



The Frequency Distribution of Celiac Autoantibodies in Alopecia Areata

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ABSTRACT

Background: Alopecia areata (AA) is a noncicatricial (nonscarring) alopecia. The association between AA and celiac disease (CD) is debatable. Several studies declare the relationship between AA and CD as measurement of celiac autoantibodies (anti-gliadin IgA and anti-gliadin IgG), but a few studies consider anti-tissue transglutaminase IgA. The aim of this study was to evaluate the frequency distribution of celiac autoantibodies (all of them) in patients with AA compared with controls.

Methods: This study is a case-control study. Thirty-five patients entered in each group. Anti-gliadin IgA, anti-gliadin IgG, and anti-tissue transglutaminase IgA were tested in all patients. Samples were examined in ELISA method with binding site's kits, and the result was reported as positive/negative. Finally, the frequency distribution of autoantibodies was examined.

Results: The age average did not show a significant difference between two groups ($P = 0.62$). In addition, there was no significant difference between the two groups based on gender ($P = 0.15$). The prevalence of antibody in case and control groups was 2.85% and 0%, respectively. There was no significant difference between the two groups ($P = 0.31$).

Conclusions: There may be a relationship between CD and AA, but the absence of statistical association between AA and CD does not mean that there is no relationship between gluten and AA in certain patients. Thus, we have shown here that the biological tests to search for CD do not bring information and proof enough, and it is why we recommend another approach to disclose gluten intolerance in AA patients.

Keywords: Alopecia areata, autoantibodies, celiac, frequency distribution

INTRODUCTION

Alopecia areata (AA) is a nonscarring alopecia that genetic and immunological causes have been suggested to be

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ffective in the pathogenesis of the disease. Prevalence of AA in the United States is 0.1–0.2% with an estimated lifetime risk of 2%.^[1-6] AA is characterized by sudden onset of hair loss in one or more regions, generally head, and some other parts of the body covered with hair that can be patchy, totalis (100% terminal hair loss on the scalp), universalis (100% terminal hair loss on the scalp and body), and ophiasis (hair loss around the periphery of the scalp). The most prevalent form is patchy.^[1,4] About 7–66% of the patients have nail involvement, and the most common form of nail involvement is pitting.^[6,7] Various studies revealed that AA can accompany with anxiety disorders, depression, and social phobia. Prevalence of these disorders is significantly higher than the others.^[3] The psychological and social role of hair, particularly scalp hair, is much more important, in comparison to the biological aspect. Hair can be a social characteristic of sex, age, values, and even being the member of a group. Beyond the social meaning of hair, it plays an important role in the identity and self-imagination of the body.^[3] Hair also plays a role in physical attraction and is an important factor in interpersonal relationships. In some studies, AA is reported accompanied with other autoimmune illnesses such as Hashimoto's thyroiditis, vitiligo, diabetes, lichen planus, and also in a few reports, celiac disease (CD) (gluten-sensitive enteropathy).^[8-10] Although diagnosis of AA is usually facile, treatment is not. Curative treatment does not exist yet.^[1]

CD is a small intestinal disease characterized by villous atrophy, mucosal inflammation, and crypt hyperplasia, which occurs upon exposure to dietary gluten and which exhibits improvement after the removal of gluten from the diet.^[11] For the diagnosis of CD, initially, serological tests are recommended. Anti-tissue transglutaminase IgA is one of the most sensitive and specific tests.^[11] Anti-gliadin IgA and IgG are other serological tests. Other diagnostic procedures include endoscopy, biopsy of the small intestine, oral tolerance tests (xylose and lactulose), and radiographic studies of small intestine.^[12,13] The gluten-free diet is a recommended treatment in CD.^[14]

Some studies declare patients with CD have a higher risk of AA. The prevalence of gliadin antibody in patients with AA is estimated to be about 1 in 116. In another study, prevalence of anti-gliadin in patients with AA is estimated to be about 18 in 100.^[15,16]

The chronic and recurrent nature of AA and its stressful effect on patients make this study important. Unfortunately, there is no cure for AA. According to most of the reports, hair regrew in patients with AA and CD after they accepted a gluten-free diet. AA is a skin disease and can be easily diagnosed, but can be a manifestation of an internal disease such as celiac, so CD can be treated before any complication.

In previous studies, all these three antibodies were not tested at the same time. Assessment of these three

antibodies at the same time can help to understand the relationship between these two diseases.

METHODS

Study design

It was a case–control study conducted at one of the biggest university of medical sciences of center of Iran, in which patients with AA referred to dermatology clinics were analyzed and studied. Thirty-five patients were selected through simple sampling in patients with AA and control group. First, in the case group, the type of AA was identified. Data such as age, sex, duration of disease (classified according to the Olsen's study),^[17] family history of AA (first degree), and nail involvement were collected in questionnaires. Next, 35 healthy people were selected randomly as control group. All patients with AA were considered to be the case group and all healthy participants without a past history and family history of AA, CD, and other autoimmune diseases (vitiligo, Hashimoto's hypothyroidism, etc.) were considered as the control group. Exclusion criteria included patients who were treated with a gluten-free diet, pregnant women, nursing mothers, and people who did not cooperate with the investigation. After an explanation of how the process works, a written informed consent was signed by the participants. Ethical approval for our study was obtained from the Isfahan University of Medical Sciences (ethical code: 393232).

Procedure

Both groups were referred to an accredited laboratory for the following tests: Anti-gliadin IgA, anti-gliadin IgG, and anti-tissue transglutaminase IgA. For this purpose, first, taking a small sample of blood (5 ml clot blood without anticoagulant) from a vein in arm was necessary and then it was centrifuged for 10 min at around 2500–3000. Finally, the laboratory examined the obtained serum samples from centrifugation in ELISA method with binding site's kits of the UK. A normal range of tests was defined according to the laboratory standards and finally was reported as positive/negative.

Statistical analysis

The statistical analyses of the results were performed using Chi-square test (for qualitative data) and *t*-test (to compare the means of two groups and for quantitative data) in SPSS 16 for Windows (IBM Corporation, NY, USA). In this study, the significance level was set at $P < 0.05$.

RESULTS

The average age in the case and control group was 28.11 ± 7.1 and 27.6 ± 7.2 years, respectively ($P = 0.62$). Nearly, 58.8% and 41.2% of the patients of the case and control groups were males, respectively ($P = 0.15$).

Regarding the type of AA, 88.6% of the patients had patchy AA, 8.6% and 2.8% of them had totalis and universalis AA, respectively.

Concerning the nail involvement, 88.5% of the patients had no involvement, but 5.7%, 2.9%, and 2.9% of them had pitting, ridging, and onycholysis, respectively.

Most of the participants in the case group did not have any positive familial history of AA (82.9%). Forty percent of the patients suffered from the disease for <3 months and 8.6% of the patients suffered from AA over 5 years [Table 1].

The serum of one AA patient (2.8%) was positive for antibodies. The control group was seronegative for these antibodies. There was no significant difference between the two groups based on Chi-square test ($P = 0.31$).

DISCUSSION

In the current study, the serum of one AA patient (2.8%) was positive for antibodies. The control group was seronegative for these antibodies. Until now, the results of studies about the relationship between AA and CD are controversial. Several studies declare an association between AA and CD. In 1995, one of the first research reports connecting AA with CD was published. They had observed that some of their patients with AA also had CD. They reported a 14-year-old boy with universalis alopecia, completely regrew after he accepted a gluten-free diet. This case report, and a few others, alerted the physicians to monitor a large group of patients with alopecia for CD. In fact, they did determine a relatively high rate of CD in their patients, much greater than accidental. On the basis of this analysis, they suggested that CD antibody testing should be carried out in all patients with AA. Since then, several medical researchers have reported the association between CD and AA.^[10] A few case reports proposed an association between CD and AA. In a prospective trial of 256 AA patients, 6 had positive tissue transglutaminase and endomysial with positive biopsy.^[11]

In another study, Volta *et al.* estimated that the prevalence of gliadin antibody in patients with AA was 1 in 116, which was about 2.5 times more than the prevalence of

this antibody in normal people.^[15] Hallaji *et al.* estimated the prevalence of anti-gliadin antibodies in patients with AA to be about 18–100.^[16] However, results of this study showed that in this population, there was no significant difference between the two groups in terms of celiac autoantibodies (anti-gliadin IgA, anti-gliadin IgG, and anti-tissue transglutaminase IgA), which could be due to different demographic compositions. In this study, the prevalence of antibodies had not been determined, but compared between the case and control groups. On the other hand, in this study, all these three antibodies had been checked at the same time, which seems to increase the accuracy of this study. If the previous studies had checked these three autoantibodies at the same time, they could not find statistically significant positive results. However, it seems that evaluating the prevalence of antibodies instead of frequency distribution of the antibodies was the advantage of other studies.

In general, AA may occur at any age, but the disease was more common in younger age and under 20 years.^[3,4] In Seirafi's study,^[4] 54% of the samples were <20 years old. In this study, the age average in the case group was 28.11 ± 7.1 years. It can be explained through the fact that children's clinics were separated from adult's clinics. In one study, more than 66% of the patients were younger than 30 years old and only 20% were over 40 years old.^[1,2] It was similar to the results of this study. AA affected both males and females.^[1,4,17] In one study, the affected men were more than women.^[1] In this study, 58.8% of the patients were men which was similar to the other studies.

The most frequent type of AA was patchy (88.6%). The second frequent form was totalis (6.8%). In Halaji's study, the most frequent form of AA was patchy which was consonant with this study.^[16]

The prevalence of nail involvement in AA patients was estimated at a wide range of 7% to 66% in different studies. The most common form of nail involvement in AA was pitting.^[16,18,19] Hallaji *et al.* estimated that the prevalence of nail involvement is about 8%. In this study, most patients (88.5%) did not have nail involvement in the study group. Perhaps, the reason was that over 50% of our patients suffered from the disease less than a year, and still there had not been enough time for nail involvement.

However, the most frequent form of nail involvement was pitting (5.7%).

Seirafi *et al.*^[4] reported that 72% of the patients had nail changes and the most common form was pitting, which was similar to this study. Some believed that AA may be inherited.^[20] In some studies, the frequency of positive familial history had been reported about 3–27%.^[4,21] In another study, the prevalence of positive familial history of AA was estimated to be about 14–22%. In this study,

Table 1: Frequency and duration of alopecia areata in the case group

Duration of disease	Frequency	Percentage
<3 months	14	40
3-12 months	5	14.3
12-24 months	9	25.7
2-5 years	4	11.4
>5 years	3	8.6
Total	35	100

17.1% of the cases had a positive familial history, which was in the range of other studies.

Forty percent of the patients suffered from AA for <3 months, and 6.8% of the patients suffered from AA over 5 years. In some studies, the average duration of disease was 10.3 months with a range within 1 week to 8 years which was similar to this study.^[22]

CONCLUSIONS

Unlike many studies, this study shows that the frequency distribution of celiac autoantibodies (anti-gliadin IgA, anti-gliadin IgG, and anti-tissue transglutaminase IgA) in patients with AA does not differ from the normal population. Thus, we show here that the biological tests to search for CD do not bring information and proof enough, and it is why we recommend another approach to disclose gluten intolerance in AA patients.

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Conflicts of interest

There are no conflicts of interest.

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