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CCL 27 level in patient with alopecia areata

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Abstract
Introduction: Alopecia areata is a chronic inflammatory disease and a common form of non-scarring recurrent hair loss, that involves hair follicles and sometimes nails. Today, studies suggest that some chemokines, expressed by epithelial cells, might have an important role in lymphocytes chemotaxis and skin inflammation. These chemokines especially might attract memory T cells toward themselves. Therefore, in this study we aim to investigate CCL 27 level in patient affected by alopecia areata and control group.
Material and Methods: In this case-control study, the study population consisted of patients with alopecia areata who referred to the private dermatology clinic in Birjand in 2019 as the case group and the control group was selected from patients referred to Birjand city Shafa laboratory. Inclusion criteria were: having informed consent, having no diabetes mellitus, thyroiditis, psoriasis, iron deficiency anemia, atopic dermatitis, and inflammatory skin diseases. Also, exclusion criteria were: topical or previous systemic treatment for the last 2 months, Patients with autoimmune diseases and systemic diseases. A blood sample of 5 ml was extracted from each case in case and control groups. The collected data were then entered into SPSS software ver. 16 and analyzed.
Results: In this study 35 cases were present in each group. There was 27 (77.1%) male and 8 (22.9%) female present in both groups. Mean age in both groups 31/57 ± 10/8 all patients lived in urban areas. According to results of this study mean serum level of CCL 27 in both case and control groups was not significantly different (P>0.05). also there were no significant relation between serum level of CCL 27 with gender and age group in both case and control groups (P>0.05).
Conclusions: There was no significant difference between serum level of CCL27 among case and control groups. Also, serum level of CCL27 showed no significant difference between gender and age groups (P>0.05).

Keywords: alopecia areata, serum level, CCL27

Introduction

Alopecia areata is a chronic inflammatory disease and a common form of non-scarring recurrent hair loss that involves hair follicles and sometimes nails. This disease can affect any part of body with hair follicles. It is a relatively common disease characterized by the appearance of one or more oval, round, finite and hairless areas. The onset of this disease is unpredictable. It begins rapidly and results in patchy hairless in a specific area [1]. According to its manifestations alopecia areata could be categorized to different types. Its most common form is alopecia areata patchy which is consist of one or more coin-sized hairless patches on the scalp or other areas of the body. It also might cause total loss of hair on scalp which is called alopecia totalis, and it may progress to universal loss of hair on face and body which is called alopecia universalis [1]. In 7 to 66 percent of the cases it might also affect nails [2].

This disease is the cause of 2-3% of new admits in dermatologic clinics [3]. The prevalence of the disease is estimated at 150 per 100,000 population, which is 0.2% of the population [4]. Alopecia areata may affect every person at any age, from infancy to elderly, its morbidity is not gender related, and is the same among men and women [3, 5].

The definite pathogenesis for this disease remains unknown, but some recent studies have suggested that autoimmunity (associated with T cells) and impaired hair growth cycle might play an important role in the development of alopecia areata. The association of alopecia areata with some other autoimmune diseases, such as thyroid disorders, might confirm such hypothesis [1, 6]. It is also suggested that genetic susceptibility and triggering factors, specially stress, might also have a role in the development of the disease [3]. According to other studies, melanocyte antigens might be of importance in the development of the disease [7, 8].

Biopsy finding include: lymphocyte infiltration around hair floccules, follicle miniaturization, fluffy telogenous rate of 1.5 to 1 and increased ztelogenous and catagenous follicles. Furthermore, presence of eosinophils in the biopsy might be a useful diagnostic marker.

Recently, some studies suggest that chemokines expressed by epithelial cells, which are widely produced by keratinocytes [9], have an important role in lymphocytic infiltration among epithelial cells and skin inflammation. These chemokines selectively, recruit memory T cells [10, 11].

One of these chemokines, CCL27, is limited to skin basal layer and is involved in formation of keratinocyte's outer sheath [11]. In alopecia areata this chemokine increases in the root of outer sheath. Its expression increases by IL-1β and TNF-α and

Decreases by IL-10 (12). Some studies suggest that this chemokine might have an important role in adhesion of memory T cells to CD4+, CLA receptors. Thereby, our aim in this study was to assess CLA27 serum level in alopecia areata patients in comparison to control group.

Method

In this case-control study, the case group considered that alopecia patients were diagnosed with alopecia areata by a dermatologist based on clinical symptoms. The inclusion criteria were as follows:

1. Alopecia areata patients who had informed consent to participate in the study.
2. Not affected by diabetes mellitus, thyroiditis, psoriasis iron deficiency anemia, atopic dermatitis, and other inflammatory skin diseases.

Exclusion criteria were as follows

1. Patients who had received 2 weeks of topical or previous systemic treatment in the last 2 months
2. Patients with autoimmune diseases and systemic diseases.

Control group was selected from patients referring to Birjand Shafa Laboratory for regular checkup. Control group was matched for age and sex with cases. Before extraction of blood sample, all patents were introduced with study implementation steps as well as its aims, then an informed consent received from the participants. A blood sample of 5 ml of peripheral blood from basal vein were received from each participant by an experienced laboratory technician according to standard principles. Then serum was extracted and kept in the condition of -80C until the participant numbers reached to appropriate amount. CCL27 level was measured by CCL27 plate ELISA containing monoclonal antibody for CCL27. After preparation of CCL27 ELISA Kit the serum sample was introduced to the kit following the measurement steps described by company's protocol. At the end, the absorbance of each well was measured by ELISA reader at 450 nm and the concentration of the chemokine was calculated according to the protocol. Finally, the data for each group were entered to SPSS Software ver. 16 and analyzed. At first, the data were considered for the normal distribution using the Kolmogorov-Smirnov test. Due to lack of normal distribution at the level of error of, 0.05, the Chi-square test and the non-parametric Man-Whitney test was used for comparison.

Results

Total number 70 patients were enrolled into this study. 35 cases of alopecia areata and 35 healthy non-alopecia areata patients. As we have matched case and control groups for age and sex, there were no differences between the two groups. Mean age of both groups was **31/57 ± 10/8**. 77.1% of each group consisted of male gender (27) and 22.9% of each group were females (8) (table 1). All of the enrolled cases were lived in urban areas.

Table 1: Comparison of frequency distribution of gender in case and control Groups

Gender	Case	Control	Total
Male	27(77/1%)	27(77/1%)	54(77/1%)
Female	8(22/9%)	8(22/9%)	16(22/9%)
Total	35(100%)	35(100%)	70(100%)

The mean level of CCL27 was 775.4±732 in case group while the amount of CCL27 level for control group was 106.7±893.1. to analyze the differences between these groups we used Mann-Whitney U test which results indicate that there is no significant difference between CCL27 level between the two groups (P>0.05) (table2).

Table 2: Comparison of Mean serum level of CCL27 in case and control groups

Group	Mean	SD	Maximum	Minimum	Mann-Whitney Test
Case	775/4	732/0	2471/5	123/6	X^2= 489.000, Z=-1.451
Control	1060/7	893/1	2529/8	222/1	P=-0.147

We used the same test for comparison of CCL27 level between gender groups. According to the results of Mann-Whitney U test there was no significant difference for CCl27 level between men and women in each group (P>0.05) (table 3).

Table 3: Comparison of Mean serum level of CCL27 in case and control groups according to gender

Group	Gender	Mean	SD	Minimum
Case	Male	825/881	814/117	X^2= 100.000, Z=-0.314 P=-0.753
	Female	605/225	312/436	
Control	Male	1149/219	936/21	X^2= 97.000, Z=-0.432 P=-0.666
	Female	761/925	697/19	

We also compared CCL27 level between age groups as it is shown in table 4. According to Kruska Wallis test results CCL27 level have no significant difference between age groups in both groups (P>0.05).

Table 3 Compassion of Mean serum level of CCL27 in case and control groups according to age groups

Table 4: Compassion of Mean serum level of CCL27 in case and control groups according to age groups

Group	Age Group	Mean	SD	Kruska Wallis Test
Case	0-10 years	708/9	194/87	X2= 3.286 df=5 P=0.656
	10-20 years	505/63	228/90	
	20-30 years	1053/30	918/503	
	30-40 years	886/86	850/31	
	40 years and more	385/14	284/22	
Control	0-10 years	1410/7	1336/573	X2= 5.492 df=5 P=0.359
	10-20 years	395/433	181/464	
	20-30 years	1185/867	902/879	
	30-40 years	1251/312	963/683	
	40 years and more	505/460	350/225	

Discussion

Alopecia areata is a relatively common disease with several features including oval, round, restricted and hairless areas in some parts of the body. This chronic inflammatory disease affect Hair follicle and sometimes nails. Alopecia areata has an unpredictable course that might be fast or slow [13, 14]. A wide range of cytokines and chemokines are involved in the inflammatory process which is mediated by CD4 +. These chemokines play a role in the recruitment and activation of immune cells around the hair follicle [15]. Thus, the aim of this study was to evaluate the serum level of CCL 27 in patients with alopecia areata in comparison with healthy control subjects.

According to the results of our study, there was no significant difference between the mean serum levels of CCL 27 between the two groups. In a study, among alopecia areata patients by mirzaei *et al*. on HSP70, which is an inflammatory factor, it was suggested that mean serum level of HSP70 was significantly higher among alopecia areata patients in comparison to controls ($P<0.05$) [16]. The result of our study is not consistent with the result of mirzaei's study. In another study conducted by Bilgic *et al*. under the title of Serum cytokine and chemokine profiles in patients with alopecia areata, it was indicated that mean serum level of CCL27 in patient group is significantly higher in comparison to control group ($P<0.05$). the result of this study, also are inconsistent with ours, some of the reasons for given differences might be unreliable answer of selected control group about their health condition or undetected inflammatory conditions in members of control group which might cause a rise in serum chemokine level in the blood samples taken. In a study by Simonetti *et al*. it was mentioned that serum level of ligand factor 27 in affected tissue had significantly lower level in comparison to control tissue ($P<0.05$). This data is also not consistent with our results, which might be associated with ethnic and genetic differences among cases, as the mean serum levels of this factor in both control and patient subjects were much higher in our study than in the Simonetti study [11].

Also, according to our study there was no significant relation between gender and mean serum level of CCL27. No significant relation found between mean serum level of CCL27 and age groups among both alopecia affected patients and healthy control participants in our study.

Conclusion

The result of this study suggest that there is no significant difference in CCL27 mean serum level between case and control group. Also mean serum level of CCl27 does not differ significantly among gender and age groups ($P>0.05$).

Conflict of interest

The author declares that there is no conflict of interest.

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