R programming language (version 3.3.1 for Windows) and the rattle graphical user interface (GUI) package were applied for statistical analysis. We used the chi-square test, two-sided Fisher's exact test, and descriptive methods for statistical assessments. A *P*-value ≤ 0.05 was considered statistically significant. The strength of the association of autoimmune diseases in first degree relatives of psoriatic patients was estimated by odds ratio (OR) and 95% confidence intervals (95% CIs).

RESULTS

This study was conducted on 955 first degree relatives of 109 psoriatic patients and 934 first degree relatives of 109 age-sex matched healthy individuals. The occurrence of autoimmune diseases was 13.2% in first degree relatives of psoriatic patients, which was significantly higher compared to 5.2% in controls' first degree relatives (OR: 2.74; 95% CI: 1.95-3.87; *P*<.0001). This difference was also observed when we compared male relatives of psoriatic patients to with male relatives of controls (OR: 2.63; 95% CI: 1.54-4.49; *P*=.0004) and in a comparison of female relatives of psoriatic patients to female relatives of controls (OR: 2.84; 95% CI: 1.81-4.44; *P*< .0001). The familial clustering of psoriasis was higher in psoriasis families (4%) compared to control families (0.01%) with an OR of 38.66 (95% CI: 5.3-282.19; *P*<.0001). This finding was also the same for the separate assessment of male gender (OR: 20.42; 95% CI: 2.73-152.87; *P*<.0001) and female gender (OR: 37.52; 95% CI: 2.25-624.42; *P*<.0001). There was no statistically significant difference regarding type 1diabetes, lupus erythematosus, rheumatoid arthritis, multiple sclerosis, vitiligo, Crohn's disease, and ulcerative colitis. However, lupus erythematosus was significantly more prevalent among first degree female relatives of the psoriasis group (OR: 12.87; 95% CI: 0.72-229.1; *P*= .0308). Autoimmune thyroid disease was more prevalent in first degree relatives of psoriatic patients (OR: 2.81; 95% CI: 1.36-5.83; *P*=.0066), particularly in female relatives (OR: 2.67; 95% CI: 1.17-6.08; *P*=.0255) as seen in Table 2.

Table 2. Comparison of autoimmune diseases in first degree relatives of the case and control groups.

	Male [a]		Female [b]		Total		
	Case (n=444)	Control (n=434)	Case (n=511)	Control (n=500)	Case (n=955)	Control (n=934)	*P*-value*
Type 1 diabetes	12 (2.7%)	9 (2.1%)	16 (3.1%)	8 (1.6%)	28 (2.9%)	17 (1.8%)	NS** - NS - NS
Lupus erythematosus	2 (0.45%)	2 (0.5%)	6 (1.2%)	0	8 (0.8%)	2 (0.2%)	NS - 0.0308 - NS
Autoimmune thyroid disease	7 (1.6%)	2 (0.5%)	21 (4.1%)	8 (1.6%)	28 (2.9%)	10 (1.1%)	NS - 0.0225 -0.0066
Rheumatoid arthritis	7 (1.6%)	3 (0.7%)	11 (2.1%)	13 (2.6%)	18 (1.9%)	16 (1.7%)	NS - NS - NS
Multiple sclerosis	2 (0.45%)	0	0	0	0	0	NS - NS - NS
Psoriasis	20 (4.5%)	1 (0.2%)	18 (3.5%)	0	38 (4%)	1 (0.1%)	<0.0001 - <0.0001 - <0.0001
Crohn's disease	0	0	0	0	0	0	NS - NS - NS
Ulcerative colitis	0	0	0	0	0	0	NS - NS - NS
Vitiligo	0	3 (0.7%)	4 (0.8%)	0	4 (0.4%)	3 (0.3%)	NS - NS - NS
Total	50 (11.3%)	20 (4.7%)	76 (14.9%)	29 (5.8%)	126 (13.2%)	49 (5.2%)	0.0004 - <0.0001 - <0.0001

[a] Father, brother, and son
[b] Mother, sister, and daughter
* First and second values stand for case and control group comparison based on gender (male and female). The third value is for comparison of total count of 9 autoimmune diseases between first degree relatives of cases and controls.
** NS: Not statistically significant difference; *P*> .05

DISCUSSION

The concept of a correlation between various autoimmune diseases has been investigated in previous studies. A large epidemiological study in Germany evaluated co-morbidities and other inflammatory disorders in patients with psoriasis. They observed an elevated frequency of rheumatoid arthritis, Crohn's disease, and ulcerative colitis [14]. A Swedish study of approximately 29000 patients over 50 years showed an increased risk of psoriasis in patients with celiac disease that was independent of a temporal relationship [15]. Another cross-sectional study on more than 12000 patients with inflammatory bowel disease revealed that those patients were at greater risk of psoriasis, asthma, rheumatoid arthritis, and multiple sclerosis [16]. These findings have supported the hypothesis that stated autoimmune diseases are interrelated and share common etiologic factors; patients with one autoimmune disease are more susceptible to other types of immune-mediated disorders.

Studies on first degree relatives have also yielded similar results. In a case-control study in first degree relatives of 773 multiple sclerosis patients, it was shown that the prevalence of other autoimmune diseases, including psoriasis, was significantly higher. The researchers proposed that common genetic susceptibility factors for autoimmunity co-existed with disease specific genetic or environmental factors, which determined the clinical phenotype of this disease [17]. Another case-control study was conducted on first degree relatives of patients with celiac disease from 1969 to 2008 at 28 pathology departments in Sweden. The patients' diagnoses were confirmed by histopathology evaluations. The researchers determined that first degree relatives with celiac disease were at increased risk for non-celiac autoimmune diseases [18].

Despite the significant difference in total autoimmune diseases in cases versus controls in our study, only psoriasis and autoimmune thyroid disease had statistically meaningful higher prevalence in the case group. Although this difference was observed for lupus erythematosus in females, this finding might not be reliable due to the bias of zero measure in the control group, which was compatible. There was no evidence of this relation between psoriasis and lupus erythematosus in previous studies. However, in a case-control study, Gul et al. assessed psoriatic patients without psoriatic arthritis which compared thyroid hormones and auto-antibody levels. They observed significantly increased free thyroxine (FT4) levels in the patient group, while antithyroglobulin (AbTG) and antithyroid peroxidase antibody (AbTPO) levels did not show a statistical difference between the two groups. Their finding brings the controversy over plausible thyroid autoimmunity in patients with psoriasis compared with healthy individuals [19]. In a study by Zoabi et al., there was no statistical difference in thyroid function observed between psoriatic patients and controls, even though there were increased TSH levels and positive auto-antibody titers in patients with severe psoriasis in comparison to patients with mild psoriasis [20].

The expected finding of an overall higher prevalence of autoimmune diseases in female relatives of psoriatic patients is in concordance with the belief that female gender is by itself a risk factor for autoimmune diseases. However, unlike some other studies, this predominance was not disease specific in our study [21].

CONCLUSION

There were significantly higher total autoimmune diseases in first degree relatives of patients with psoriasis. In psoriasis, there was familial aggregation and clustering of psoriasis and autoimmune thyroid disease. We suggest that further studies with larger sample sizes along with clinical and para-clinical evaluation of first degree relatives might better achieve more definite results and contribute to counseling families with affected psoriasis members.

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Conflict of Interest: None declared.

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