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Study of total serum immunoglobulin E level and prevalence of atopy in alopecia areata patients

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Background: Alopecia areata (AA) is non-scarring hair loss. Its etiopathology is not fully known, most evidence considered AA an immunologically mediated disease. To compare serum levels of total immunoglobulin E (IgE) between AA patients and healthy subjects, and to assess whether AA is associated with atopy.

Methods: 50 AA patients and 50 healthy subjects were included in this study. Presence of atopy was elicited by detailed family and/or personal history of atopy. Clinically patients were divided into 2 groups: patients with single patch of AA (alopecia unilocularis, AU), or with multiple patches (alopecia multilocularis, AM). Serum levels of IgE were measured in both groups.

Results: Serum levels of total IgE were significantly higher in patients than in controls (178 ± 154 ku/l vs. 118 ± 57 ku/l; $P < 0.05$). Evidence of atopy was present in 48% of AA patients compare to 18% of control subjects ($P < 0.05$). Patients with disease duration more than one year had significantly higher serum IgE levels ($P < 0.05$), and patients with AM had significantly higher serum IgE levels than patients with AU (267 ± 189 ku/l vs. 102 ± 32.3 ku/l; $P < 0.05$). Mean value of serum IgE did not vary significantly with patient's age at onset, gender, history of atopy or family history of AA. Atopy was significantly associated with AM.

Conclusion: Total serum IgE is elevated in AA patients with significant association with severe and chronic disease irrespective of the presence of atopy. Atopic diseases were more frequent in AA patients with severe clinical presentation.

Keywords: alopecia areata, IgE, chronic disease

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INTRODUCTION

Alopecia areata (AA) is a chronic disease characterized by non-scarring hair loss on the scalp or other parts of the body with a wide range of clinical presentations [1]. It affects 1–2% of the population of both genders and occurs in all age groups [1]. AA can detrimentally affect the patient's self-esteem and quality of life, making the diagnosis and control of this condition of utmost importance [2]. About 10–22% of patients with AA have concomitant atopy, twice the prevalence as that of the general population [3]. The most commonly reported associated atopic diseases with AA are atopic dermatitis, asthma, and allergic rhinitis [3]. Moreover, patients with an associated atopic disease have an earlier age of onset and more severe disease than non-atopic subjects [4]. The pathogenesis of AA is uncertain, though auto-immunity has been suggested [1]. Moreover, environmental factors such as infection and psychological stress may play important roles [2]. A previous study suggested that the initiation phase of AA includes a heavily Th1-based immune response, and the maintenance of

destruction of the hair follicles by cytotoxic cells may be due to a shift from the initial Th1 response to a more chronic Th2 immune profile [5,6].

Serum immunoglobulin E (IgE) concentrations are high in many dermatological and systemic diseases [6]. The production of IgE is usually determined by Th2 cells. The Th2 cytokines, IL (interleukin)-4 and IL-13, are required signals for IgE synthesis. Different studies have measured IgE in AA patients, providing controversial results [5,6,7]. The present study aimed to estimate the total serum IgE and prevalence of atopic diseases among AA patients, and to shed light on the relationship of IgE level with disease chronicity and severity.

PARTICIPANTS AND METHODS

This was a case-control study conducted in the Department of Dermatology at El-Jumhoria hospital in Benghazi, Libya. The study included 50 patients with a diagnosis of patchy AA. A detailed history was obtained from each patient, including demographic data, disease duration, history of atopic disease, and family history of AA. Patients with alopecia totalis, alopecia universalis, as well as patients with any other autoimmune skin disease or systemic disease that might elevate the serum IgE were excluded from the study. According to the clinical type of AA, patients were divided into two groups: patients with a single patch of AA (alopecia unilocularis, AU) and patients with multiple patches (alopecia multilocularis, AM). According to the duration of disease, the patients were divided into two groups: duration of 1 year or less, and more than 1 year. The control group consisted of 50 sex- and age-matched healthy subjects. Blood samples were taken from each patient and control subject for measurement of serum IgE. Signed consent was obtained from all patients and subjects after explaining the nature of the study to them. The work was done in accordance with the Declaration of Helsinki.

Statistical Analysis

Data analysis was performed using SPSS version 22. The data were expressed as mean ± standard deviation. The chi-squared test and independent t-test were used for statistical analysis. Differences were considered statistically significant with P-values < 0.05.

RESULTS

The demographic data of patients under study and control subjects are shown in Table 1. Of the total 50 patients with AA, 27 (54%) had AU and 23 (46%) had AM. Patients with AA had a significantly higher prevalence of atopy as compared to control subjects (48% vs. 18%; P = .003), and a family history of AA was reported in 12 (24%) patients (Table 1). Allergic rhinitis was present in 26% of the patients (Figure 1). Serum levels of IgE were

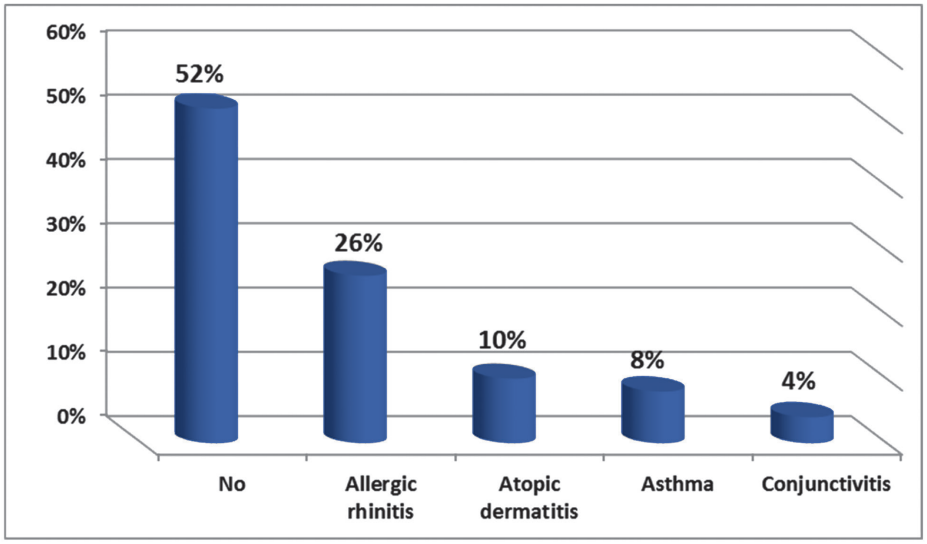

Figure 1. Prevalence of atopy diseases in the alopecia areata (AA) patients of this study

Table 1. The demographic data of the alopecia areata (AA) patients of this study

Demographic data	AA* patients (50)	Control subjects (50)	*P*-value
Age mean ± SD † yrs	28 ± 7 yrs	29 ± 6 yrs	.338
Sex			
Female	22 (44%)	26 (52%)	.548
Male	28 (56%)	24 (48%)	
Duration yrs ± SD	2.3 ± 1.6 yrs	NA ‡	
H/O Atopy	24 (48%)	9 (18%)	.003
Family H/O AA*	12 (24%)	NA ‡	
Clinical type			
Unilocularis	27 (54%)	NA ‡	
Multilocularis	23 (46%)		

Alopecia areata*, standard deviation †, not applicable ‡

significantly higher in patients relative to control subjects (Table 2). A significant association was found between high serum IgE levels and a disease duration of more than one year as well as AM (Table 3). There was no statistically significant difference in serum IgE level between AA patients with atopy and those without atopic diseases (Table 3). There were insignificant differences in mean values of IgE among AA patients regarding age at onset, sex of the patients, and family history of AA (Table 4). A significant association was found between a history of atopy and AM, but this parameter had no significant association with other variables (Table 5)

Table 2. Serum IgE levels in alopecia areata (AA) patients and control subjects

	Patients (50)	Control subjects (50)	*P*-value
Mean serum IgE (kU/L)	178 ± 154	118 ± 57	.01
High serum IgE	13 (26%)	4 (8%)	.03

Table 3. Serum IgE in alopecia areata (AA) patients in relation to other variables

Variables (n*)			*P*-value
Duration of AA †			
≤1yr (20)		>1yrs (30)	.004
Serum IgE (kU/L)	103 ± 39	228 ± 179	
H/O atopy			
Yes (24)		No (26)	.877
Serum IgE (kU/L)	181 ± 139	175 ± 171	
Family H/O atopy			
Yes (16)		No (34)	.530
Serum IgE (kU/L)	158 ± 164	187 ± 150	
Type of AA			
AU ‡ (27)		AM § (23)	.000
Serum IgE (kU/L)	102 ± 32.3	267 ± 189	

Number of patients*, Alopecia areata †, Alopecia unilocularis ‡, Alopecia multilocularis §

Table 4. Serum IgE in alopecia areata (AA) patients in relation to other variables.

Variables (n*)			*P*-value
Age at onset			
High serum IgE (13)		Normal IgE (37)	.872
Age (yrs)	23.4 ± 7	24 ± 6	
Sex of patients			
	Female (22)	Male (28)	.529
Serum IgE (kU/L)	156 ± 123	141 ± 116	
Family history of AA			
	Yes (12)	No (38)	.729
Serum IgE (kU/L)	191 ± 168	174 ± 150	

Number of patients*

Table 5. Atopy in AA patients in relation to other variables.

History of atopy 24 (48%)			*P*-value
Sex of patients			
	Female	Male	.569
n* (%)	12 (24%)	12 (24%)	
Age at onset (Yrs)			
	H/O atopy (24)	No H/O atopy (26)	.933
Mean ± SD	24 ± 7	24 ± 8	
Duration of AA †			
	≤1Yr	> 1Yr	.565
n* (%)	11 (22%)	13(26%)	
Clinical type of AA			
	AU ‡	AM §	.009
n* (%)	9 (18%)	15 (30%)	

Number of patients*, Alopecia areata †, Alopecia unilocularis ‡, Alopecia multilocularis §

DISCUSSION

The discovery of IgE was a breakthrough in the field of allergy and immunology; apart from allergic diseases, IgE is involved in the pathogenesis of several other disorders [8]. The highest IgE concentrations have been found in atopic diseases, scabies, ichthyosis vulgaris, and pruritic dermatoses [9]. Furthermore, elevated total IgE was reported in psoriasis, pyogenic skin infections, systemic lupus erythematosus, and AA [9].

The association of serum IgE levels and AA has been investigated in previous studies with varying results [5,6,7]. In the present study, the serum levels of IgE were significantly higher in patients relative to control subjects; this was consistent with previous studies [6,10,11]. Moreover, serum IgE was elevated in 26% of AA patients, which is in agreement with the

study of O'Loughlin *et al.*, who found elevated total serum IgE in 30% of AA patients [12]. Furthermore, Przybilla *et al.* found elevated total IgE in 19.7% of AA patients [9], and Kasumagic-Halilovıc and Prohi´c found elevated total IgE in 37% of AA patients [7]. A higher prevalence of elevated serum IgE in AA patients compared with controls has been reported in multiple studies [6,11]. However, elsewhere in the literature, such a difference was not found between AA patients and normal subjects [1,13,14].

Concerning the clinical presentation of AA, in the present study, patients with AM had significantly higher serum IgE levels than patients with AU. This is in agreement with the study of Attia *et al.*, which reported significantly elevated serum IgE levels in AA patients, particularly among those with a severe presentation [5]. However, other studies reported insignificant differences in serum IgE among AA cases with different disease severity [6,7,11].

In the present study, patients with a disease duration of more than one year had significantly higher serum IgE levels, which is in agreement with previous reports [5,11]. However, the study of Bakry *et al.* reported insignificant differences in serum IgE among AA cases with different disease duration [6]. In agreement with previous studies, we found no correlation between serum IgE levels and age at onset, sex of the patients, history of atopy, and family history [5,6].

Atopy has been reported to occur with an increased frequency in patients with AA [15,16]. It has been suggested that AA in atopic subjects tends to occur at an earlier age and with greater severity relative to non-atopic subjects [3,16].

In the present study, a history of atopy was significantly more common among patients relative to control subjects. In fact, 48% of our patients had a history of atopy, with allergic rhinitis being seen in 26% of patients with AA. These are in agreement with the findings of Kaur *et al.* [17] Among patients with a history of atopy, 62.5% had AM, confirming the results of previous studies that reported severe AA in up to 75% of patients who had associated atopy [16,17]. There was no significant correlation between a history of atopy and age at onset, sex, and duration of alopecia, corresponding with the literature [15,17].

It is believed that AA is an organ-specific autoimmune disease targeting hair follicles and leading to their disruption [10]. Although increased levels of Th1 cytokines (interferon-γ and IL 2) in lesional AA skin have been reported, the Th2 immune response has also been incriminated in the pathogenesis of AA [18]. The mechanism of IgE elevation in AA is not well known. A variety of cytokines control IgE production; IL4, IL6, IL7, IL9, and IL13 enhance IgE production. In contrast, IFNγ and IL10 inhibit IgE synthesis [6].

The production of IgE is usually determined by Th2 cells. IL-4, a Th2 cytokine, is a required signal for IgE synthesis. Previous studies reported a significant elevation of serum IL-4 level in patients with localized AA, while its serum level tended to decrease in patients with extensive forms [18]. However, Attia *et al.* reported that elevated levels of total serum IgE and IL-4 were more common in severe AA [5]. Moreover, the observed underexpression of IL-10 mRNA in the skin of patients with AA may reflect IL-10 deficiency associated with B cell stimulation [5].

Tumor necrosis factor (TNFα) is known to fulfill a key role in the pathogenesis of AA [7]. TNFα may enhance IgE levels by creating a microenvironment rich in IL4 and IL13 as Th2 cytokines, stimulating IgE class switching in patients with AA [19].

IgE elevation in AA patients may be also due to the overexpression of CD40 on B cells. A previous study suggested that CD40 stimulation could enhance IgE production; moreover, CD40 was also found to be expressed in hair structures including the dermal papilla of AA lesions, confirming a possible role in IgE elevation in some AA patients [20].

In the present study, patients with a disease duration of more than one year had significantly higher serum IgE levels. A previous study suggested that the initiation phase of AA is a heavily Th1-based immune response, while the maintenance of destruction of hair follicles by cytotoxic cells is due to a shift from the Th1 response to a more chronic Th2 immune profile [21]. Thus, AA is a cell-mediated autoimmune disease with late, possibly secondary, humoral responses [5].

Additionally, genetic mechanisms have also been proposed for the association between atopy and AA. It is well known that AA seems to be a polygenic disease where several genes such as the IL-4 gene and the gene for the β subunit of the type 1 IgE receptor play roles in determining the disease susceptibility and the association of AA with atopic disease [22].

CONCLUSION

This study supports the evidence that elevation of total serum IgE is associated with AA, particularly with severe presentations, irrespective of the presence of atopy. Atopic diseases have frequently been associated with AA. Allergic rhinitis was more frequent than asthma or atopic dermatitis in AA patients, and this association seemed to be higher for the more severe forms of AA. Further studies on a larger scale and on different AA presentations are required for firmer conclusions.

Conflict of interest: None declared.

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