

EVALUATION OF TOTAL SERUM IMMUNOGLOBULIN E IN ATOPIC AND NONATOPIC ALOPECIA AREATA PATIENTS

MOHAMMAD S. NAYAF

Rezumat

Istoric: Etiologia AA s-a schimbat considerabil de-a lungul anilor, diferite școli medicale desemnând diferite etiologii bolii. Mecanismul prin care imunoglobulina E ar putea interveni în patogenia AA este necunoscut. IgE total seric a fost măsurat în studii anterioare, cu rezultate controversate.

Obiectiv: Acest studiu are ca obiectiv evaluarea serică a IgE total la atopici și neatopici, dintre pacienții cu AA; compararea rezultatelor cu un grup de control, subiecți aparent sănătoși; verificarea asocierii dintre imunoglobulinele E și AA.

Pacienți și Metodă: După acordarea consimțământului informat, au fost investigați 135 pacienți cu AA și 100 sănătoși, selectați din cadrul Clinicii de Dermatologie în perioada aprilie 2013–aprilie 2015. Toți subiecții studiului (pacienți și grup de control) au fost împărțiți în două grupuri, un grup cu atopie și altul fără atopie. Toți subiecții au fost supuși determinării nivelului seric de IgE. S-au recoltat 5 ml sânge de la fiecare participant pentru determinarea prin ELISA a IgE total (EIA-1788, DRG International Inc. SUA).

Rezultate: Pacienții atopici au fost în număr de 38 (28,15%) și cei neatopici au fost în număr de 97 (71,85%). Douăzeci și doi (57,9%) dintre cei 38 pacienți AA cu atopie au avut nivele crescute ale concentrației IgE. Comparația între cazuri și grupul de control a arătat că există o diferență semnificativă între ambele grupuri ($p < 0,05$) dar nu au existat diferențe semnificative între tipurile de gravitate ale AA.

Concluzii: IgE total seric este crescut în atopie precum și la pacienții neatopici cu AA. Hipersensibilitatea poate fi implicată în patogenia AA. Rolul exact al IgE total în AA va trebui investigat ulterior, studiile viitoare fiind

Summary

Background: The etiology of AA has experienced considerable drift over the years and different schools of thought have assigned varied etiologies to the condition. The mechanism by which IgE might interact in the pathogenesis of AA is unknown. Total serum IgE was measured in previous studies with controversial results.

Objective: This study has objectives to evaluate the serum IgE level in atopics and nonatopics, within AA patients; compare the result with apparently healthy control; and verify association between IgE and AA.

Patients And Methods: After giving informed consent, 135 patients with AA and 100 healthy, collected from the Dermatology Outpatient Clinic, during the period from April 2013 till April 2015. All subjects of the study (patients and controls) were divided into two groups, one group with atopy and the other group without atopy. Patients and controls were subjects to determination of total serum IgE level. Five ml of blood was taken from each participants for determination of total serum IgE using the DRG® IgE (EIA-1788) (DRG International Inc, USA) by ELISA.

Results: Atopic patients were 38 (28.15%) and nonatopic patients were 97 (71.85%). Twenty two (57.9%) of 38 AA patients with atopy had elevated serum concentrations of total IgE, compared to controls group were eight (32%) of 25 had elevated serum IgE levels. Thirty four (35%) of 97 AA patients without atopy had elevated serum concentrations of total IgE compared to controls group, were sixteen (21.33%) of 75 had elevated serum IgE levels. Comparison between total cases and controls revealed that there was a significant difference between both groups as $p < 0.05$; but there were insignificant difference between severity types of AA.

* Dermatology, Department of Medicine, College of Medicine, University of Tikrit, Iraq.

utile în clarificarea înțelegerii mecanismelor AA, ducând la îmbunătățirea diagnosticului și a tratamentului.

Cuvinte cheie: Alopecia areata (AA); Imunoglobulina E (IgE).

Conclusions: Total serum IgE is elevated in atopy and without atopy of AA patients. Hypersensitivity may be involved in pathogenesis of AA. The exact role of serum IgE in AA should be additionally investigated in future studies will be helpful in clarifying our understanding of AA, leading to improvements in diagnosis and treatment.

Key words: Alopecia areata (AA); Immunoglobulin E (IgE).

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Introduction

Alopecia areata (in Franch, pelade) is characterized by rapid and complete loss of hair in one or more round or oval patches, usually on the scalp, bearded area, eyebrows, eyelashes, and less commonly, on the hairy area of the body [1].

Alopecia areata is one of the most common human autoimmune diseases, with a lifetime risk of ~2%. In the United States, > 4.5 million people are affected with AA (National Alopecia Areata Foundation), which affects both sexes at all ages and in all ethnic groups [2].

The etiology of AA has experienced considerable drift over the years and different schools of thought have assigned varied etiologies to the condition. A viral etiology was proposed in the late 1970s but subsequent articles have demonstrated no connection. A genetic study by Yang et al. found that 8.4% of the patients had a positive family history of AA, suggesting a polygenic additive mode of inheritance. It has now been widely postulated that AA is an organ-specific autoimmune disease with genetic predisposition and an environmental trigger [3]. Previous attempts to confirm autoantibodies directed against hair follicle components in sera from AA patients have met with difficulty. In addition, the majority of perilesional inflammatory cells around hair follicles in AA are either CD4 or CD8 positive lymphocytes [4].

Diseases of atopy affect up to 60% of AA patients, and a recent study revealed that patients with a history of atopic dermatitis (AD) or autoimmune disease are, in turn, at an increased risk of developing AA. Twelve percent of AA patients develop co-existing autoimmune

diseases; predominantly thyroid disease, but also vitiligo and pernicious anemia, among other conditions [5].

Serum IgE levels in dermatologic condition other than atopic dermatitis usually have been reported as normal, although increased serum IgE concentrations have been documented in patients with contact allergic dermatitis, systemic lupus erythematosus, and alopecia areata [6]. Several dermatological and inflammatory disorders have been associated with IgE dysregulation and elevated IgE levels. Alopecia areata, erythema nodosum (especially due to streptococcus), acral dermatitides and blistering diseases, such as pemphigus, have been associated with IgE elevation [7].

Determination of total serum IgE levels is used as a screening tool for atopy, although the sensitivity and specificity of serum IgE determination still remains controversial. With normal values differing in their range, an upper limit of 120-180 U.mL for serum-IgE levels is generally accepted to provide a feasible tool to distinguish atopics from nonatopics. Besides atopy, elevated IgE levels are occasionally observed in disorders like parasitic infection, myeloma, chronic inflammatory bowel diseases, human immunodeficiency virus (HIV) infection or rare disorders like Job's syndrome [8].

The aim of our study was to evaluate serum concentrations of IgE in atopic and nonatopic within AA patients and healthy subjects.

Patients and methods

After giving informed consent, 135 patients with AA and 100 healthy, age- and sex-matched subjects as a control group were included in the

present study, collected from the Dermatology Outpatient Clinic, during the period from April 2013 till April 2015. The patients group were 82 males and 53 females and control group consisted of 78 males and 22 females. The control group did not have any scalp lesions in their personal history or on clinical examination.

All subjects of the study (patients and controls) were divided into two groups, one group with atopy and the other group without atopy. All subjects of the study were subjected to complete history taking, general, and dermatological examination.

Patients and controls with one or more of the following were excluded: Bacterial, viral infection and/or parasitic infestations; smokers; hyper IgE syndrome and acute phase of acute coronary syndromes; PUVA; past or present history of malignancy. The patients and controls who had received any treatment within previous 5 months were excluded from the study; as well as patients with any diseases based on the immune pathomechanism. Excluded from the study were patients and controls with other skin disorders and/or another cause of alopecia (tinea capitis, trichotillomania, androgenic alopecia, scarring alopecia, traction alopecia, secondary syphilis, telogen effluvium, female androgenic alopecia). No patient and controls was accepted for the study who had more than one type of atopic diseases (atopic dermatitis; asthma; or allergic rhinoconjunctivitis).

According to the severity of AA, patients were classified as follows: 1) Mild: Three or less patches of alopecia with a widest diameter of <3 cm or disease limited to eyelashes and eyebrows. 2) Moderate: Existence of more than three patches of alopecia or a patch greater than 3 cm at the widest diameter without alopecia totalis or universalis. 3) Severe: Alopecia totalis or alopecia universalis. 4) Ophiasis: Severe form in which loss of hair occurs in the shape of a wave at the circumference of the head [9].

All subjects of the study were subjected to: stool analysis to exclude parasitic infestation, complete blood count to determine the number of eosinophils. Patients and controls were subjects to determination of total serum IgE level. Five ml of blood was taken from each participants for determination of total serum IgE using the DRG®

IgE (EIA-1788) (DRG International Inc, USA) by ELISA. According to the instruction of the manufacturer, blood was centrifuged and serum was stored till testing. Total serum IgE levels <150 IU/ml was considered normal or borderline range, amount of ≥ 150 IU/ml was considered pathological according to manufacturer.

Results were collected, tabulated, statistically analyzed. Data were considered statistically significant at $p < 0.05$.

Results

Atopic patients were 38 (28.15%) their ages ranged from 5 years to 65 years with a mean \pm SD age of 25.33 ± 7.24 years. Disease duration ranged from 3 weeks to 22 months with a mean \pm SD duration of 3.48 ± 2.65 months. Regarding disease severity, 20 (52.63%) cases had mild AA, 13 cases (34.21%) had moderate AA, 3 cases (7.9%) had severe AA and 2 cases (5.26%) had ophiasis. Atopic control group were 25 (25%) their ages ranged from 7 years to 53 years with a mean \pm SD age of 25.43 ± 8.28 years as shown in the table 1.

Nonatopic patients were 97 (71.85%) their ages ranged from 8 years to 55 years with a mean \pm SD age of 27.42 ± 9.35 years. Disease duration ranged from 5 weeks to 24 months with a mean \pm SD duration of 4.37 ± 3.70 months. Regarding disease severity, 50 cases (51.55%) had mild AA, 45 cases (46.39%) had moderate AA, one case (1.03%) had severe AA and one case (1.03%) had ophiasis. Nonatopic control group were 75 (75%) their ages ranged from 9 years to 59 years with a mean \pm SD age of 22.52 ± 6.43 years as shown in the table 1.

Comparison between cases and controls revealed that there was no significant difference between both groups as $p < 0.05$; as shown in the table 1.

Table 2 showed laboratory (IgE) data for the atopic AA and control. Twenty two (57.9%) of 38 AA patients with atopy had elevated serum concentrations of total IgE, compared to controls group were eight (32%) of 25 had elevated serum IgE levels. Concerning severity types of atopic AA patients, in mild form twelve (54.55%), in moderate form seven (31.82%), in severe form two (9.09%), and in ophiasis one (4.55%) had elevated serum IgE levels. Comparison between

Table 1. Correlation between AA types and atopic and nonatopic patients

AA-types	Atopic	Nonatopic	Total
Mild	20 (52.63%)	50 (51.55%)	70 (51.85%)
Moderate	13 (34.21%)	45 (46.39%)	58 (42.96%)
Severe	3 (7.9%)	1 (1.03%)	4 (2.96%)
Ophiasis	2 (5.26%)	1 (1.03%)	3 (2.22%)
Total cases	38 (28.15%)	97 (71.85%)	135 (100%)
Control	25 (25%)	75 (75%)	100 (100%)

Table 2. Laboratory data comparing between atopic AA patients according to the severity and control

AA-Types	Normal/borderline <150 IU/ml	Pathological >150IU/ml	Total
Mild	8 (50%)	12 (54.55%)	20 (52.63%)
Moderate	6 (37.5%)	7 (31.82%)	13 (34.21%)
Severe	1 (6.25%)	2 (9.09%)	3 (7.89%)
Ophiasis	1 (6.25%)	1 (4.55%)	2 (5.26%)
Total cases	16 (42.1%)	22 (57.9%)	38 (100%)
Control	17 (68%)	8 (32%)	25 (100%)

total cases and controls revealed that there was a significant difference between both groups as $p < 0.05$; but there were insignificant difference between severity types of AA.

Table 3 showed laboratory (IgE) data for the nonatopic AA and control. Thirty four (35%) of 97 AA patients without atopy had elevated serum concentrations of total IgE compared to controls group, were sixteen (21.33%) of 75 had elevated serum IgE levels. Concerning severity types of non-atopic AA patients, in mild form eighteen

(52.94%), in moderate form eleven (32.35%), in severe form three (8.82%), and in ophiasis two (5.89%) had elevated serum IgE levels. Comparison between total cases and controls revealed that there was a significant difference between both groups as $p < 0.05$; but there were insignificant difference between severity types of AA.

The IgE level was most elevated in mild type within atopic (54.55%) and nonatopic (52.94%) among severity types of alopecia areata.

Table 3. Laboratory data comparing between non-atopic AA patients according to the severity and control

AA-Types	Normal/borderline <150 IU/ml	Pathological >150IU/ml	Total
Mild	29 (46.03%)	18 (52.94%)	47 (48.45%)
Moderate	31 (49.21%)	11 (32.35%)	42 (43.30%)
Severe	2 (3.17%)	3 (8.82%)	5 (5.15%)
Ophiasis	1 (1.59%)	2 (5.89%)	3 (3.09%)
Total cases	63 (65%)	34 (35%)	97 (100%)
Control	59 (78.67%)	16 (21.33%)	75 (100%)

Discussion

At present, to our knowledge, there has been no published study evaluating the IgE in atopic and nonatopic patients in connection with severity type of AA.

Although the etiopathogenesis of AA is poorly understood, most researches think that it is connected with immune processes. It has been reported that various autoimmune diseases often coexist with AA, and various autoantibodies against different tissues, including those directly against hair follicle, have been noticed in AA patients [10].

Evidence of atopy, including nasal and nasobronchial allergy, bronchial asthma, and atopic dermatitis was detected in 18% of the patients in the study of Sharma; Yang et al, observed a higher incidence (36.8%) [11]. The association with atopy, which was positive only in 11% of cases in the study of Intiha Mohamed Almously and Ban Antwan Behnan in Erbil [12]; in the present study, the incidence of atopic diseases were 28.15% within AA patients. Previous studies report frequencies of atopy in AA patients ranging from 1% to 52%, although a recent study in Singapore reported atopy in 60.7% of patients [13].

These apparent associations between AA and atopy and other autoimmune diseases could be the result of a nonspecific increase in immune system sensitivity coupled to genetic predispositions [14]. AA and atopy share a Th2 cytokine pattern and increased levels of IgE antibodies, mast cells, and eosinophils. In addition, a biphasic pattern of T helper response in both AA and atopic dermatitis has been observed [15].

Our study clearly demonstrated that total serum IgE was significantly increased in AA patients with atopy (57.9%) and without atopy (35%) in comparison to healthy subjects (32%) and (21.33%) respectively. Regarding IgE comparison between total cases and controls, and between atopic and nonatopic, revealed that there was a significant difference as $p < 0.05$.

The association of serum IgE levels and AA has been previously investigated with varying results. Przybilla et al. found elevated total IgE in 19.7% of studied AA patients. Later on, O'Loughlin et al. found elevated total serum IgE in 30% of AA patients. Kasumagić-Halilović and Prohić also found elevated total IgE in 37% of AA patients. Attia et al. found elevated total IgE in 48.3% of nonatopic AA cases. Zuel Fakkar et al. found elevated total IgE in 50% of studied Egyptian cases. Zhao et al. demonstrated significant elevation of IgE in patchy AA than healthy control. Bork et al. also recorded a significant increase in serum IgE (32%) in children with AA [16]. However, in contrast to these results, total serum IgE levels were not elevated in AA patients in other previous studies [17].

In summary, serum IgE was significantly elevated in atopy and without atopy within AA, may reflect the genetic and autoimmunity background of the pathogenesis of AA. Accordingly, our results suggest that elevation of total serum IgE might be a common feature in AA, may be limited to a selected patient population. The exact role of serum IgE in AA should be additionally investigated in future studies.

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Conflict de interese
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Correspondance address: Assist.Prof. Mohammad S.Nayaf
Dermatology, Department of Medicine, College of Medicine, University of Tikrit, Iraq.
E-mail: nayaf_mohammad@yahoo.com.