University of Thi-Qar Journal Vol.12 No.3 SEP 2017
Web Site: https://jutq.utq.edu.iq/index.php/main
Email: journal@jutq.utq.edu.iq

Prevalence of anti-tissue Transglutaminase antibodies among patients with alopecia areata in Nassiriah city.

https://doi.org/10.32792/utq/utj/vol12/3/17

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Abstract

Background: alopecia areata is an autoimmune disease in which hair is lost from some or all areas of the body, usually from the scalp due to the body's failure to recognize its own body cells and subsequent destruction of its own tissue as if it were an aggressor. The Anti- tissue transglutaminase antibodies, antibodies against the enzyme tissue transglutaminase (tTG), are found in the blood of some patients with alopecia areata. Serological blood tests such as anti- tissue transglutaminase antibodies are the first-line non-invasive investigation required to make a diagnosis of celiac disease.

Aims: the aim of the study is to establish the prevalence of Anti-*tissue transglutaminase antibodies in* patients with alopecia areata.

Methods: we evaluated 96 serum samples. The samples were collected from two groups; group I of sixty five patients with alopecia areata and group II of thirty one control patients who were referred to dermatology department in al-hussaien teaching hospital for different dermatological diseases other than alopecia areata. All participants were evaluated for anti-tissue transglutaminase IgA and anti-tissue transglutaminase IgG antibodies.

Results: out of the 65 patients with alopecia areata included in the study, tTGA was positive in 13 patients (20%) and tTGG was positive in 8 patient (12.4%). The prevalence of positivity in patients with alopecia areata was

higher compared to the control group in which tTGA was positive in 3 patients (9.7%) and the tTGG was positive in 2 patients (6%).

Conclusion: we conclude that patients with alopecia areata have higher prevalence of serum anti-tissue transglutaminase antibodies compared with control which support the autoimmune basis for alopecia areata, however, we were unable to demonstrate an increased risk of celiac disease in those patients.

Keywords: alopecia areata (AA), autoantibody, celiac disease (CD), anti-tissue transglutaminase antibody IgA (tTGA), anti-tissue transglutaminase antibody IgG (tTGG)

Introduction

Alopecia areata (AA) is a recurrent non-scarring type of hair loss that affect any hair bearing area. A prevalence of AA in the united states is 0.1-0.2%[1]. Many evidences support the hypothesis that alopecia areata is an autoimmune disease and the process appears to be a T cell mediated through controlling the activation and proliferation of regulatory T cells, cytotoxic T lymphocyte-associated antigen 4, interleukin-2, interleukin-2 receptor A, and Eos (also known as Ikaros family zinc finger 4), as well as the human leukocyte antigen. For autoimmunity, either auto reactive T-cells are not suppressed, or antigens escape the protective process. Several observational studies have recently demonstrated that alopecia areata is associated with other disorders such as pernicious anemia, vitiligo, atopic dermatitis, collagen vascular diseases and thyroid diseases[2] . The tissue transglutaminase is widely distributed in human organs and is a multifunctional enzyme involved in the cross linking of extracellular matrix protein, fibrogenesis and wound healing. The Antibodies to this tissue transglutaminase enzyme are found in patients with several conditions, including celiac disease, juvenile diabetes[3], inflammatory bowel diseases[4] and various forms of arthritis[5]. High levels (titers) of tTG are found in almost all instances of celiac disease [6] which support the association of tTG with celiac disease. It is believed that the accumulation of tTG in the enterocytes as well as its release to the extracellular matrix is consequences of the induction of apoptosis in those regions undergoing the

destruction typical of severe CD-associated lesions. It is recommended to evaluate patients suspected of having celiac disease for tTG including patients with compatible clinical symptoms, patients with an atypical symptoms, and individuals at increased risk (family history, previous diagnosis with associated disorder, positivity for HLA DQ2 and/or DQ8)[6]. The antibodies to tissue transglutaminase follow a complex pathway of generation. In terms of serology, celiac disease is associated with a variety of autoantibody, including anti-endomysial, anti-tissue transglutaminase (tTG), and deamidated gliadin antibodies. Although the IgA isotype of tTG usually predominates in celiac disease, individuals may also produce IgG isotypes, particularly if the individual is IgA deficient. The most sensitive and specific serologic tests are tTG and deamidated gliadin antibodies [7].

AIMS

The aim of this study was to establish the prevalence of anti-tissue transglutaminase antibodies in patients with alopecia areata and compare them with controls.

Materials and methods

It was a case –control study in which the sera of 96 patients (divided into two groups; 65 alopecia areata patients group, and 31 control group) were obtained during the study period. Patients and controls groups were attending the Dermatology Department outpatient clinic at Al-hussan teaching hospital in Nassiriah city which is located in the south of Iraq. The patients enrolled after obtaining an informed consent from the patients and/or their parents. The study was conducted over a period of 20 months between February 2014 and July 2016. A relevant data such as age, sex, duration of disease and family history of disease, for example, alopecia areata, diabetes mellitus and thyroid dysfunction were collected in a Proforma. Both groups were referred to laboratory for the following parameters: anti-tissue transglutaminase IgA antibody and anti-tissue transglutaminase IgG antibody which were assessed by the ELISA method. A rang of normal values was defined according to the laboratory standards.

Reference Values for anti-tissue transglutaminase IgA antibody:

<4.0 U/mL (negative)

4.0-10.0 U/mL (weak positive)

>10.0 U/mL (positive)

Reference values apply to all ages.

Reference Values for anti-tissue transglutaminase IgG antibody:

<6.0 U/mL (negative)

6.0-9.0 U/mL (weak positive)

>9.0 U/mL (positive)

Reference values apply to all ages.

The statistical analyses of the data were made using chi-squire test and t-test in SPSS (version 17, SPSS Inc. Chicago, Illinois, USA), Graphpad (version 3.06, Graphpad software, San Diego, California, USA). In this study, the significance level was set at $p < 0.05$.

Results

The average age in the case and control groups was 23.61 years (±10.20) and 25.3years (±11.3) respectively (p =0.34).

Out of the 65 case group which consist of 70 % male and 30% female , the family history of AA was 8 out of 65, 14 patient have a positive family history of diabetes and 8 patients have a positive family history of thyroid diseases, with age ranging from 9 years to 56 years (44.6% ≤20 years and 55.4% above 20 years) . While out of the 31 control group which consist of 59% male and 41% female, 5 individuals have a positive family history of diabetes and 3 individuals have a positive family history of thyroid diseases (Table 1). The mean duration of AA was (11.33 months)

In cases group, tTGA test was positive in 20% (13 out of 65), weak positive in 24.6% (16 out of 65) and negative in 55.4% (37 of 65). In control group, tTGA test was positive in 3 out of 31(9.7%), weak positive 6 out 31 (19.3%) and negative in 22 out of 31(70.9%). There was no significant difference between the two groups based on Chi-square test (P = 0.058).Table 2

tTGG test of cases group was positive in 12.4% (8 out of 65), weak positive in 15.3% (10 out of 65) and negative in 72.3% (47out of 65) while tTGG test

of control group was positive in 2 out of 31 (6%), weak positive in 4 out of 31 (13%) and negative in 25 out of 31 (81%). There was no significant difference between the two groups based on Chi-square test (P = 0.27). Table3

Table 1: Characteristics of case- control population.

	Case(n=65)	Control(n=31)
Family history of diabetes	8	5
Family history of thyroid disorders	8	3
Male: female ratio	46:19	18:13 P=0.077
Mean age	23.6 years	25.3 years P=0.34

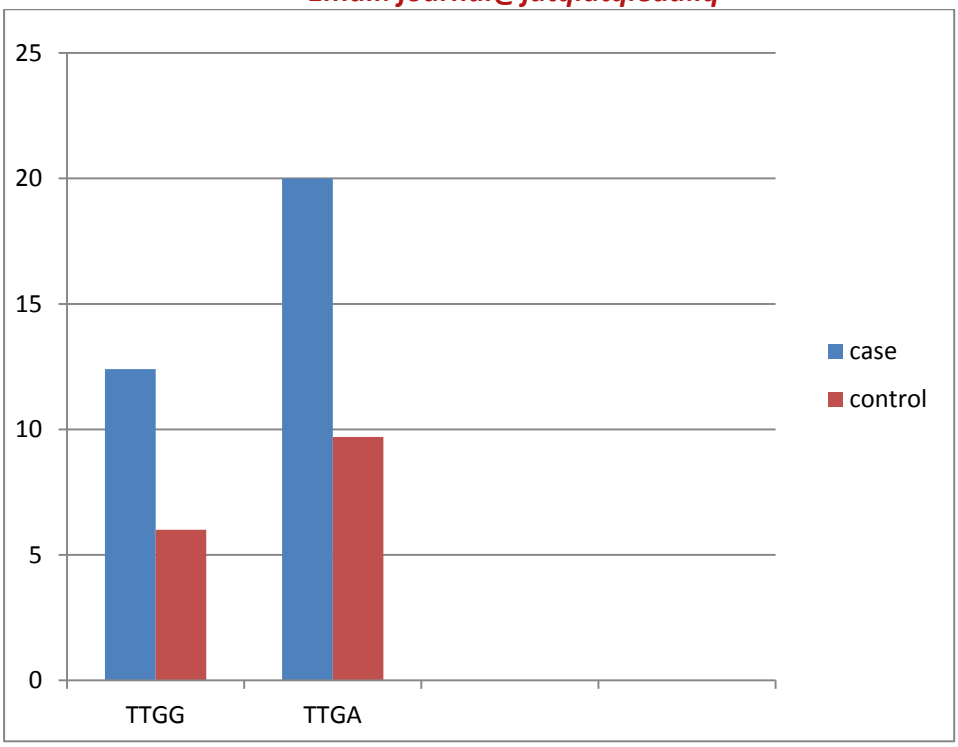
Table 2: comparison between case and control anti-tissue transglutaminase IgA antibody.

tTGA test	Case	Control
Number of subjects	65	31
<4.0 U/mL (negative)	36 (55.4%)	22(70.9%)
4.0-10.0 U/mL (weak positive)	16 (24.6%)	6 (19.3%)
>10.0 U/mL (positive)	13 (20%)	3(9.7%)

Table 3: comparison between case and control anti-tissue transglutaminase IgG antibody.

tTGG test	Case	Control
Number of subjects	65	31
<6.0 U/mL (negative)	47 (72.3%)	25(81%)
6.0-9.0 U/mL (weak positive)	10 (15.3%)	4 (13%)
>9.0 U/mL (positive)	8 (12.4%)	2(6%)

Figure: Levels of tTGG and tTGA autoantibody in cases (n = 65) compared with controls (n = 31).



Discussion

In the present study, the serum of 13 AA patients (20%) was positive for anti-tissue transglutaminase IgA antibodies. In comparison, the control group were sero-positive in 9.7% for these antibodies with (Pvalue=0.058). While the anti-tissue transglutaminase IgG antibody was positive in 12.6 % of AA patients and the control group was found to be seropositive in 6%(Pvalue = 0.27). The data reported here indicates that the presence of anti-tTG antibodies is not an exclusive event occurring in CD patients only but is also related to dermatitis herpetiformis in addition to other diseases such as diabetes mellitus, thyroiditis, and multiple sclerosis [8]. Dermatitis herpetiformis is associated with other disorders and complications that likely reflect the spectrum of CD. Some diseases occur more frequently in CD patients, for example, autoimmune thyroid diseases occur in 20–30% of the CD cases[8] and Insulin-dependent diabetes and lymphoma occur in less than 5 % of CD cases, while other autoimmune diseases such as alopecia areata, Addison's disease, vitiligo, and psoriasis occur infrequently[8], [9]. Results of this study indicate an association between AA and CD tests, and these

studies are similar to several studies which state a relationship between AA and CD. The first research reports linking AA with CD was published in 1995[10]. In this study, they reported a 14-year-old boy with alopecia universalis totally re-grew after he received a gluten-free diet. 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 and a few case reports proposed an association between CD and AA. In a prospective trial of 256 AA patients, 6 had positive anti-tissue transglutaminase and endomysial antibodies with positive biopsy for CD[11]. In another study, Volta et al. estimated that the prevalence of anti-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 [12]. Hallaji et al. estimated the prevalence of anti-gliadin antibodies in patients with AA[13] .In general, AA may occurs at any age, but the disease was more common in younger age and under 20 years [14],[15]. In our study, 44.6% of the samples were <20 years old and the age average in the case group was 23.61 ± 10.2 years. Some researchers supposed that AA may be a hereditary disease [20]. In a number of studies, the occurrence of positive family history had been reported about 3–27% [16]. In this study, the occurrence of positive familial history of AA was 12.4% of the cases, which was in the range of other studies [17]. The male /female ratio in case group was 70% male: 30% female. The limitations of this study include its inability to demonstrate an increased risk of celiac disease in patients with alopecia areata owing to lack of intestinal biopsy.

Conclusion

We concluded that patients with alopecia areata have a higher prevalence of serum anti-tTG antibodies compared with control, which further supports the autoimmune basis of alopecia areata and raises the need for including gastrointestinal systematic review when taking the history from patients with alopecia areata and consequently investigating them for anti-tTG antibodies when indicated. However, large-scale studies which include doing an intestinal biopsy for the patients with alopecia areata and positive anti-tTG antibodies are recommended to substantiate the results of the present study.

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مدى شيوع الأجسام المضادة لانزيم ترانسغلوتاميناس الانسجه لدى مرضى الثعلبة في مدينة الناصريه

نبذة مختصرة

الخلفية:مرض الثعلبة هو مرض المناعة الذاتية الذي يسبب فقدان الشعر من بعض أو جميع مناطق الجسم وعادة من فروة الرأس بسبب فشل الجسم في التعرف على خلاياه والذي يسبب لاحقا تدمير في انسجة الجسم. هذه الدراسه وجدت أجسام مضادة لانزيم ترانسغلوتاميناس الأنسجة في دم بعض مرضى الثعلبه خلال اختبارات الدم المصلية وتعتبرهذه الاجسام المضاده ذات اهميه تشخيصيه لمرض الاضطرابات الهضمية.

الأهداف: الهدف من الدراسة لتأكيد احتمالية وجود الأجسام المضادة لانزيم الترانسغلوتاميناس الانسجه في دم المرضى الذين يعانون من مرض الثعلبة.

الطريقة: قمنا بتقييم 96 عينة من مصل الدم تم جمعها من مجموعتين والتي تشمل المجموعة الأولى التي احتوت خمسة وستين مريضا يعانون من مرض الثعلبة و المجموعة الثانية التي تتكون من إحدى و ثلاثون مريض لايعانون من مرض الثعلبه وهي مجموعه الضبط وقد تم جمع العينات في قسم الأمراض الجلدية في مستشفى الحسين التعليمي في محافظة ذي قار الواقعه في جنوب العراق .

النتائج: من اصل 65 مريضا مصابين بداءالثعلبه, وجدنا ان الاجسام المضاده لانزيم ترانزكلوتاميناس الانسجه (نوع أ) كانت إيجابية في 13 مريضا (20٪)، وكانت الاجسام المضاده لانزيم ترانزكلوتاميناس الانسجه (نوع ج) إيجابيه في 8 مرضى (12.4٪) أي ان انتشار الإيجابية لدى مرضى الثعلبه كان أعلى مقارنة مع مجموعة الضبط.

الاستنتاج: نخلص إلى أن المرضى المصابين بداء الثعلبة لديهم ارتفاع معدل الاجسام المضاده لانزيم ترانسغلوتاميناس الأنسجة ، والتي تسند فكرة ان داء الثعلبه مرض مناعي ومع ذلك، لم نتمكن من إثبات زيادة خطر الإصابة بمرض الاضطرابات الهضميه في هؤلاء المرضى.

الكلمات الرئيسية: الثعلبة ، الأجسام المضادة لانزيم ترانسغلوتاميناس الانسجه (نوع أ و نوع ج)، مرض الاضطرابات الهضمية.